

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

AMENDMENT NO. 1
TO
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Metagenomi Technologies, LLC

(to be succeeded by Metagenomi, Inc. in the reorganization)
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2836
(Primary Standard Industrial
Classification Code Number)

83-2735153
(I.R.S. Employer
Identification No.)

Metagenomi Technologies, LLC
1545 Park Avenue
Emeryville, California 94608
(510) 871-4880
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Securities Exchange Act of 1934.

Large Accelerated filer Accelerated filer
Non-accelerated filer Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant files a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

Purpose of this Amendment

This Amendment No. 1 to the registration statement on Form S-1 (the "Registration Statement") that was filed with the Securities and Exchange Commission on January 5, 2024, is being filed solely for the purpose of replacing certain images appearing in the preliminary prospectus contained in the Registration Statement with higher resolution images. The contents of the images remain unchanged in all respects.

Reorganization

Metagenomi Technologies, LLC, the registrant whose name appears on the cover of this registration statement, is a Delaware limited liability company. Prior to the effectiveness of this registration statement, Metagenomi Technologies, LLC will complete a series of transactions pursuant to which Metagenomi Technologies, LLC will merge with and into its wholly-owned subsidiary, Metagenomi, Inc., a Delaware corporation, with Metagenomi, Inc. continuing as the surviving corporation. We refer to this reorganization throughout the prospectus included in this registration statement as the "Reorganization." Except as disclosed in the prospectus, the consolidated financial statements and summary consolidated financial data and other financial information included in this registration statement are those of Metagenomi Technologies, LLC and its subsidiaries and do not give effect to the Reorganization. Shares of the common stock of Metagenomi, Inc. are being offered by the prospectus included in this registration statement.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the Securities and Exchange Commission declares our registration statement effective. This preliminary prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated January 8, 2024

PRELIMINARY PROSPECTUS

Shares



Metagenomi

Common Stock

This is an initial public offering of shares of common stock of Metagenomi, Inc.

We are offering _____ shares of our common stock. We expect that the initial public offering price will be between \$ _____ and \$ _____ per share.

Prior to this offering, there has been no public market for our common stock. We have applied to list our common stock on the Nasdaq Global Select Market under the symbol "MGX." We believe that upon the completion of this offering, we will meet the standards for listing on the Nasdaq Global Select Market, and the closing of this offering is contingent upon such listing.

We are an "emerging growth company" under the federal securities laws and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and for future filings.

	Per share	Total
Initial public offering price	\$ _____	\$ _____
Underwriting discounts and commissions(1)	\$ _____	\$ _____
Proceeds, before expenses, to Metagenomi, Inc.	\$ _____	\$ _____

(1) See "Underwriting" beginning on page 268 of this prospectus for additional information regarding underwriting compensation.

We have granted the underwriters an option for a period of 30 days to purchase an additional _____ shares of our common stock from us at the initial public offering price, less underwriting discounts and commissions.

Investing in our common stock involves a high degree of risk. Before buying any shares, you should read carefully the discussion of the material risks of investing in our common stock under the heading "Risk Factors" starting on page 18 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares against payment in New York, New York on _____, 2024.

J.P. Morgan Jefferies TD Cowen Wells Fargo Securities BMO Capital Markets
Chardan

Prospectus dated _____, 2024.

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We have not, and the underwriters have not, authorized anyone to provide any information or to make any representation other than those contained in this prospectus, any amendment or supplement to this prospectus or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares of common stock offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus, any amendment or supplement to this prospectus or any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

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For investors outside the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

Market data and certain other statistical information used throughout this prospectus are based on independent industry publications, governmental publications, reports by market research firms, or other independent sources that we believe to be reliable sources. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We are responsible for all of the disclosure contained in this prospectus, and we believe that these sources are reliable; however, we have not independently verified the information contained in such publications. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed under the section entitled "Risk Factors" and elsewhere in this prospectus. Some data are also based on our good faith estimates.

We intend to apply for various trademarks that we use in connection with the operation of our business. This prospectus may also contain trademarks, service marks and trade names of third parties, which are the property of their respective owners. Our use or display of third parties' trademarks, service marks, trade names or products in this prospectus is not intended to, and does not imply a relationship with, or endorsement or sponsorship by us. Solely for convenience, the trademarks, service marks and trade names referred to in this prospectus may appear without the TM or SM symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable owner of these trademarks, service marks and trade names.

PROSPECTUS SUMMARY

This summary highlights information contained in greater detail elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes thereto included elsewhere in this prospectus. You should also consider, among other things, the information set forth under the sections entitled "Risk Factors," "Special Note Regarding Forward-Looking Statements," and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case included elsewhere in this prospectus.

Prior to the effectiveness of this registration statement, we will complete a series of transactions pursuant to which Metagenomi Technologies, LLC will merge with and into its wholly-owned subsidiary, Metagenomi, Inc., a Delaware corporation, with Metagenomi, Inc. continuing as the surviving corporation. See "Reorganization." Except where the context otherwise requires or where otherwise indicated, the terms "Metagenomi," "we," "us," "our," "our company," "the company," and "our business" refer, prior to the Reorganization discussed below, to Metagenomi Technologies, LLC and, after the Reorganization, to Metagenomi, Inc.

Overview

We are a precision genetic medicines company committed to developing curative therapeutics for patients using our proprietary, comprehensive metagenomics-derived genome editing toolbox. Genetic diseases are caused by a diverse set of mutations that have been largely inaccessible by genome engineering approaches to date. Genetic mutations are seen in a variety of forms, including deletions, insertions, single-base-pair changes and sequence repeats, and are found throughout the genome and across a variety of different cell types, tissues, and organ systems. Additionally, many diseases lack a genetic origin but have the potential to be effectively and permanently addressed through genome editing. We are harnessing the power of metagenomics, the study of genetic material recovered from the natural environment, to unlock four billion years of microbial evolution to discover and develop a suite of novel editing tools capable of correcting any type of genetic mutation found anywhere in the genome. Our comprehensive genome editing toolbox includes programmable nucleases, base editors, and RNA and DNA-mediated integration systems (including prime editing systems and clustered regularly interspaced short palindromic repeat ("CRISPR")-associated transposases ("CASTs")). We believe our diverse and modular toolbox positions us to access the entire genome and select the optimal tool to unlock the full potential of genome editing for patients.





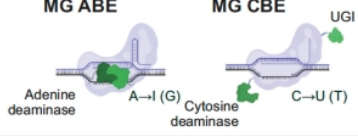

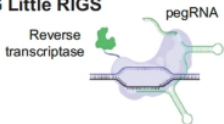

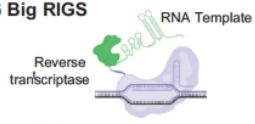

The company was founded by pioneers in the field of metagenomics, a powerful science that allows us to tap into the diversity of microbial life on this planet. The metagenomics process starts by collecting samples from microbe-rich ecosystems ranging from simple home gardens to extreme locations such as hydrothermal vents below the ocean. We then extract the DNA from these environmental samples and deeply sequence them to fully reconstruct the genomes of the resident microbes. Each sample may include thousands of distinct genomes from previously unknown organisms revealing novel cellular machinery that we utilize as building blocks for our editing systems. Using high-throughput screening, artificial intelligence ("AI"), and proprietary algorithms, we rapidly mine through billions of novel proteins from our genome-resolved metagenomics database to create genome editing tools. To date, we have analyzed over 460 trillion base pairs, predicted over 7.4 billion proteins, including over 322 million CRISPR-associated ("Cas") proteins and over 1.75 million CRISPRs, which we estimate has resulted in the identification of over 20,000 novel genome editing systems. Simultaneously, we have assembled extensive libraries of millions of nucleases, deaminases, reverse transcriptases ("RTs") and over one thousand CASTs. Our platform is designed to enable us to rapidly and

effectively find, screen, and select tools with the highest potential targetability, specificity, and efficiency in order to develop them into genetic medicines. The iterative nature of our process, underpinned by AI, allows us to continuously push the boundaries of innovation.

Our proprietary toolbox of editing systems

We have developed an expansive and modular toolbox of next-generation genome editing systems that will allow us to interact with the human genome in a site-specific manner, where each tool can be matched to specific disease targets. Figure 1 summarizes our diverse and versatile toolbox of different editing capabilities with the potential to address the full spectrum of genetic diseases.

Figure 1. Our Toolbox.

Gene Edit	Tool / System	Examples	Our Advantages
Knockdown / Gene inactivation Knock-in / Gene insertion Exon skipping / Gene modification 	Programmable nucleases, including ultra-small type V and SMART systems	MG Type II & SMART Nucleases  MG Type V Nucleases 	<ul style="list-style-type: none"> Efficient and precise genome editing systems Diverse nucleases have extensive genome targeting capabilities Compact and ultra-small systems will enable delivery via a single AAV Function as programmable modules for base editing and RIGS
Nucleotide changes 	Base editors, including ultra-small systems	MG ABE Adenine deaminase A→I (G) MG CBE Cytosine deaminase C→U (T) 	<ul style="list-style-type: none"> Extensive genome targetability enabled by Metagenomi nucleases/nickases SMART base editors are smallest nickase-based systems characterized to-date, will enable more efficient delivery via a single AAV
Small replacements/corrections (1-100 base pair replacement, insertion, or deletion) 	Prime editing with RNA-mediated integration systems for small corrections ("Little RIGS")	MG Little RIGS Reverse transcriptase pegRNA 	<ul style="list-style-type: none"> Extensive genome targetability enabled by Metagenomi nucleases/nickases Ultra-small RTs are highly active and accurate for prime editing
Large insertions (>100 base pair integrations) 	RNA-mediated integration systems for large integrations ("Big RIGS") DNA-mediated integration with CRISPR associated transposases ("CAST")	MG Big RIGS Reverse transcriptase RNA Template  MG CAST DNA Template Transposase 	<ul style="list-style-type: none"> Potential to accurately and efficiently integrate large transgenes without the need for double-stranded DNA breaks Potential to address genetic diseases driven by loss of function mutations <p>Big RIGS</p> <ul style="list-style-type: none"> Potentially extensive genome targetability enabled by Metagenomi nucleases/nickases RNA-templated integrations Will enable 'all RNA' delivery of genome editing system and integration template <p>CAST</p> <ul style="list-style-type: none"> DNA-templated integrations, potentially including templates much larger than what can be accomplished with RIGS

Our programmable nucleases are the backbone of our broad set of genome editing tools. These novel nucleases including type II and type V Cas nucleases, of which some are ultra-small systems that we call Small Arginine-Rich systems ("SMART") nucleases, have unique targeting abilities and can be programmed by guide RNAs ("gRNA") to target and cut at specific locations in any genome sequence. Targeted genomic breaks trigger DNA repair pathways that can be used for genome editing, for example, to integrate a gene at a target site (knock-in) or for gene inactivation (knockdown).

Our toolbox contains thousands of CRISPR nucleases with diverse abilities to target different parts of the genome, allowing us to select the ideal nuclease for targeting any given gene in a site-specific manner and potentially overcome a major limitation of first-generation CRISPR/Cas9 systems.

We also modify our nucleases to either nick the genome (i.e., a nickase that cuts one strand of the DNA) or to simply bind to target sites (i.e., a nuclease dead variant). These capabilities (e.g., searching, cutting, nicking, and binding) can be leveraged as a chassis by adding on additional effector enzymes to create base editors for single nucleotide changes and RNA-mediated integration systems ("RIGS") for both small and large genomic

integrations using “Little RIGS” for prime editing and “Big RIGS” for large integrations. Using modular engineering, we match nickases with deaminases and RTs for base editing and RIGS, respectively. Furthermore, nucleases can be engineered by swapping the search modules of the enzyme to expand the targetability of the chassis, which is critical for site-specific genomic modifications. Given the measured targeting density of our toolbox, we believe that essentially any codon in the human genome could be addressed with our gene editing systems.

Our highly active nucleases have gone through extensive preclinical evaluation for both *in vivo* and *ex vivo* applications, with demonstration of broad potency of these systems across human primary cells, mouse, and nonhuman primate (“NHP”) models. Our base editors, RIGS, and CAST systems have demonstrated activity across various cell-based models. In addition to evaluating system activity, we have undertaken detailed characterization of guide-specific on- and off-target effects. We routinely identify guides that have no or minimal verifiable off-target editing, thus overcoming another limitation of first-generation CRISPR/Cas9 systems.

In addition to overcoming the activity, targetability, and specificity limitations of first-generation systems, our nuclease toolbox was designed to have broad compatibility with viral and nonviral delivery technologies. This compatibility is accomplished by having a variety of nuclease and gRNA structures, which range in terms of their size and biochemistry. For example, small guides for some type V Cas systems streamline manufacturing for delivery by lipid nanoparticle (“LNP”) approaches, and SMART nickases can be used to construct base editors that are small enough to fit within the packaging limitations of adeno-associated viruses (“AAV”). SpCas9, which is currently used in most base editing applications, is roughly three times the size of some of our smallest SMART nickases and cannot be efficiently packaged into a single AAV. Combined, we believe these features will facilitate delivery of our genome editing tools to previously inaccessible tissue types and organ systems.

While nucleases, base editors, and prime editors can precisely address a wide variety of genomic modifications required to treat disease, the fact that many diseases are caused by a multitude of mutations across a gene means that a diverse set of editing tools are required to fully address these patient populations. The integration of a complete and functional gene through targeted genome editing may provide a way in which every patient with a given disease could potentially be treated by a single genetic medicine. Big RIGS and CASTs are novel genome editing systems that are under development to achieve what has been a major challenge for the genome editing field—large, targeted genomic integrations. Initial preclinical readouts conducted in mammalian cells indicate that these systems could potentially have a major impact on how diseases caused by loss-of-function mutations, the most common cause of genetic diseases, can be addressed through genome editing.

Therapeutic translation roadmap and initial programs

We are taking a stepwise approach deploying our genome editing toolbox to develop potentially curative therapies for patients. Our lead programs are selected to both address important diseases and to establish new standards in targetability, precision, efficiency, and scope of editing capabilities. Figure 2 summarizes the portfolio of programs that we and our partners are advancing, as we aim to match the optimal genome editing tools for each indication. Each of these indications were chosen based on our conviction in the underlying biology, existence of validating preclinical and clinical data, availability of pharmacodynamic and translational tools to assess early proof-of-concept, relevant value supporting outcome measures, and ongoing clinical unmet need. While we do not currently have any approved products and all of our product candidates are preclinical, our lead programs capture an ever-growing set of translational learnings and insights that will inform and accelerate future programs.

Figure 2: Therapeutic Translation.



Hemophilia A—novel, durable, knock-in approach for expression of Factor VIII

Hemophilia A is the most common X-linked inherited bleeding disorder and is caused by mutations in the Factor VIII ("FVIII") gene leading to loss of functional FVIII protein that impacts the body's ability to form normal clots in response to injury. FVIII is normally produced in the liver within sinusoidal endothelial cells and is then secreted into the bloodstream where it acts as a cofactor for the catalytic activation of Factor X in the clotting pathway. The lack of functional FVIII disrupts the normal clotting cascade and predisposes patients to increased risk of bleeding, either spontaneously or in response to injury or surgery. Repeated bleeding episodes in joints or soft tissues can lead to progressive joint damage, inflammation, pain, and mobility impairment. Intracranial bleeding is of greatest concern as this can be rapidly fatal or lead to major morbidity.

Rather than provide the FVIII gene in an episomal location, which risks dilution from cell division or cell death as well as episomal transcriptional silencing, our approach is to insert a FVIII DNA cassette into a "safe harbor location," within an intron of the albumin gene that is not expected to have deleterious effects. FVIII expression is then driven by the strong native albumin promoter. This approach has previously been demonstrated in preclinical studies to lead to therapeutically relevant expression of a different clotting factor (Factor IX) with negligible impact to systemic circulating albumin levels. Our FVIII knock-in approach is designed to provide stable expression and clinically relevant circulating levels of FVIII, even at low integration rates because of the strength of the albumin promoter. We have demonstrated the feasibility of the FVIII gene knock-in approach in mice with several mouse specific guides and different FVIII DNA donor cassettes, with integration of the FVIII gene leading to FVIII mRNA expression and therapeutically relevant levels of FVIII protein in the blood. In an ongoing NHP study we demonstrated integration of a surrogate cynomolgus-FVIII cassette (used to avoid immune response that would occur with a foreign human FVIII protein) and observed therapeutically relevant levels of the cyno-FVIII protein encoded by the integrated cassette in all 3 treated animals that has extended for 4.5 months following a single dose of the AAV-cFVIII virus followed five weeks later by a liver trophic LNP encapsulating the mRNA encoding MG29-1 and guide 2 at a dose of 1mg/kg body weight. We intend to continue measuring FVIII levels in these monkeys up to the 12 month time point to generate a robust data set on durability.

Evaluation of different human FVIII donor DNA cassettes has been completed in mice resulting in the selection of 2 lead cassettes that will be compared in another NHP study, potentially leading to a development candidate selection anticipated in Q2 2024.

In parallel, we are manufacturing mRNA, gRNA, AAV and LNP to support future investigational new drug ("IND") enabling studies.

Primary Hyperoxaluria, Type 1 ("PH1")—a durable knockdown of HAO1 for substrate reduction therapy

PH1 is a rare autosomal recessive metabolic disease arising from loss of function mutations in the alanine-glyoxylate aminotransferase ("AGXT") gene that encodes alanine glyoxylate aminotransferase. This enzyme is found in peroxisomes of the liver where it catalyzes the conversion of glyoxylate to glycine and pyruvate. Lack of functional AGXT leads to an accumulation of glyoxylate substrate, which is then converted to oxalate and excreted in the kidney. The excess urinary oxalate forms an insoluble complex with urinary calcium that leads to the production of calcium oxalate crystal precipitates. This pathologic process results in the formation of repeated calcium oxalate urolithiasis and nephrolithiasis, which in turn leads to obstructive uropathy, inflammation, fibrosis, tubular toxicity, and progressive loss of kidney function. PH1 is a serious disease that causes kidney failure. More than 70% of individuals with PH1 mutations will develop end-stage renal disease, with a median age in young adulthood.

The goal of our genome editing approach is to durably knock down HAO1 resulting in stable and permanent reduction of oxalate levels to effect a lifelong benefit. We have performed nuclease and guide screening to select an optimal nuclease and gRNA combination. Along with our partner ModernaTX, Inc. ("Moderna"), we have achieved preclinical proof-of-concept in an AGXT knock-out mouse which is an accepted disease model of PH1. We are in the final stages of confirming the candidate to take into NHP studies and expect to have NHP data in 2024 to support final development candidate selection.

Transthyretin Amyloidosis—a single treatment to knockdown TTR gene expression

Transthyretin amyloidosis is a disease of misfolded and aggregated transthyretin ("TTR") protein that can deposit in tissues causing organ dysfunction, primarily in the heart and/or peripheral nerves. The TTR protein is normally produced in the liver and circulates in a homotetramer (four copies of the same TTR protein bound together) where it serves as a carrier protein for vitamin A and thyroxine. Certain mutations have been identified that can cause TTR homotetramers to fall apart, misfold, and aggregate into insoluble fibrils that deposit in cardiac tissue and peripheral nerves. However, more commonly, the normal aging process is associated with an increased propensity for TTR misfolding and aggregation in the heart without any known genetic sequence variation. These distinctions lead to TTR amyloidosis being characterized as either hereditary transthyretin amyloidosis ("ATTRv") caused by mutations in TTR, or wild-type ATTR amyloidosis ("ATTRwt"). It is estimated that globally there are approximately 50,000 patients with ATTRv and between 300,000 and 500,000 patients with ATTRwt. Among the larger ATTRwt patient population, the most common presentation is a rapidly progressive, restrictive, and hypertrophic cardiomyopathy due to progressive deposition of insoluble TTR fibrils, which result in thickening of the myocardium and stiffening of the ventricles. These pathologic processes lead to impaired diastolic function and progressive cardiomyopathy that typically leads to progressive heart failure and often death within three to five years from disease onset. Although cardiac manifestations are more common and severe, patients with neurologic manifestations also experience significant morbidity, loss of functionality, and impaired quality of life.

Using our novel nucleases, we aim to provide efficient TTR knockdown and halt further deposition of amyloid fibrils. Previous experience suggests a clinical correlation between the degree of TTR knockdown and potential

for benefit in familial forms of the disease, which are expected to translate similarly to wild type forms. The high degree of *in vivo* editing efficiency and specificity of our nuclease platform suggest the potential for a single treatment to knockdown TTR gene expression and remove the requirement for life-long therapy. Along with our partner Ionis Pharmaceuticals, Inc. ("Ionis"), we are currently in advanced stages of nuclease and guide selection, having achieved more than 90% knockdown of human TTR protein after a single dose in a humanized TTR mouse model, and expect to move into NHP studies in 2024.

Further areas of therapeutic activity and interest

In parallel with our translation efforts in our lead programs using our novel programmable nucleases to knock-in or knockdown gene expression in liver-associated targets, we are developing more complex editing systems for liver associated targets as well as moving beyond the liver. Given that our genome editing toolbox contains small editing systems designed to be amenable to viral vector delivery, and given the progress established in targeting the central nervous system and muscle with established AAV capsids, our first extrahepatic indications will be neurodegenerative and neuromuscular diseases.

Building on our experience delivering our nucleases to the liver via LNP systems, we are extending that experience delivering novel RIGS to the liver to potentially correct ATP7B mutations in Wilson's disease and PiZ mutations in alpha-1-antitrypsin deficiency ("A1AT deficiency"). We are also exploring addressing A1AT deficiency via a base editor approach given the predominant mutation involves a single base pair. Both of these liver diseases have well-defined biology, readily available translational biomarkers for early proof-of-concept, established development pathways based on prior drug approvals, and important unmet medical needs.

Building on our experience with our novel type II and type V programmable nucleases, we are extending that experience by working to deliver these nucleases via AAV to the central nervous system to potentially knockdown genetic targets important for both spontaneous and familial amyotrophic lateral sclerosis (SOD1, ATXN2) and Charcot-Marie-Tooth Type 1a (PMP22). In addition, we are working to address a series of mutations common in Duchenne Muscular Dystrophy with our programmable nucleases through exon skipping approaches. In diseases outside of the liver, we intend to initially leverage known biology and clinical validation achieved with RNA-targeted approaches like antisense and small interfering RNA ("siRNA") to advance more potent and definitive one-time genome editing treatments.

Building on our experience with both knock-in gene expression and smaller gene corrections with RIGS, we are progressing our larger RNA- and DNA-mediated integration systems to potentially provide a single curative approach to cystic fibrosis. As opposed to currently-available therapies limited to subsets of patients with individual mutations, we intend to deliver a full copy of a functional cystic fibrosis transmembrane conductance regulator ("CFTR") gene. This approach can similarly be pursued across many other diseases characterized by loss of function mutations.

Our Team

We have assembled a world-class team that is driven by a passion to create potentially curative genetic medicines through the discovery of novel genome editing technologies by harnessing the power of metagenomics. Key members of our executive and leadership team include:

- **Brian C. Thomas, Ph.D., Chief Executive Officer and Founder**, prior to co-founding the company, Dr. Thomas spent more than 20 years in academic research at UC Berkeley helping to pioneer the field of metagenomics. Dr. Thomas has been cited over 16,000 times and listed as an inventor in 28 patent families.
- **Jian Irish, Ph.D., MBA, President and Chief Operating Officer**, has held biopharma executive leadership roles for nearly 20 years at Kite Pharma / Gilead, Sanofi, and Amgen in drug development and global operations, and has helped launch several breakthrough medicines.

- **Pamela Wapnick, MBA, Chief Financial Officer**, has over 20 years of diversified financial leadership experience spanning strategic and operational finance roles at public and private companies including life sciences and biotechnology companies, Diality Inc, Capsida Biotherapeutics, True North Therapeutics and Amgen.
- **Sarah Noonberg, M.D., Ph.D., Chief Medical Officer**, has spent more than 20 years in translational and clinical development leadership roles with a track record of advancing therapeutic programs from discovery to commercialization, including at Medivation and BioMarin.
- **Simon Harnest, Chief Investment Officer and SVP of Strategy**, has held leadership roles in corporate finance and strategy in the life sciences sector, having raised over \$1 billion in public and private capital, including leading Collectis' U.S. IPO and subsequent spin-out and IPO of Calyxt.
- **Luis G. Borges, Ph.D., Chief Scientific Officer**, has over 27 years of experience in the biotechnology industry, including Amgen, Five Prime Therapeutics, Cell Medica, and Century Therapeutics, where he held leadership roles in the research and development of multiple therapeutic candidates.
- **Simren Delaney, Ph.D., LL.M., VP of Legal**, is specialized in Intellectual Property and Patent law, having previously worked at Wilson Sonsini Goodrich & Rosati, and plays an instrumental role in driving the development of the company's growing IP portfolio.
- **Christopher T. Brown, Ph.D., VP of Discovery**, is a former scientist at the Jill F. Banfield laboratory at UC Berkeley and an expert in using metagenomics to discover novel microbial systems for use in genome editing. Dr. Brown's research has resulted in over 35 publications and over 20 patent family filings.
- **Michael Conway, MBA, CPA, VP of Finance**, has spent nearly 20 years in finance leadership positions at life science and technology companies, including Adamas Pharmaceuticals, InterMune, and Intel.
- **Alan Brooks, Ph.D., SVP of Preclinical**, has worked on genetic medicines providing scientific leadership in translational research for more than 25 years, including at Casebia Therapeutics and Bayer Healthcare. Dr. Brooks' research has led to 20 publications and numerous patent filings.

Our company is supported by our board of directors, Scientific Advisory Board, and a leading syndicate of investors, with more than 30 funds supporting our Series B and Series B-1 preferred unit financings.

Our Strategy.

Our goal is to harness the power of our proprietary metagenomics platform to create curative genetic medicines for patients. Key components of our strategy to achieve this goal include:

- Leverage our leadership position in metagenomics to continually advance and expand innovative genome editing tools.
- Develop and deliver products that make precise modifications to the human genome to cure disease.
- Build a fully integrated genome editing company.
- Expand therapeutic impact to patients through continued investment in business development and enabling partnerships, including with our existing partners Moderna, Ionis, and Affini-T Therapeutics, Inc.
- Maintain our entrepreneurial outlook, scientifically rigorous approach, and culture of tireless commitment to patients.

Risks Associated with Our Business

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We have never generated revenue from product sales and may never become profitable.
- We will need substantial additional funding in addition to the net proceeds we receive from this offering. If we are unable to raise additional capital when needed on acceptable terms, or at all, we may be forced to delay, reduce, or terminate certain research and product development programs, future commercialization efforts or other operations.
- We are very early in our development efforts, and we have not yet initiated IND-enabling studies or clinical development of any product candidate. As a result, we expect it will be many years before we commercialize any product candidate, if ever. If we are unable to advance our current or future product candidates into and through clinical trials, obtain regulatory approval and ultimately commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.
- We are subject to additional development challenges and risks due to the novel nature of our genome editing technology.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. Because genome editing is novel and the regulatory landscape that will govern our potential product candidates is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for our potential product candidates.
- The genome editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on genome editing using programmable nucleases, base editing, and RNA and DNA-mediated integration systems (including prime editors and Cas transposases), but other genome editing technologies may be discovered that provide significant advantages over such technologies, which could materially harm our business.
- If any of the product candidates we may develop or the delivery modes we rely on cause undesirable side effects, it could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential regulatory approval.
- Positive results from early preclinical studies of any product candidates we may develop are not necessarily predictive of the results of later preclinical studies and any future clinical trials of such product candidates. If we cannot replicate the positive results from our earlier preclinical studies of any product candidates we may develop in our later preclinical studies and future clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize such product candidates.
- We may find it difficult to enroll patients in our future clinical trials given the limited number of patients who have the diseases any product candidates we identify or develop are intended to target. If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical development activities and our receipt of necessary regulatory approvals could be delayed or prevented.
- Genetic therapies are novel, and any product candidates we develop may be complex and difficult to manufacture. We could experience delays in satisfying regulatory authorities or production problems that result in delays in our development programs, limit the supply of the product candidates we may develop or otherwise harm our business.

- We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.
- While we intend to seek designations for our potential product candidates with the U.S. Food and Drug Administration (the "FDA") and comparable foreign regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our potential product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.
- Because we are developing product candidates in the field of genetic medicines in which there is little clinical experience, there is increased risk that the FDA, the European Medicines Agency or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.
- If preclinical studies or clinical trials of any product candidates we may identify and develop fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.
- Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate we may develop in the United States or any other jurisdiction, and any such approval may be for a more narrow indication than we seek.
- If conflicts arise between us and our collaborators or strategic partners, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.
- We have entered into collaborations, and may enter into additional collaborations, with third parties for the research, development, manufacture and commercialization of programs or product candidates. If these collaborations are not successful, our business could be adversely affected.
- Our collaborators and strategic partners may control aspects of our clinical trials, which could result in delays and other obstacles in the commercialization of our proposed products and materially harm our results of operations.
- Our future success depends on our ability to retain our Chief Executive Officer and other key executives and to attract, retain, and motivate qualified personnel.
- Our commercial success depends on our ability to obtain, maintain, enforce, and otherwise protect our intellectual property and proprietary technology, and if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products and product candidates similar to ours and our ability to successfully develop and commercialize our genome editing systems may be adversely affected.
- Intellectual property rights do not necessarily address all potential threats to our business.

Corporate Information

We commenced our current operations and converted to a Delaware limited liability company in September 2018. We were originally founded as Metagenomi.co, a Delaware corporation, in September 2016. Prior to the

effectiveness of this registration statement, we intend to engage in a series of transactions, which we refer to collectively as the Reorganization. As a result of the Reorganization, Metagenomi Technologies, LLC will merge with and into its wholly-owned subsidiary, Metagenomi, Inc., a Delaware corporation, with Metagenomi, Inc. continuing as the surviving corporation. In connection with the Reorganization, (i) all of the outstanding common unitholders of Metagenomi Technologies, LLC will receive shares of common stock of Metagenomi, Inc., (ii) all of the outstanding preferred unitholders of Metagenomi Technologies, LLC will receive shares of preferred stock of Metagenomi, Inc. and (iii) all of the outstanding holders of profits interest units in Metagenomi Technologies, LLC will receive shares of common stock and restricted common stock in Metagenomi, Inc. as determined by the applicable provisions of the Metagenomi Technologies, LLC operating agreement in effect immediately prior to the Reorganization. Immediately prior to the completion of this offering, all outstanding shares of preferred stock of Metagenomi, Inc. will be converted into shares of common stock.

Metagenomi, Inc. will become the registrant for purposes of this offering, and our consolidated financial statements will be reported from Metagenomi, Inc. See "Reorganization" and "Description of Capital Stock" for additional information, including a description of the terms of our capital stock following the Reorganization and the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will be in effect upon the completion of this offering.

Our principal executive offices are located at 1545 Park Avenue Emeryville, California 94608, and our telephone number is (510) 871-4880.

Our website address is <https://www.metagenomi.co>. The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"). As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- being permitted to present only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's discussion and analysis of financial condition and results of operations" disclosure in this prospectus;
- reduced disclosure about our executive compensation arrangements;
- not being required to hold advisory votes on executive compensation or to obtain stockholder approval of any golden parachute arrangements not previously approved;
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002; and
- an exemption from compliance with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on the financial statements.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of

(i) the last day of the fiscal year in which we have total annual gross revenues of \$1.235 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission (the "SEC"). We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. Additionally, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, therefore, while we are an emerging growth company we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies. As a result of this election, our financial statements may not be comparable to those of other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

THE OFFERING

Shares of common stock offered by us	shares.
Shares of our common stock to be outstanding after this offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full).
Underwriters' option to purchase additional shares	We have granted the underwriters a 30-day option to purchase up to additional shares of our common stock at the initial public offering price, less underwriting discounts and commissions on the same terms as set forth in this prospectus.
Use of proceeds	We estimate that the net proceeds to us from the sale of shares of our common stock in this offering will be approximately \$ million, or \$ million if the underwriters exercise their option to purchase additional shares in full, assuming an initial public offering price of \$ per share, the estimated midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds of this offering, together with our existing cash and cash equivalents and available-for-sale marketable securities, to and for general corporate purposes. See "Use of Proceeds."
Proposed Nasdaq Global Select Market symbol	We have applied to list our common stock on the Nasdaq Global Select Market under the symbol "MGX." The closing of this offering is contingent upon such listing.
Risk factors	Investment in our common stock involves substantial risks. You should read this prospectus carefully, including the section entitled "Risk Factors" and the consolidated financial statements and the related notes to those statements included in this prospectus, before investing in our common stock.
<p>The number of shares of our common stock outstanding after this offering assumes the Reorganization takes place prior to the effectiveness of this registration statement and is based on shares of our common stock (including shares of unvested restricted common stock) issued in exchange for common units and profits interests outstanding as of September 30, 2023, and after giving effect to the conversion of shares of our redeemable convertible preferred stock, issued in connection with the Reorganization in exchange for redeemable convertible preferred units outstanding as of September 30, 2023, into an equivalent number of shares of our common stock immediately prior to the completion of this offering:</p>	
<p>The number of shares of common stock to be outstanding after this offering excludes:</p> <ul style="list-style-type: none"> • shares of common stock reserved for future issuance under our 2024 Stock Option and Incentive Plan, which will become effective on the date immediately prior to execution of the underwriting agreement related to this offering; and 	

- shares of common stock reserved for future issuance under our 2024 Employee Stock Purchase Plan, which will become effective immediately prior to execution of the underwriting agreement related to this offering.

Except as otherwise noted, all information in this prospectus:

- assumes no vesting of the restricted common stock described above;
- assumes no exercise of the underwriters' option to purchase up to additional shares of common stock in this offering;
- assumes the filing of our amended and restated certificate of incorporation and the effectiveness of our amended and restated bylaws, which will occur upon the closing of this offering; and
- assumes a -for- reverse stock split of our common stock effected on , 2024.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables present the summary consolidated financial data for Metagenomi Technologies, LLC and its consolidated subsidiary. You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes appearing elsewhere in this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the consolidated statements of operations for the years ended December 31, 2022 and 2021 from our audited consolidated financial statements appearing elsewhere in this prospectus. The consolidated statements of operations for the nine months ended September 30, 2023 and 2022 and the consolidated balance sheet data as of September 30, 2023 have been derived from our unaudited condensed consolidated financial statements appearing elsewhere in this prospectus, which have been prepared on the same basis as the audited consolidated financial statements. In the opinion of management, the unaudited data reflect all adjustments, consisting only of normal recurring adjustments, necessary for a fair statement of the financial information in those statements. Our historical results are not necessarily indicative of the results that may be expected in any future period. The summary consolidated financial data included in this section are not intended to replace the consolidated financial statements and the related notes included elsewhere in this prospectus.

	Year Ended		Nine Months Ended	
	December 31,		September 30,	
	2021	2022	2022	2023
(in thousands, except share and per share data)				
Consolidated Statements of Operations Data:				
Collaboration revenue	\$ 243	\$ 17,200	\$ 11,605	\$ 32,357
Operating expenses:				
Research and development	14,478	43,139	28,082	69,648
General and administrative	9,712	18,701	12,397	21,005
Total operating expenses	24,190	61,840	40,479	90,653
Loss from operations	(23,947)	(44,640)	(28,874)	(58,296)
Other income (expense):				
Interest expense	(302)	(98)	(98)	—
Interest income	43	3,419	1,489	11,836
Change in fair value of long-term investments	2,760	94	94	2,870
Other income (expense), net	4	201	146	(70)
Total other income	2,505	3,616	1,631	14,636
Net loss before provision for income taxes	(21,442)	(41,024)	(27,243)	(43,660)
Provision for income taxes	—	(2,569)	(1,723)	(5,301)
Net loss	\$ (21,442)	\$ (43,593)	\$ (28,966)	\$ (48,961)
Net loss per unit attributable to common unitholders, basic and diluted(1)	\$ (3.77)	\$ (7.34)	\$ (4.88)	\$ (8.23)
Weighted-average common units outstanding, basic and diluted(1)	5,691,431	5,938,654	5,935,673	5,947,500
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)(2)		\$		\$
Pro forma weighted-average common stock outstanding, basic and diluted (unaudited)(2)				

(1) See Note 16 to our audited consolidated financial statements and Note 14 to our unaudited condensed consolidated financial statements included elsewhere in this prospectus for details on the calculation of basic and diluted net loss per unit attributable to common unitholders.

(2) See "Unaudited Pro Forma Net Loss Per Share Attributable to Common Stockholders" subsection below for details on our unaudited pro forma calculations.

Unaudited Pro Forma Net Loss Per Share Attributable to Common Stockholders

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2022 and for the nine months ended September 30, 2023 has been computed to give effect to (i) the Reorganization, (ii) the conversion of and shares of our redeemable convertible preferred stock outstanding as of December 31, 2022 and September 30, 2023, respectively, into an equivalent number of shares of our common stock as if such conversion occurred on January 1, 2022 and (iii) the filing and effectiveness of our amended and restated certificate of incorporation that will be in effect immediately prior to

the completion of this offering. The unaudited pro forma net loss attributable to common stockholders gives effect to the adjustments described below. The unaudited pro forma net loss per share attributable to common stockholders, basic and diluted, does not include the effect of the shares of our common stock expected to be sold in this offering.

The following table sets forth the computation of the unaudited pro forma basic and diluted net loss per share assuming the offering is completed on January 1, 2022:

	Year Ended December 31, 2022 (unaudited)	Nine Months Ended September 30, 2023 (unaudited)
(in thousands, except share and per share data)		
Numerator:		
Net loss	\$ (43,593)	\$ (48,961)
Denominator:		
Weighted-average common units outstanding, basic and diluted	5,938,654	5,947,500
Pro forma adjustment to reflect the issuance of common stock in exchange for common units in connection with the Reorganization(1)		
Pro forma adjustment to reflect the issuance of common stock in exchange for vested profits interests in connection with the Reorganization(1)		
Pro forma adjustment to reflect the conversion of redeemable convertible preferred stock issued in connection with the conversion of the redeemable convertible preferred units from the Reorganization into common stock(2)		
Pro forma weighted-average common shares outstanding, basic and diluted (unaudited)	<u> </u>	<u> </u>
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)	<u>\$</u>	<u>\$</u>

- (1) Reflects the exchange of (i) 5,947,500 common units for shares of our common stock and (ii) vested profits interests for shares of our common stock in connection with the Reorganization, as if such exchange had occurred on January 1, 2022.
- (2) Reflects the conversion of shares of our redeemable convertible preferred stock, issued in connection with the Reorganization in exchange for redeemable convertible preferred units, into an equivalent number of shares of our common stock, as if such conversion had occurred on January 1, 2022.

	As of September 30, 2023		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2)
	(in thousands)		
Condensed Consolidated Balance Sheet Data:			
Cash and cash equivalents	\$ 101,897	\$	\$
Available-for-sale marketable securities	191,030		
Working capital(3)	231,221		
Total assets	386,433		
Total liabilities	154,696		
Redeemable convertible preferred units	350,758		
Redeemable convertible preferred stock	—		
Accumulated deficit	(125,650)		
Total members'/shareholders' equity (deficit)	(119,021)		

- (1) The consolidated pro forma balance sheet data gives effect to (i) the Reorganization, (ii) the conversion of _____ shares of our redeemable convertible preferred stock, issued in connection with the Reorganization in exchange for redeemable convertible preferred units outstanding as of September 30, 2023, into an equivalent number of shares of our common stock immediately prior to the closing of this offering, and (iii) the filing and effectiveness of our amended and restated certificate of incorporation upon the closing of this offering.
- (2) The pro forma as adjusted consolidated balance sheet data gives effect to the pro forma adjustments set forth in footnote (1) above and our issuance and sale of _____ shares of our common stock offered in this offering at an assumed initial public offering price of \$ _____ per share, which is the estimated midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information set forth in the table above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of this offering as determined at pricing.
- (3) We define working capital as current assets less current liabilities. See our consolidated financial statements included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

Each \$1.00 increase or decrease in the assumed initial public offering price of \$ _____ per share, which is the estimated midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, the pro forma as adjusted amount of each of our cash and cash equivalents, working capital, total assets, and total members'/shareholders' equity (deficit) by \$ _____ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase or decrease of 1,000,000 shares in the number of shares offered by us as set forth on the cover page of this prospectus, would increase or decrease, as applicable, the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets, and total members'/shareholders' equity (deficit) by \$ _____ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our consolidated financial statements and related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the events or developments described below were to occur, our business, prospects, operating results and financial condition could suffer materially, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks Related to Financial Position and Need for Capital

We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was \$21.4 million and \$43.6 million for the years ended December 31, 2021 and 2022, and \$29.0 million and \$49.0 million for the nine months ended September 30, 2022 and 2023, respectively. As of September 30, 2023, we had an accumulated deficit of \$125.7 million. We have financed our operations primarily through issuing redeemable convertible preferred units and convertible promissory notes and entering into collaboration agreements. Substantially all of our losses have resulted from expenses incurred in connection with our research and development and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- advance our current research activities and further develop our platform;
- continue preclinical development and initiate clinical trials for any product candidates we may identify;
- seek regulatory approval for any product candidates for which we successfully complete clinical trials;
- establish our manufacturing capabilities, including internal manufacturing facilities and contracting with other vendors;
- ultimately, commercialize our future product candidates requiring significant marketing, sales, and distribution infrastructure expenses;
- hire additional research and development, clinical, commercial, general and administration personnel;
- develop, maintain, expand, protect, and enforce our intellectual property portfolio;
- acquire or in-license product candidates, intellectual property and technologies;
- confirm, maintain or obtain freedom to operate for any of our owned or licensed technologies and product candidates;
- establish and maintain collaborations;
- add operational, financial and management information systems and personnel; or
- incur additional legal, audit, accounting, compliance, insurance, investor relations and other expenses to operate as a public company that we did not incur as a private company.

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As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, which may include collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, reduce or eliminate the development and commercialization of our platform or delay our pursuit of potential in-licenses or acquisitions.

We have not initiated clinical development of any potential product candidate and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must develop and, either directly or through collaborators, eventually commercialize a therapy or therapies with market potential. This will require us to be successful in a range of challenging activities, including identifying product candidates, completing preclinical studies and clinical trials of product candidates, obtaining regulatory approval for these product candidates, manufacturing, marketing and selling those therapies for which we may obtain regulatory approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability.

Because of the numerous risks and uncertainties associated with developing our technology and any potential product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We have never generated revenue from product sales and may never become profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, product candidates we may identify for development. We may not generate revenues from product sales for many years, if ever. Our ability to generate future revenues from product sales depends heavily on our or our collaborators' ability to successfully:

- identify product candidates and successfully complete research development of any product candidates we may identify;
- seek and obtain regulatory approvals for any product candidates for which we successfully complete clinical trials;
- launch and commercialize any product candidates for which we may obtain regulatory approval by establishing a sales force, marketing and distribution infrastructure, or alternatively, collaborating with a commercialization partner;
- qualify for adequate coverage and reimbursement by government and third-party payors for any product candidates for which we may obtain regulatory approval;
- establish and maintain supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for any product candidates for which we obtain regulatory approval;

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- develop, maintain and enhance a sustainable, scalable, reproducible and transferable manufacturing process for the product candidates we may develop;
- address competing technological and market developments;
- negotiate favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- receive market acceptance by physicians, patients, healthcare payors, and others in the medical community;
- maintain, protect, enforce, defend and expand our portfolio of intellectual property and other proprietary rights, including patents, trade secrets and know-how;
- defend against third-party intellectual property claims of infringement, misappropriation or other violation; and
- attract, hire and retain qualified personnel.

Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration (the "FDA") or other regulatory authorities to perform preclinical studies or clinical trials in addition to those that we currently anticipate. Even if one or more of the product candidates we may develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Additionally, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives. Even if we are able to generate revenues from the sale of any approved product candidates, we may not become profitable and may need to obtain additional funding to continue operations.

We will need substantial additional funding in addition to the net proceeds we receive from this offering. If we are unable to raise additional capital when needed on acceptable terms, or at all, we may be forced to delay, reduce, or terminate certain of our research and product development programs, future commercialization efforts or other operations.

Developing gene editing products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate and conduct clinical trials of, and seek regulatory approval for, any product candidates we may identify. In addition, if we obtain regulatory approval for any product candidates we may identify, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, manufacturing, and distribution are not the responsibility of a collaborator. Other unanticipated costs may also arise. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce, or eliminate our research and product development programs, future commercialization efforts or other operations.

As of September 30, 2023, our cash, cash equivalents and available-for-sale marketable securities were \$292.9 million. We expect that the net proceeds from this offering, together with our existing cash, cash equivalents, and available-for-sale marketable securities, will enable us to fund our operating expenses and capital expenditure requirements into . However, our operating plan may change as a result of factors currently unknown to us, and we may need to seek funding sooner than planned. Our future capital requirements will depend on many factors, including:

- the timing and progress of research and development, preclinical and clinical development activities;

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- the number, scope and duration of clinical trials required for regulatory approval of our future product candidates;
- the costs, timing, and outcome of regulatory review of any of our future product candidates;
- the costs of manufacturing clinical and commercial supplies of our future product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our future product candidates for which we receive regulatory approval;
- the costs of preparing, filing and prosecuting our patent applications, maintaining and enforcing our patents and other intellectual property rights and defending intellectual property-related claims;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements, and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- our ability to establish and maintain collaboration and license agreements on favorable terms, if at all;
- the extent to which we acquire or in-license other product candidates and technologies;
- any product liability or other lawsuits related to our future product candidates;
- our implementation of various computerized informational systems and efforts to enhance operational systems;
- expenses incurred to attract, hire and retain skilled personnel;
- the costs of operating as a public company;
- our ability to establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payers;
- the extent to which we acquire or invest in businesses, products, and technologies;
- the effect of competing technological and market developments; and
- the impact of the COVID-19 pandemic, as well as other factors, including economic uncertainty and geopolitical tensions, which may exacerbate the magnitude of the factors discussed above.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, and possibly other restrictions.

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Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We have no committed sources of additional capital and, if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our future product candidates or other research and development initiatives. Without sufficient funding, our license agreements and any future collaboration agreements may also be terminated if we are unable to meet the payment or other obligations under such agreements.

If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Additionally, if we raise funds through additional collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates we develop, or we may have to grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock.

Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are an early-stage company. We commenced our operations in September 2018. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, and research and development activities such as acquiring and developing our platform and technology and identifying and beginning to advance preclinical testing of potential product candidates. All of our programs are still in the research or lead optimization stage of development and their risk of failure is high. We have not yet demonstrated an ability to initiate or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial-scale therapy, arrange for a third party to do so on our behalf or conduct sales and marketing activities necessary for successful commercialization.

Our limited operating history, particularly in light of the rapidly evolving genome editing field, may make it difficult to evaluate our technology and industry and predict our future performance. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by very early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

In addition, as a new business that is rapidly growing, we may encounter other unforeseen expenses, difficulties, complications, and delays in our product development. We will need to transition from a company with a research focus to a company capable of conducting clinical trials and ultimately supporting commercial activities if any of our future product candidates are approved. We may not be successful in such a transition.

Our future ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Since our inception, we have incurred losses and we may never achieve profitability. As of December 31, 2022, we had U.S. federal net operating loss carryforwards of \$0.02 million (which are not subject to expiration) and state net operating loss carryforwards of \$8.3 million (which begin to expire in various amounts in 2037), and \$2.8 million of research credit carryforwards for state income tax purposes (which do not expire and can be carried forward indefinitely). To the extent that we continue to generate taxable losses, under current law, our unused U.S. federal net operating losses ("NOLs") may be carried forward to offset a portion of future taxable income, if any. Additionally, we continue to generate business tax credits, including research and development tax credits, which generally may be carried forward to offset a portion of future taxable income, if any, subject

to expiration of such credit carryforwards. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), if a corporation undergoes an "ownership change," generally defined as one or more shareholders or groups of shareholders who own at least 5 percent of the corporation's equity increasing their equity ownership in the aggregate by more than 50 percentage points (by value) over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. Similar rules may apply under state tax laws. Our prior equity offerings and other changes in our stock ownership have resulted in such ownership changes in the past. In addition, we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOLs or other pre-change tax attributes to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. Additional limitations on our ability to utilize our NOLs to offset future taxable income may arise as a result of our corporate structure whereby NOLs generated by our subsidiary may not be available to offset taxable income earned by our subsidiary. There is a risk that due to changes under the tax law, regulatory changes or other unforeseen reasons, our existing NOLs or business tax credits could expire or otherwise be unavailable to offset future income tax liabilities. At the state level, there may also be periods during which the use of NOLs or business tax credits is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For these reasons, we may not be able to realize a tax benefit from the use of our NOLs or tax credits, even if we attain profitability.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our business and our financial condition. In recent years, many such changes have been made and changes are likely to continue to occur in the future. We cannot predict whether, when, in what form or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided or whether they could increase our tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

Risks Related to Business, Technology, and Industry

We are very early in our development efforts, and we have not yet initiated IND-enabling studies or clinical development of any product candidate. As a result, we expect it will be many years before we commercialize any product candidate, if ever. If we are unable to advance our future product candidates into and through clinical trials, obtain regulatory approval and ultimately commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts and have focused our research and development efforts to date on research efforts including preclinical studies. Currently, all of our programs are still in the research or lead optimization stage of development. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of our future product candidates, which may never occur. We have not yet generated revenue from product sales, and we may never be able to develop or commercialize a marketable product.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an investigational new drug ("IND") application and finalizing the trial design based on discussions with the FDA. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests prior

to commencing clinical trials, the start of our first clinical trials may be delayed or we may be unsuccessful obtaining clearance to proceed into clinical development. Even after we receive and incorporate guidance from the FDA, the FDA could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials, delay the enrollment of our clinical trials, abandon our clinical development plans or meet stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union.

In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. We may conduct one or more of our clinical trials with one or more trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA, and there can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

Commercialization of any product candidates we may develop will require preclinical and clinical development; regulatory approval in multiple jurisdictions; manufacturing supply, capacity and expertise; a commercial organization; and significant marketing efforts. The success of product candidates we may identify and develop will depend on many factors, including the following:

- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for any product candidates we may develop;
- successful enrollment and completion of clinical trials, including under the FDA's current Good Clinical Practices ("GCPs"), current Good Laboratory Practices ("GLPs"), and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our future clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishment of arrangements through our own facilities or with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for any product candidates we may develop;
- commercial launch of any product candidates we may develop, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our product candidates we may develop, including method of administration, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies;

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- maintenance of a continued acceptable safety, tolerability and efficacy profile of any product candidates we may develop following approval; and
- establishment and maintenance of healthcare coverage and adequate reimbursement by payors.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates we may develop, which would materially harm our business. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are subject to additional development challenges and risks due to the novel nature of our genome editing technology.

Because our *in vivo* technology potentially involves genome editing across multiple cell and tissue types, we are subject to many of the challenges and risks that other genome editing therapeutics and gene therapies face, including:

- regulatory guidance regarding the requirements governing gene and genome editing therapy product candidates have changed and may continue to change in the future;
- to date, only a limited number of products that involve *in vivo* gene transfer have been approved globally;
- improper modulation of a gene sequence, including unintended editing events or insertion of a sequence into certain locations in a patient's chromosome, could lead to cancer, other aberrantly functioning cells or other diseases, including death;
- corrective expression of a missing protein in patients' cells could result in the protein being recognized as foreign, and lead to a sustained immunological reaction against the expressed protein or expressing cells, which could be severe or life-threatening; and
- regulatory agencies may require extended follow-up observation periods of patients who receive treatment using genome editing product candidates including, for example, the FDA's recommended 15-year follow-up observation period for these patients, and we will need to adopt such observation periods for product candidates we develop if required by the relevant regulatory agency, which could vary by country or region.

Furthermore, our technology has potential application for *ex vivo* immune cell editing strategies. Because *ex vivo* application of our technology potentially involves editing human cells and then delivering modified cells to patients, we may be subject to many of the challenges and risks that engineered cell therapies face. For example, clinical trials using engineered cell-based gene therapies may require unique products to be created for each patient and such individualistic manufacturing may be both inefficient and cost-prohibitive.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. Because genome editing is novel and the regulatory landscape that will govern our potential product candidates is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for our potential product candidates.

The time required to obtain approval for any of our potential product candidates from the FDA, the European Medicines Agency ("EMA") or other comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. For more information on the regulatory approval process, see "Business—Government Regulation." Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. Even if initial clinical trials in any of our product candidates we may develop are successful, such product candidates may fail to show the desired safety and efficacy in

later stages of clinical development despite having successfully advanced through preclinical studies and initial clinical trials. There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials.

Because genome editing is novel, the regulatory requirements that will govern any novel genome editing product candidates we develop may continue to evolve. Within the broader genetic therapy field, a limited number of gene therapy products have received marketing authorization from the FDA and the EMA to date. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and may continue to change in the future. For example, in January 2020, the FDA issued several new guidance documents on gene therapy products, and in March 2022, the FDA published a draft guidance document providing recommendations for human genome editing gene therapy products. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Therapeutic Products ("OTP") within its Center for Biologics Evaluation and Research ("CBER") to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials may also be subject to review and oversight by an institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees certain basic and clinical research conducted at the institution participating in the clinical trial. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies, such as an IBC or institutional review board ("IRB"), can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. For example, more recently, some genome editing companies have seen significant delays in receiving FDA authorization to allow the initiation of their clinical trials, and has suspended ongoing trials, due to the FDA's placement of clinical holds on their INDs.

The same applies in the European Union. The EMA's Committee for Advanced Therapies ("CAT") is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products (i.e. gene therapy, somatic-cell therapy or tissue-engineered medicines). The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the Committee for Medicinal Products for Human Use ("CHMP") before CHMP adopts its opinion which is submitted to the European Commission for the final decision on whether to grant a marketing authorization or not. In the European Union, the EMA publishes guidelines for the development and evaluation of gene therapy medicinal products to assist in preparing marketing authorization applications, however these are continually under review. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines.

Adverse developments in post-marketing experience or in clinical trials conducted by others of gene therapy products, cell therapy products or products developed through the application of genome editing technology may cause the FDA, the EMA and other regulatory bodies to revise the requirements for development or approval of our potential product candidates or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing genome editing technology in a timely manner or under

technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the commercialization of resulting products.

The regulatory review committees and advisory groups described above and any new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop.

The genome editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on genome editing using programmable nucleases, base editing, and RNA and DNA-mediated integration systems (including prime editors and CRISPR-associated (“Cas”) transposases), but other genome editing technologies may be discovered that provide significant advantages over such technologies, which could materially harm our business.

To date, we have focused our efforts on genome editing technologies using programmable nucleases, base editing, and RNA and DNA-mediated integration systems (including prime editors and Cas transposases backed by our metagenomics database. Other companies have previously undertaken research and development of genome editing technologies using zinc finger nucleases, engineered meganucleases and transcription activator-like effector nucleases, but to date none have obtained regulatory approval for a product candidate. There can be no certainty that genome editing technology will lead to the development of genetic medicines or that other genome editing technologies will not be considered better or more attractive for the development of medicines. A number of alternative approaches are being developed by others. Our investments may not be consistent with the expectations of our stockholders and may not produce the benefits that we expect, in which case our growth, business, financial condition, and results of operations could be adversely affected. See “Risk Factors—Risks Related to Business, Technology and Industry—We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.” Similarly, another new genome editing technology that has not been discovered yet may be more attractive than programmable nucleases, base editing, and RNA and DNA-mediated integration systems. Moreover, if we decide to develop genome editing technologies other than those involving such technologies, we cannot be certain we will be able to obtain rights to such technologies. Any of these factors could reduce or eliminate our commercial opportunity, and could have a material adverse effect on our business, financial condition, results of operations and prospects.

If any of the product candidates we may develop or the delivery modes we rely on cause undesirable side effects, it could delay or prevent their development or potential regulatory approval, limit the commercial potential or result in significant negative consequences following any potential regulatory approval.

To date, we have not evaluated any product candidates in human clinical trials. It is impossible to predict when or if any product candidates we may develop will ultimately prove safe in humans. In the genomic medicine field, there have been several significant adverse events from gene therapy treatments in the past, including reported cases of leukemia and death. Product candidates we may develop may be associated with undesirable side effects, unexpected characteristics or other serious adverse events, including off-target cuts of DNA, or the introduction of cuts in DNA at locations other than the target sequence. These off-target cuts could lead to

disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off-target cut events, DNA from such repair template could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. There is also the potential risk of delayed adverse events following exposure to genome editing therapy due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Possible adverse side effects that could occur with treatment with genome editing products include an immunologic reaction after administration which could substantially limit the effectiveness of the treatment. If any of our genome editing technologies demonstrate a similar effect, we may decide or be required to halt or delay preclinical development or clinical development of any product candidates we may develop. In addition to serious adverse events or side effects caused by any product candidate we may develop, the administration process or related procedures also can cause undesirable side effects. If any such events occur, our preclinical studies or clinical trials could be delayed, suspended or terminated. There can be no assurance that our genome editing technologies will not cause severe or undesirable side effects.

If in the future we are unable to demonstrate that such adverse events were caused by factors other than our product candidate, the FDA, the EMA or other comparable foreign regulatory authorities could order us to cease further clinical studies of, or deny approval of, any product candidates we develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we may develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, result of operations and prospects significantly.

Viral vectors, including the adeno-associated virus ("AAV"), which are relatively new approaches used for disease treatment, also have known side effects, and for which additional risks could develop in the future. In past clinical trials that were conducted by others with non-AAV vectors, significant side effects were caused by gene therapy treatments, including reported cases of myelodysplasia, leukemia and death. Other potential side effects could include an immunologic reaction and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of cancer. If the vectors we use demonstrate a similar side effect, or other adverse events, we may be required to halt or delay further clinical development of any potential product candidates. Such delayed adverse events may also occur in other viral vectors, including AAV vectors.

In addition to side effects and adverse events caused by our product candidates, the conditioning, administration process or related procedures which may be used to condition a patient for gene therapy treatment also can cause adverse side effects and adverse events. A gene therapy patient is generally administered cytotoxic drugs to remove stem cells from the bone marrow to create sufficient space in the bone marrow for the modified stem cells to engraft and produce new cells. This procedure compromises the patient's immune system, and conditioning regimens have been associated with adverse events in clinical trial participants.

Additionally, if we successfully develop a product candidate and it receives regulatory approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy ("REMS") to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan

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to healthcare practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any product candidate that we may develop that receives regulatory approval, several potentially significant negative consequences could result, including:

- regulatory authorities may revoke licenses or suspend, vary or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our genome editing technology and any product candidates we may identify and develop and could have a material adverse effect on our business, financial condition, results of operations and prospects.

Positive results from early preclinical studies of any product candidates we may develop may not necessarily be predictive of the results of later preclinical studies and any future clinical trials of such product candidates. If we cannot replicate the positive results from our earlier preclinical studies of any product candidates we may develop in our later preclinical studies and future clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize such product candidates.

Any positive results from our preclinical studies of any product candidates we may develop may not necessarily be predictive of the results from later preclinical studies and clinical trials of such product candidates. Similarly, even if we are able to complete our planned preclinical studies or any future clinical trials of any product candidates we may develop according to our current development timeline, the positive results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain regulatory approval.

We may also consider additional delivery modes, which may carry additional known and unknown risks.

We may also consider additional delivery modes, which may carry additional known and unknown risks. For example, we intend to use lipid nanoparticles (“LNPs”) to deliver our nucleases. While LNPs have been used to deliver smaller molecules, such as small interfering RNA (“siRNA”), they have not been clinically proven to deliver large RNA molecules. Furthermore, as with many AAV-mediated gene therapy approaches, certain patients’ immune systems might prohibit the successful delivery, thereby potentially limiting treatment outcomes of these patients. Even if initial clinical trials in any of our potential product candidates we may develop are successful, these product candidates we may develop may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through preclinical studies and initial clinical trials.

We may find it difficult to enroll patients in our future clinical trials given the limited number of patients who have the diseases any product candidates we identify or develop are intended to target. If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical development activities and our receipt of necessary regulatory approvals could be delayed or prevented.

As we progress our programs, we may not be able to initiate or continue clinical trials for any product candidates we identify or develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, the EMA or other comparable regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. Enrollment may be particularly challenging for some of the rare genetically defined diseases we are targeting in some of our discovery programs. In addition, if patients are unwilling to participate in our genome editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy or genome editing fields, competitive clinical trials for similar patient populations, clinical trials in competing product candidates or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our potential product candidates may be delayed. Moreover, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our potential product candidates, and patients who would otherwise be eligible for our future clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors, some of which may include:

- severity of the disease under investigation;
- size of the patient population and process for identifying patients, including proximity and availability of clinical trial sites for prospective patients with conditions that have small patient pools;
- design of the trial protocol, including efforts to facilitate timely enrollment in clinical trials;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients and ability to monitor patients adequately during and after treatment;
- ability to obtain and maintain patient informed consent;
- risk that enrolled patients will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial and genome editing as a therapeutic approach; and
- patient referral practices of physicians.

In addition, our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, some of which may include:

- difficulty in establishing or managing relationships with clinical research organizations ("CROs") and physicians;
- different standards for the conduct of clinical trials;
- different standard-of-care for patients with a particular disease;
- difficulty in locating qualified local consultants, physicians and partners; and
- potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment and of genome editing technologies.

Enrollment delays in our future clinical trials may result in increased development costs for our potential product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our future clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials or entire clinical programs, any of which would have an adverse effect on our business, financial condition, results of operations and prospects.

Genetic therapies are novel, and any product candidates we develop may be complex and difficult to manufacture. We could experience delays in satisfying regulatory authorities or production problems that result in delays in our development programs, limit the supply of the product candidates we may develop or otherwise harm our business.

Any product candidates we may develop will likely require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as the product candidates we intend to develop generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate will perform in the intended manner. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims, insufficient inventory or potentially delay progression of our potential IND filings. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet the FDA, the EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. For example, the current approach of manufacturing AAV vectors may fall short of supplying required number of doses needed for advanced stages of preclinical studies or clinical trials, and the FDA may ask us to demonstrate that we have the appropriate manufacturing processes in place to support the higher-dose group in our preclinical studies or clinical trials. In addition, any product candidates we may develop will require complicated delivery methods, each of which will introduce additional complexities in the manufacturing process.

In addition, the FDA, the EMA and other regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

Given the nature of biologics manufacturing there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. Some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of any product candidates we may develop could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations and prospects.

Any problems in our manufacturing process or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic

research institutions, which could limit our access to additional attractive development programs. Problems in third-party manufacturing process or facilities also could restrict our ability to ensure sufficient clinical material for any clinical trials we may be conducting or are planning to conduct and meet market demand for any product candidates we develop and commercialize.

We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.

The development and commercialization of new drug products is highly competitive. Moreover, the genome editing field is characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We will face competition with respect to any product candidates that we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent or other intellectual property protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, while others are based on entirely different approaches.

Amongst publicly traded peers, there are several companies utilizing CRISPR/Cas technology, including Caribou Biosciences, Inc., Editas Medicine, Inc., CRISPR Therapeutics AG, Intellia Therapeutics, Inc. and Graphite Bio, Inc. Several additional companies such as Sangamo Therapeutics, Inc., Precision BioSciences, Inc., bluebird bio, Inc., and Cellectis Inc. utilize alternative nuclease-based genome editing technologies, including zinc finger nucleases ("ZFNs"), engineered meganucleases and transcription-activator like effector nucleases ("TALENs"). Beam Therapeutics utilizes base editing technology. Prime Medicine utilizes prime editing technology.

In addition, other private companies such as Tessera Therapeutics, Inc. and Tome Biosciences, Inc. have announced their work in recombinase DNA and RNA gene writers, although little is known publicly about their science or portfolio. Other companies have announced intentions to enter the genome editing field, such as Moderna, Inc. and Pfizer Inc. Most recently, new epigenetic editing companies have emerged, such as Chroma Medicine, Inc. and Tune Therapeutics, Inc. In addition, we face competition from companies utilizing gene therapy, oligonucleotides and cell therapy therapeutic approaches.

Several private companies such as Arbor Biotechnologies, Inc., Scribe Therapeutics Inc., and Mammoth Biosciences, Inc. are actively searching for novel genome editing components and have reported the discovery of new DNA-cutting enzymes. Other companies are active in LNP delivery technologies and advancing those into therapeutics using genetic therapies, including Recode Therapeutics, Inc., Verve Therapeutics, Inc., Generation Bio Co. and Beam Therapeutics, among others.

Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for any product candidates we may develop. This may include other types of therapies, such as small molecule, antibody and/or protein therapies.

Many of our current or potential competitors, either alone or with their collaboration partners, may have significantly greater financial resources and expertise in research and development, manufacturing, conducting preclinical studies and clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage

companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize product candidates that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any product candidates that we may develop or that would render any product candidates that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent or other intellectual property rights, we could face risks relating to our ability to successfully prevent or delay launch of competitors' products. The availability of our competitors' products could limit the demand and the price we are able to charge for any product candidates that we may develop and commercialize.

Adverse public perception of genome editing and cellular therapy products may negatively impact demand for, or regulatory approval of, any product candidates we may develop.

The product candidates we may develop will involve editing the human genome. The clinical and commercial success of any product candidates we may develop will depend in part on public acceptance of the use of genome editing therapies for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that genome editing is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy in general could result in greater government regulation and stricter labeling requirements of genome editing products, including any of our product candidates, and could cause a decrease in the demand for any products we may develop. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Additionally, ethical, social and legal concerns about genome editing and gene therapy could result in additional regulations restricting or prohibiting any product candidates we may develop.

The commercial success of any of the product candidates we may develop will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Even if we obtain the requisite approvals from the FDA in the United States, the EMA in the European Union and other regulatory authorities internationally, the commercial success of any product candidates we may develop will depend, in part, on the acceptance of physicians, patients and health care payors of genome editing and gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community who may opt for existing treatments with which they are already familiar and for which greater clinical data may be available. The degree of market acceptance of genome editing and gene therapy products and, in particular, any product candidates we may develop, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in any future clinical trials;
- the potential and perceived advantages of such product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;

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- the clinical indications for which the product candidate is approved by the FDA, the EMA or other regulatory authorities;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of physicians to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA, the EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party payor coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and future clinical trials, market acceptance of the product will not be fully known until after it is launched. If any product candidates we may develop do not achieve an adequate level of acceptance following regulatory approval, if ever, we may not generate significant product revenue and may not become profitable.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We have limited financial and managerial resources. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market products based on our technologies, we may not be successful in commercializing our future product candidates if and when any such product candidates are approved and we may not be able to generate any revenue.

We do not currently have a sales or marketing infrastructure and, as a company, have no experience in the sale, marketing or distribution of therapeutic products. To achieve commercial success for any potential approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

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There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future product that we may develop;
- the lack of complementary treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

Due to the novel nature of our technology and the potential for any product candidates we may develop to offer therapeutic benefit in a single administration or limited number of administrations, we face uncertainty related to pricing and reimbursement for such product candidates.

Our initial target patient populations are relatively small, as a result of which the pricing and reimbursement of any product candidates we may develop, if approved, must be adequate to support the necessary commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to any product candidates we may develop (e.g., for administration of our product candidate to patients) is also important. Inadequate reimbursement for such services may lead to physician and payor resistance and adversely affect our ability to market or sell our product candidates. In addition, we may need to develop new reimbursement models in order to realize adequate value. Payors may not be able or willing to adopt such new models, and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary but we are unsuccessful in developing them, or if such models are not adopted by payors, our business, financial condition, results of operations, and prospects could be adversely affected.

We expect the cost of a single administration of a genome editing therapy, such as those we are seeking to develop, to be substantial, when and if they achieve regulatory approval. We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of any such product candidates will depend substantially, both domestically and

abroad, on the extent to which the costs of any of our product candidates will be paid by government authorities, private health plans, and other third-party payors. Payors may not be willing to pay high prices for a single administration. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective, and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical, and cost-effectiveness data. There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any of our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

In the United States, no uniform policy exists for coverage and reimbursement for products among third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate a payor will pay for the product. One third-party payor's decision to cover a particular product or service does not ensure that other payors will also provide coverage for the medical product or service. Third-party payors may limit coverage to specific products on an approved list or formulary, which may not include all FDA-approved products for a particular indication.

Further, third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of any product candidates we may develop, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Despite our best efforts, any product candidates we may develop may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Finally, in some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing product pricing vary widely from country to country. For example, in the EU, pricing and reimbursement of pharmaceutical products are regulated at a national level under the individual EU Member States' social security systems. Some foreign countries provide options to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and can control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A country may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price

controls or reimbursement limitations for products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Even if approved for reimbursement, historically, product candidates launched in some foreign countries, such as some countries in the EU, do not follow price structures of the United States and prices generally tend to be significantly lower.

If we are not able to establish collaborations on a timely basis, on commercially reasonable terms, or at all, we may have to alter, reduce or delay our development and commercialization plans, or increase our expenditures to fund development or commercialization activities at our own expense.

For some of the product candidates we may develop, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborations and collaborations are complex and time-consuming to negotiate and document. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, the EMA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us.

We may also be restricted under existing collaboration agreements from entering into future collaboration agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators, which further increases competition we face in seeking potential collaborations.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to develop product candidates or bring them to market and generate product revenue.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy, geopolitical tensions and in the global financial markets. A severe or prolonged economic downturn or additional global financial and political crises could result in a variety of risks to our business, including weakened demand for any product candidates we develop or our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers or other third parties and create import and export issues, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We face risks related to health epidemics, pandemics and other widespread outbreaks of contagious disease, including the COVID-19 pandemic, which could significantly disrupt our operations, impact our financial results or otherwise adversely impact our business.

Significant outbreaks of contagious diseases and other adverse public health developments could have a material impact on our business operations and operating results. For example, the spread of COVID-19 has affected segments of the global economy and our operations. As a result of the COVID-19 pandemic or similar public health crises that may arise, we may experience disruptions that could adversely impact our operations, research and development, and as we continue developing, any preclinical studies, clinical trials and manufacturing activities we may conduct, some of which may include:

- delays or disruptions in research programs, preclinical studies, clinical trials or IND-enabling studies that we or our collaborators may conduct;
- interruption or delays in the operations of the FDA, the EMA and comparable foreign regulatory agencies;
- interruption of, or delays in receiving and distributing, supplies of drug substance and drug product from our contract manufacturing organizations (“CMOs”), to preclinical or clinical research sites or delays or disruptions in any preclinical studies or clinical trials performed by CROs;
- limitations imposed on our business operations by local, state or federal authorities to address a pandemic or similar public health crises; and
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations, and cybersecurity and data accessibility or security issues.

In addition, the trading prices for biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic and we may face similar volatility in our stock price after we complete this public offering. We cannot predict the scope and severity of any economic recovery after the COVID-19 pandemic abates, including following any additional “waves” or other intensifying of the pandemic. If we or any of the third parties with whom we engage were to experience additional shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business, financial condition, our results of operations and prospects. Furthermore, the COVID-19 pandemic could exacerbate the other risks described in this section.

Our operations are vulnerable to interruption by disasters, terrorist activity, pandemics and other events beyond our control, which could harm our business.

Our facilities are located in California. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major flood, power loss, terrorist activity, pandemics or other regional or global disasters and generally do not have a recovery plan for such events. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

We may use artificial intelligence in our business, and challenges with properly managing its use, as well as uncertainty regarding the legal landscape surrounding the use of AI could result in reputational harm, competitive harm, and legal liability, and adversely affect our results of operations.

We incorporate artificial intelligence (“AI”) solutions into our platform, and these applications may become important in our operations over time. There are significant risks involved in utilizing AI and no assurance can be provided that the usage of such AI will enhance our business or assist our business in being more efficient or profitable. Known risks of AI currently include inaccuracy, bias, toxicity, intellectual property infringement or

misappropriation, data privacy and cybersecurity and data provenance. In addition, AI may have errors or inadequacies that are not easily detectable. AI may also be subject to data herding and interconnectedness (i.e., multiple market participants utilizing the same data), which may adversely impact our business. If the data used to train AI or the content, analyses, or recommendations that AI applications assist in producing are or are alleged to be deficient, inaccurate, incomplete, overbroad or biased, our business, financial condition, and results of operations may be adversely affected. The legal landscape and subsequent legal protection for the use of AI remains uncertain, and development of the law in this area could impact our ability to enforce our proprietary rights or protect against infringing uses. If we do not have sufficient rights to use the data on which AI relies or to the outputs produced by AI applications, we may incur liability through the violation of certain laws, third-party privacy or other rights or contracts to which we are a party. Our use of AI applications may also, in the future, result in cybersecurity incidents that implicate the personal data of customers or patients. Any such cybersecurity incidents related to our use of AI applications could adversely affect our reputation and results of operations.

Risks Related to Regulatory, Legal, and Clinical Trials

While we intend to seek designations for our potential product candidates with the FDA and comparable foreign regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our potential product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA and comparable foreign regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. However, there can be no assurance that we will successfully obtain such designations for any potential product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for one or more of our potential product candidates, there can be no assurance that we will realize their intended benefits. For example, we may seek fast track designation for some of our potential product candidates. If a therapy is intended for the treatment of a serious or life threatening condition and the therapy nonclinical or clinical data demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a fast track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Additionally, we may seek a breakthrough therapy designation for some of our potential product candidates. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA may also be eligible for accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our potential product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and

instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our potential product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification. In addition, we may seek a regenerative medicine advanced therapy ("RMAT") designation for some of our potential product candidates. An RMAT is defined as cell therapies, therapeutic tissue engineering products, human cell and tissue products and combination products using any such therapies or products. Gene therapies, including genetically modified cells that lead to a durable modification of cells or tissues may meet the definition of a regenerative medicine therapy. The RMAT program is intended to facilitate efficient development and expedite review of RMATs, which are intended to treat, modify, reverse or cure a serious or life-threatening disease or condition. A new drug application or a biologics license application ("BLA") for an RMAT may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with the FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine therapy that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical trials, patient registries or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. RMAT designation is within the discretion of the FDA. Accordingly, even if we believe one of our potential product candidates meets the criteria for designation as a regenerative medicine advanced therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of RMAT designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our potential product candidates qualify as for RMAT designation, the FDA may later decide that the biological products no longer meet the conditions for qualification. We may also seek rare pediatric disease designation for some of our potential product candidates. The FDA defines "rare pediatric disease" as a (i) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (ii) a rare disease or condition within the meaning of the Orphan Drug Act. Designation of a product candidate as a product for a rare pediatric disease does not guarantee that a marketing application for such product candidate will meet the eligibility criteria for a rare pediatric disease priority review voucher ("PRV") at the time the application is approved. Under the U.S. Federal Food, Drug, and Cosmetic Act ("FDCA"), we will need to request a rare pediatric disease PRV in our original marketing application for any potential product candidates for which we have received rare pediatric disease designation. The FDA may determine that a marketing application for any such product candidates, if approved, does not meet the eligibility criteria for a PRV. Under the current statutory sunset provisions, after September 30, 2024, the FDA may only award a PRV for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the drug or biologic that is the subject of such application, and that designation was granted by September 30, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease PRVs. However, it is possible the authority for FDA to award rare pediatric disease PRV will be further extended by Congress. As such, if we do not obtain approval of a marketing application for any of our potential product candidates on or before September 30, 2026, and if the PRV program is not extended by Congressional action, we may not receive a PRV.

In the future, we may also seek approval of product candidates under the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and generally provides a meaningful advantage over available therapies upon a determination that the

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product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality ("IMM") that is reasonably likely to predict an effect on IMM or other clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as IMM. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. There can be no assurance that the FDA would allow any of the product candidates we may develop to proceed on an accelerated approval pathway, and even if the FDA did allow such pathway, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. Moreover, even if we received accelerated approval, any post-approval studies required to confirm and verify clinical benefit may not show such benefit, which could lead to withdrawal of any approvals we have obtained. Receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for the product candidates that we may develop. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

In addition, in the European Union, we may seek to participate in the PRiority Medicines ("PRIME") scheme for our potential product candidates. The PRIME scheme is intended to encourage development of products in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation, where the marketing authorization application will be made through the centralized procedure in the European Union. Products from small-and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies on the basis of compelling non-clinical data and tolerability data from initial clinical trials. Eligible products must target conditions for which there is an unmet medical need (no treatment option exists in the European Union or, they can offer a major therapeutic advantage over existing treatments). Many benefits accrue to sponsors of product candidates with PRIME designation, including but not

limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. There is no guarantee, however, that our potential product candidates would be deemed eligible for the PRIME scheme and even if we do participate in the PRIME scheme, where during the course of development a product no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn. PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

Healthcare and other reform legislation may increase the difficulty and cost for us and any collaborators we may have to obtain regulatory approval of and commercialize any product candidates we may develop and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be ongoing efforts to implement legislative and regulatory changes regarding the healthcare system. Such changes could prevent or delay regulatory approval of any product candidates that we may develop, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain regulatory approval. Although we cannot predict what healthcare or other reform efforts will be successful, such efforts may result in more rigorous coverage criteria, in additional downward pressure on the price that we, or our future collaborators, may receive for any approved products or in other consequences that may adversely affect our ability to achieve or maintain profitability.

Within the United States, the federal government and individual states have aggressively pursued healthcare reform, as evidenced by the passing of the Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA"), and the ongoing efforts to modify or repeal that legislation. The ACA significantly changed the way healthcare is financed by both governmental and private insurers and contains a number of provisions that affect coverage and reimbursement of drug products and/or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. Other aspects of healthcare reform, such as expanded government enforcement authority and heightened standards that could increase compliance-related costs, could also affect our business. Modifications have been implemented under the former Trump administration and additional modifications or repeal may occur.

There have also been executive, judicial, and congressional challenges to certain aspects of the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business. There is no assurance that federal or state healthcare reform will not adversely affect our future business and financial results, and we cannot predict how future federal or state legislative, judicial or administrative changes relating to healthcare reform will affect our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the American Rescue Plan Act of 2021 eliminates the statutory Medicaid drug rebate cap, currently set at 100 percent of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. The U.S. Budget Control Act of 2011 and subsequent legislation, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which remain in effect through 2032. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices, which has resulted in several U.S. Congressional inquiries and federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of

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prescription drugs, and review the relationship between pricing and manufacturer patient programs. The Inflation Reduction Act of 2022 (the "IRA"), for example, includes several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries to \$2,000 starting in 2025, eliminating the prescription drug coverage gap; impose new manufacturer financial liability on certain drugs under Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation; and delay until January 1, 2032 the implementation of an HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The effects of the IRA on our business and the healthcare industry in general is not yet known.

In addition, President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. In February 2023, HHS issued a proposal in response to an October 2022 Biden executive order that proposes a Medicare drug pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through the FDA's accelerated approval pathway. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

Because we are developing product candidates in the field of genetic medicines in which there is little clinical experience, there is increased risk that the FDA, the EMA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.

In order to proceed into clinical development of any product candidates we identify, we will need to submit INDs or clinical trial applications to regulatory authorities and obtain regulatory clearance to commence clinical

development. Because the product candidates we identify are based on novel gene-editing technology, we may be unsuccessful in obtaining clearance from regulatory authorities to proceed into clinical development. In order to commence clinical development, we will need to identify success criteria and endpoints such that the FDA, the EMA or other regulatory authorities will be able to determine the clinical efficacy and safety profile of any product candidates we may develop. As we are initially seeking to identify and develop product candidates to treat diseases in which there is little clinical experience using new technologies, and while we may have opportunities to discuss our clinical development plans with regulatory authorities prior to commencing clinical development, there is heightened risk that the FDA, the EMA or other regulatory authorities may not consider the clinical trial endpoints that we propose to provide clinically meaningful results (reflecting a tangible benefit to patients). In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoints to a degree of statistical significance. This may be a particularly significant risk for many of the genetically defined diseases for which we plan to develop product candidates because many of these diseases such as PH1 have small patient populations, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Furthermore, even if we do achieve the pre-specified criteria, we may produce results that are unpredictable or inconsistent with the results of the non-primary endpoints or other relevant data. The FDA also weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. Other regulatory authorities in the European Union and other countries may make similar comments with respect to these endpoints and data. Any product candidates we may develop will be based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. No genome editing therapeutic product has been approved in the United States or in Europe. Within the broader genome product field, only a limited number of gene therapy products, such as uniQure N.V.'s Glybera and Abecma from Bristol Myers Squibb and bluebird bio, have received marketing authorization or regulatory approval from the European Commission or the FDA. Some of these products have taken years to register and have had to deal with significant issues in their post-marketing experience.

If preclinical studies or clinical trials of any product candidates we may identify and develop fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

Before obtaining regulatory approval from regulatory authorities for the sale of any product candidates we may identify and develop, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain regulatory approval of their product candidates.

We and our collaborators, if any, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive regulatory approval or commercialize any product candidates we may identify and develop, including:

- delays in reaching a consensus with regulators on trial design;
- regulators, IRBs, or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective CROs and clinical trial sites;

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- clinical trials of any product candidates we may develop may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development or research programs;
- difficulty in designing well-controlled clinical trials due to ethical considerations which may render it inappropriate to conduct a trial with a control arm that can be effectively compared to a treatment arm;
- difficulty in designing clinical trials and selecting endpoints for diseases that have not been well-studied and for which the natural history and course of the disease is poorly understood;
- the number of patients required for clinical trials of any product candidates we may develop may be larger than we anticipate; enrollment of suitable participants in these clinical trials, which may be particularly challenging for some of the rare genetically defined diseases we are targeting in our most advanced programs, may be delayed or slower than we anticipate; or patients may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, IRBs, or independent ethics committees may require that we or our investigators suspend or terminate clinical research or clinical trials of any product candidates we may develop for various reasons, including noncompliance with regulatory requirements, a finding of undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks or after an inspection of our clinical trial operations or trial sites;
- the cost of clinical trials of any product candidates we may develop may be greater than we anticipate;
- the supply or quality of any product candidates we may develop or other materials necessary to conduct preclinical studies or clinical trials of any product candidates we may develop may be insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing, and delivery of any product candidates we may develop to the preclinical study sites or clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of serious adverse events associated with any product candidates we may develop that are viewed to outweigh their potential benefits;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors; and
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

If we or our collaborators are required to conduct additional clinical trials or other testing of any product candidates we may develop beyond those that we currently contemplate, if we or our collaborators are unable to successfully complete clinical trials or other testing of any product candidates we may develop, or if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we or our collaborators may:

- be delayed in obtaining regulatory approval for any such product candidates we may develop or not obtain regulatory approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to changes in the way the product is administered;

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- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a REMS, or through modification to an existing REMS;
- be sued; or
- experience damage to our reputation.

Product development costs will also increase if we or our collaborators experience delays in clinical trials or other testing or in obtaining regulatory approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates we may develop, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize any product candidates we may develop, any of which may harm our business, financial condition, results of operations, and prospects.

Failure to access or a significant delay in accessing animal research models may materially adversely affect our ability to advance our preclinical programs and successfully develop any product candidates we may identify, which could result in significant harm to our business.

Consistent with various rules, regulations and current good manufacturing practices ("cGMP"), our ability to advance our preclinical programs and successfully develop any product candidates we may identify requires access to animal research models sufficient to assess safety and in some cases to establish the rationale for therapeutic use. Failure to access or a significant delay in accessing animal research models that meet our needs or that fulfil regulatory requirements may materially adversely affect our ability to advance our preclinical programs and successfully develop any product candidates we may identify and this could result in significant harm to our business. During the COVID-19 pandemic, researchers and CROs (including those engaged by us) experienced significant limitations in their access to animal research models, specifically including a sharp reduction in the availability of non-human primates ("NHPs") originating from breeding farms in Southeast Asia and limited access to the generation of genetically-modified rodent models used in efficacy evaluations. Prior to the pandemic, China was the leading exporter of NHPs employed in basic and applied research; however, early in 2020, China ceased exportation of cynomolgus monkeys, the species most commonly involved in pharmaceutical product development. This change in the world supply of a critical research model has resulted in increased demand from breeding farms principally located in Cambodia, Vietnam, and Mauritius Island, with a resultant marked increase in unit pricing. Consequently, this has further exacerbated an already constrained NHP supply for research purposes. If we are unable to obtain NHPs in sufficient quantities and in a timely manner to meet the needs of our preclinical research programs, if the price of NHPs that are available increases significantly, or if our suppliers are unable to ship the NHPs in their possession that are reserved for us, our ability to advance our preclinical programs and successfully develop any preclinical candidates we may identify may be materially adversely affected or significantly delayed.

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate we may develop in the United States or any other jurisdiction, and any such approval may be for a more narrow indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA advisory committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may

experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require labeling that includes precautions or contraindications with respect to conditions of use, or may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially adversely affect our business, financial condition, results of operations, and prospects.

Regulatory approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product candidate testing and validation and additional administrative review periods. Seeking regulatory approval outside the United States could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our product candidates will be unrealized.

Even if we, or any of our collaborators or strategic partners, obtain regulatory approvals for any product candidates we may develop, the terms of approvals and ongoing regulation of such product candidates could require the substantial expenditure of resources and may limit how we, or they, manufacture and market such product candidates, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain regulatory approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA, the EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, facility registration and drug listing requirements, cGMP relating to quality control, quality assurance and corresponding maintenance of records and documents, applicable product tracking and tracing requirements and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, our manufacturing and testing facilities will be required to undergo pre-license inspections and pre-approval inspections. Even if regulatory approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the products may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

Accordingly, assuming we, or any collaborators we may have, receive regulatory approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the regulatory approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future

products could be limited, which could adversely affect our ability to achieve or sustain profitability. Furthermore, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition and prospects.

We may not be able to obtain orphan drug designation or exclusivity for our potential product candidates, and even if we do, that designation may not provide an expedited development or regulatory review or approval process and any orphan drug exclusivity we may receive for approved products may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan product candidates by the EMA in the European Union. Generally, if a product with an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA (as applicable) from approving another marketing application for another similar product candidate for the same orphan therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if at the end of the fifth year it is determined that a product no longer meets the criteria for orphan designation, including if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our potential product candidates, the agency must find that the product candidate is indicated for the treatment of a condition or disease that affects fewer than 200,000 individuals in the United States or that affects 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product candidate available for the disease or condition will be recovered from sales of the product in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product candidate for the same condition if the FDA concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, the U.S. Foreign Corrupt Practices Act of 1977, as amended (the "FCPA"), the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell our products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities,

and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We carry pollution insurance to protect against possible biological or hazardous waste accidents. However, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws, regulations, and permitting requirements. These current or future laws, regulations, and permitting requirements may impair our research, development, or production efforts. Failure to comply with these laws, regulations, and permitting requirements also may result in substantial fines, penalties, or other sanctions or business disruption, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Any third-party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health, and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, consultants and commercial partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could

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include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the EMA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, the EMA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. Upon the effectiveness of this registration statement, we will adopt a code of conduct and an insider trading policy applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any product candidates that we may develop.

We will face an inherent risk of product liability exposure related to the testing of any product candidates we may develop in human clinical trials and will face an even greater risk if we commercially sell such product candidates. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Our internal computer and information technology systems, or those of our third-party vendors, collaborators, contractors, consultants or other third parties, may fail, become unavailable, or suffer security incidents or data breaches, loss or leakage of data and other disruptions, which could result in a material disruption of our product development programs, compromise confidential, sensitive or personal information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

Our internal computer and information technology systems and those of our current and any future third-party vendors, collaborators, contractors, consultants or other third parties, are vulnerable to damage or interruption

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from, among other things, computer viruses, computer hackers, phishing attacks, ransomware, malware, social engineering, service interruptions, system malfunction, malicious code, employee theft, fraud, misconduct or misuse, denial-of-service attacks, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we seek to protect our information technology systems from system failure, accident and security breach, we have in the past and may in the future experience phishing and other security incidents which could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary, personal or confidential information or other disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Controls employed by our information technology department and other third parties could prove inadequate, and our ability to monitor such third parties' data security practices is limited. Due to applicable laws, rules, regulations and standards or contractual obligations, we may be held responsible for any information security failure or cybersecurity attack attributed to our third-party vendors as they relate to the information we share with them.

If we were to experience a cybersecurity breach or other security incident relating to our information systems or data, the costs, time and effort associated with the investigation, remediation and potential notification of the breach to counterparties, regulators and data subjects could be material. We may incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security incident. In addition, techniques used to sabotage or to obtain unauthorized access to networks in which data is stored or through which data is transmitted change frequently, become more complex over time and generally are not recognized until launched against a target. The risk of a security breach or disruption, particularly through cyberattacks including supply chain attacks such as SolarWinds or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. As a result, we and our third-party vendors may be unable to anticipate these techniques or implement adequate preventative measures quickly enough to prevent either an electronic intrusion into our systems or services or a compromise of critical information. We cannot guarantee that we will be able to detect or prevent any such incidents, and, our remediation efforts may not be successful or timely. Our efforts to improve security and protect data from compromise may also identify previously undiscovered instances of data breaches or other cybersecurity incidents. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary, personal or confidential information. Additionally, we do not currently maintain cybersecurity insurance, and any insurance we may maintain in the future against the risk of this type of loss in the future may not be sufficient to cover actual losses, or may not apply to the circumstances relating to any particular loss.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our third-party vendors', collaborators', contractors', consultants' or other third parties' data, including personal data, or applications or inappropriate disclosure, loss, destruction or alteration of, or access to, confidential, personal or proprietary information, we could incur significant liability including litigation exposure, substantial penalties and fines, we could become the subject of regulatory action, inquiry or investigation, our competitive position could be harmed, we could incur significant reputational damage and the further development and commercialization of any product candidates we may develop could be delayed. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates we may identify outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Similarly, the U.K. Bribery Act 2010 has extra-territorial effect for companies and individuals having a connection with the United Kingdom. The U.K. Bribery Act prohibits inducements both to public officials and private individuals and organizations. Compliance with the FCPA and the U.K. Bribery Act is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to stringent and often unsettled laws, rules, regulations, policies, standards and contractual obligations related to data privacy and security and changes in such laws, rules, regulations, policies, standards and contractual obligations could adversely affect our business.

We are subject to data privacy and protection laws, rules, regulations, policies, standards and contractual obligations that apply to the collection, transmission, storage, use, disclosure, transfer, maintenance and other

processing of sensitive, personal and personally-identifying information, which, among other things, impose certain requirements relating to the privacy, security, transmission and other processing of personal information, including comprehensive regulatory systems in the United States and European Union. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. However, our data privacy program is in its early stages and we have not yet assessed the applicability of and our compliance with data privacy-related laws, rules and regulations. As a result, we cannot guarantee that we are and have been in compliance with all applicable data privacy and protection laws, rules regulations, policies and standards, and we may need to expend significant resources to implement privacy compliance measures. Additionally, we rely on certain third-party vendors to process certain confidential, sensitive or personal information on our behalf. Failure by us or our third-party vendors to comply with any of these laws, rules, regulations, contractual obligations or standards could result in notification obligations, enforcement actions, regulatory investigations or inquiries, significant fines, imprisonment of company officials and public censure, litigation and claims for damages by affected individuals, customers or business partners, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws, rules and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. The Genetic Information Nondiscrimination Act of 2008 ("GINA"), which clarified that genetic information is protected under HIPAA and restricts the use and disclosure of genetic information.

Additionally, laws in all 50 states require businesses to provide notice to customers whose personally identifiable information has been disclosed as a result of a data breach. These laws are not consistent, and compliance in the event of a widespread data breach is difficult and may be costly. Moreover, states have been frequently amending existing laws, requiring attention to changing regulatory requirements. We also may be contractually required to notify patients or other counterparties of a security breach. Although we may have contractual protections with our service providers, any actual or perceived security breach could harm our reputation and brand, expose us to potential liability or require us to expend significant resources on data security and in responding to any such actual or perceived breach. Any contractual protections we may have from our service providers may not be sufficient to adequately protect us from any such liabilities and losses, and we may be unable to enforce any such contractual protections. In addition to government regulation, privacy advocates and industry groups have and may in the future propose self-regulatory standards from time to time. These and other industry standards may legally or contractually apply to us, or we may elect to comply with such standards. Determining whether personal information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation.

If we are unable to properly protect the privacy and security of personal information, we could be alleged or actually found to have breached our contracts. Furthermore, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face significant administrative, civil and criminal penalties. HHS has the discretion to impose penalties without attempting to resolve violations through informal means, and such enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that

threaten the privacy or security of the personal information of state residents. We cannot be sure how these laws, rules and regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws, rules and regulations at the international, federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

We make public statements about our use, collection, disclosure and other processing of personal information through our privacy policies and information provided on our website. Although we endeavor to comply with our public statements and documentation, we may at times fail to do so or be alleged to have failed to do so. The publication of our privacy policies and other statements that provide promises and assurances about data privacy and security can subject us to potential government or legal action if they are found to be deceptive, unfair or misrepresentative of our actual practices.

Data privacy remains an evolving landscape at both the domestic and international level, with new laws, rules and regulations coming into effect and continued legal challenges. For example, California enacted the California Consumer Privacy Act of 2018 ("CCPA"), which went into effect on January 1, 2020 and, among other things, requires companies that process information on California residents to make new disclosures to consumers about their data collection, use and sharing practices, allow consumers to opt out of certain data sharing with third parties and provide a new cause of action for data breaches. Additionally, California voters approved the California Privacy Rights Act ("CPRA"), which went into effect on January 1, 2023. The CPRA significantly modifies the CCPA, including by introducing additional obligations such as data minimization and storage limitations and granting additional rights to California residents such as correction of personal information and additional opt-out rights. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The enactment of the CCPA is prompting a wave of similar legislative developments in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. For example, at least four such state laws (in Virginia, Colorado, Connecticut and Utah) have taken effect, or are scheduled to take effect in 2023. Certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to confidential, sensitive and personal information than federal, international or other state laws, and such laws may differ from each other, which may complicate compliance efforts.

Our efforts to comply with the evolving data protection laws, rules and regulations may be unsuccessful. It is possible that these laws, rules and regulations may be interpreted and applied in a manner that is inconsistent with our practices and our efforts to comply with the evolving data protection rules may be unsuccessful. The laws are not consistent, and compliance in the event of a widespread data breach is costly and time-consuming. States are also frequently amending existing laws, requiring attention to frequently changing regulatory requirements. We must devote significant resources to understanding and complying with this changing landscape. Failure by us or our third-party vendors to comply with laws, rules and regulations regarding data privacy and protection would expose us to risk of enforcement actions taken by data protection authorities and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws, rules and regulations in the United States regarding privacy and security of personal information could expose us to penalties under such laws, rules and regulations. Any such failure by us or our third-party vendors to comply with data protection and privacy laws, rules and regulations could result in significant government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, rules or regulations, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

Risks Related to Third Party Relationships

If conflicts arise between us and our collaborators or strategic partners, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.

If conflicts arise between our collaborators and corporate or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Some of our collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the product candidates we may develop that are the subject of these collaborations with us. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for any product candidates we may develop.

Additionally, some of our collaborators or strategic partners could also become our competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, prevent us from obtaining timely regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the collaboration efforts, including development, delivery, manufacturing and commercialization of products. Any of these developments could harm our company and product development efforts.

We have entered into collaborations, and may enter into additional collaborations, with third parties for the research, development, manufacture and commercialization of programs or product candidates. If these collaborations are not successful, our business could be adversely affected.

As part of our strategy, we have entered into collaborations and intend to seek to enter into additional collaborations with third parties for one or more of our programs or product candidates we may develop. For example, in October 2021, we entered into a Strategic Collaboration and License Agreement with ModernaTX, Inc. ("Moderna"), focused on advancing new genome editing system for *in vivo* human therapeutic applications, in June 2022, we entered into a Development, Option and License Agreement with Affini-T Therapeutics, Inc. ("Affini-T") to develop and commercialize gene edited T-cell receptor ("TCR")-based therapeutic products exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with any engineered primary TCR alpha/beta T cells and non-exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with certain other engineered immune cells worldwide, and in November 2022, we entered into a Collaboration and License Agreement with Ionis Pharmaceuticals, Inc. ("Ionis") to research, develop and commercialize investigational medicines using genome editing technologies. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We have under these agreements, and we may have under any other arrangements that we may enter into with any third parties, limited control over the amount and timing of resources that collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements may depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations that we enter into may not be successful, and any success will depend heavily on the efforts and activities of such collaborators. Collaborations pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;

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- collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may not pursue commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;
- collaborators may delay preclinical studies and clinical trials, provide insufficient funding for a preclinical study or clinical trial program, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new preclinical studies or clinical trials or require a new formulation of a product candidate for preclinical or clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates on a discretionary basis;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership of intellectual property or other rights developed pursuant to our collaborations;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and

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- collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If any current or future collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus also apply to the activities of our collaborators.

Collaboration agreements may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. For more information, see the section titled "Business—Our License and Collaboration Agreements."

We could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

We may also be restricted under existing collaboration agreements from entering into future collaboration agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators, which further increases competition we face in seeking potential collaborations.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

Our collaborators and strategic partners may control aspects of our clinical trials, which could result in delays and other obstacles in the commercialization of our proposed products and materially harm our results of operations.

For some programs, we will depend on third party collaborators and strategic partners to design and conduct our clinical trials. As a result, we may not be able to conduct these programs in the manner or on the time schedule we currently contemplate, which may negatively impact our business operations. In addition, if any of these collaborators or strategic partners withdraw support for our programs or proposed products or otherwise impair their development, our business could be negatively affected.

In October 2021, we entered into a Strategic Collaboration and License Agreement with Moderna focused on advancing new genome editing system for *in vivo* human therapeutic applications, in June 2022, we entered into a Development, Option and License Agreement with Affini-T to develop and commercialize gene edited TCR-based therapeutic products exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with any engineered primary TCR alpha/beta T cells and non-exclusively in the field of

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treatment, prevention or diagnosis of any human cancer using products with certain other engineered immune cells worldwide, and in November 2022, we entered into a Collaboration and License Agreement with Ionis to research, develop and commercialize investigational medicines for up to eight potential genetic targets using genome editing technologies. Our lack of control over the clinical development in our agreements with Moderna, Affini-T and Ionis could cause delays or other difficulties in the development and commercialization of product candidates, which may prevent completion of intended IND applications in a timely fashion, if at all.

In addition, the termination of these agreements would prevent us from receiving any milestone, royalty payments and other benefits under that agreement, which would have a materially adverse effect on our results of operations.

Our collaborators or strategic partners may decide to adopt alternative technologies or may be unable to develop commercially viable products with our technology, which would negatively impact our revenues and our strategy to develop these products.

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of our genome editing technology. Additionally, because our current or future collaborators or strategic partners are likely to be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our genome editing technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators would prevent us from receiving future milestone and royalty payments which would negatively impact our revenues.

We expect to rely on third parties to conduct our clinical trials and some aspects of our research, as well as some aspects of our delivery methods, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We expect to rely on third parties, such as CROs, clinical data management organizations, medical institutions, preclinical laboratories and clinical investigators, to conduct some aspects of our research. For example, we may rely on a third party to supply LNPs or AAVs, or to conduct our preclinical animal experiments. Any of these third parties may terminate their engagements with us at any time under certain criteria. If we need to enter into alternative arrangements, it may delay our product development activities.

Our reliance on these third parties for clinical research and other development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA, the EMA and other regulatory authorities require us and the study sites and investigators we work with to comply with standards, commonly referred to as GLPs and GCPs for conducting, recording and reporting the results of preclinical studies and clinical trials to assure, amongst other things, that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. In the United States, we also are required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we intend to design the preclinical studies and clinical trials for our potential product candidates, CROs will conduct some or all of the preclinical studies and clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third

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parties to conduct preclinical studies and future clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Among other reasons that may delay or impact the development of our potential product candidates, outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs and other third parties do not perform such preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our potential product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our potential product candidates or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs and other third parties, we could be required to repeat, extend the duration of or increase the size of any preclinical studies or clinical trials we conduct and this could significantly delay commercialization and require greater expenditures.

We may also expect to rely on other third parties to store and distribute drug supplies for our future clinical trials. Any performance failure on the part of our distributors could delay clinical development or regulatory approval of any product candidates we may develop or commercialization of our therapies, producing additional losses and depriving us of potential product revenue.

Manufacturing biologic products is complex and subject to product loss for a variety of reasons. We contract with third parties for the manufacture of certain materials for our development programs and expect to continue to do so for clinical trials and commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our future product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We operate and are expanding our cGMP manufacturing facility which is currently capable of manufacturing clinical grade nucleases and mRNA to supply both wholly-owned and collaboration programs. We also partner with CMOs for guide RNA ("gRNA") and DNA template development and supply. We also rely, and expect to continue to rely, on third parties for gRNA and DNA template development and supply, as well as for preclinical and clinical testing and commercial manufacture if any of our product candidates receive regulatory approval. We also expect to rely on these third parties for certain logistics, including packaging, labeling, storage, and distribution. This reliance on third parties increases the risk that we will not have sufficient quantities of our materials or future product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;

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- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

We or our third-party manufacturers may encounter shortages in the raw materials or active pharmaceutical ingredients necessary to produce our future product candidates in the quantities needed for our preclinical studies or clinical trials or, if our future product candidates are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or active pharmaceutical ingredients, including shortages caused by the purchase of such raw materials or active pharmaceutical ingredient by our competitors or others. The failure of us or our third-party manufacturers to obtain the raw materials or active pharmaceutical ingredients necessary to manufacture sufficient quantities of our future product candidates may have a material adverse effect on our business.

Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. We, along with our third-party manufacturers, are subject to inspection and approval by regulatory authorities before we can commence the manufacture and sale of any of our future product candidates, and thereafter subject to ongoing inspection from time to time. We or our third-party manufacturers may not be able to comply with cGMP or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in regulatory actions, such as the issuance of FDA Form 483 notices of observations, warning letters or sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Manufacturing biologic products, such as the product candidates we intend to develop, is complex, especially in large quantities. Biologic products must be made consistently and in compliance with a clearly defined manufacturing process. Accordingly, it is essential to be able to validate and control the manufacturing process to assure that it is reproducible. Any product candidates and products that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or regulatory approval. We do not currently have arrangements in place for redundant supply or a source for bulk drug substance nor do we have any agreements with third-party manufacturers for long-term commercial supply. If any of our contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture materials or future product candidates or products we may develop, we may incur added costs and delays in identifying and qualifying any such replacement or be unable to reach agreement with an alternative manufacturer. If we are required to change third party-manufacturers for any reason, we will be required to verify that the new third party-manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our materials or future product candidates or products according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new third party-manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a third party-manufacturer may possess technology related to the manufacture of

our materials or future product candidates or products that such third party-manufacturer owns independently. This would increase our reliance on such third party-manufacturer or require us to obtain a license from such third party-manufacturer in order to have another third party-manufacturer manufacture our materials or future product candidates or products, which may not be available on commercially reasonable terms, or at all. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

Our current and anticipated future dependence upon others for the manufacture of materials and any future product candidates or products we may develop may adversely affect our future profit margins and our ability to commercialize any products that receive regulatory approval on a timely and competitive basis.

Our relationships with healthcare providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, anti-bribery and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.

Our relationships with healthcare providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, anti-bribery and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.

Healthcare providers, including physicians, and third-party payors play a primary role in the recommendation and prescription of any product candidates that we may develop for which we obtain regulatory approval and marketing approval. Our current and future arrangements with third-party payors, healthcare providers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our products for which we obtain regulatory approval. Restrictions under applicable federal and state healthcare laws and regulations, including certain laws and regulations applicable only if we have marketed products, include the following:

- the civil FCA, prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the FCA may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the FCA can result in very significant monetary penalties, for each false claim and treble the amount of the government's damages. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims;
- the federal Anti-Kickback Statute prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. A violation of the federal Anti-Kickback Statute can also form the basis for FCA liability;
- HIPAA, which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

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- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and its implementing regulations, including the final omnibus rule published on January 25, 2013, imposes, among other things, certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain, transmit, or obtain, protected health information in connection with providing a service for or on behalf of a covered entity, and their covered subcontractors. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions;
- the FDCA, which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;
- federal transparency laws, including the federal Physician Payment Sunshine Act created under the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), and its implementing regulations, which requires manufacturers of certain drugs, devices, medical supplies, and biologics, among others, to track and disclose payments under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) and other transfers of value they make to U.S. physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. This information is subsequently made publicly available in a searchable format on a Centers for Medicare & Medicaid Services ("CMS") website. Failure to disclose required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians and/or other healthcare providers; and
- analogous state and foreign laws and regulations, such as state anti-kickback, anti-bribery and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws also require pharmaceutical companies to comply with specific compliance standards, restrict financial interactions between pharmaceutical companies and healthcare providers or require pharmaceutical companies to report information related to payments to healthcare providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices may not comply with healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to significant penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government healthcare programs, such as

Medicare and Medicaid, individual imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to also induce or reward improper performance generally is governed by the national anti-bribery laws of European Union Member States, and the Bribery Act 2010 in the United Kingdom. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the United Kingdom despite its departure from the EU.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Risks Related to Personnel, Operations, and Growth

Our future success depends on our ability to retain our Chief Executive Officer and other key executives and to attract, retain, and motivate qualified personnel.

We are highly dependent on Brian C. Thomas, our Chief Executive Officer as well as the other principal members of our management and scientific teams. Dr. Thomas and such other principal members are engaged "at will," meaning we or they may terminate the relationship at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. For us to successfully compete and grow, we must recruit, retain, and develop talent who can provide the necessary expertise across a broad spectrum of disciplines. In addition, we must develop, maintain and, as necessary, implement appropriate succession plans to ensure we have the necessary human capital capable of maintaining continuity in our business.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. In addition, our company-building efforts and establishment of a company culture will also be important to developing an innovative company in a high-evolving area. We may not be able to succeed in these efforts to build Metagenomi as an attractive and exciting place to build a career or to attract and retain these types of personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. We may also encounter problems hiring and retaining the

experienced scientific, quality control and manufacturing personnel needed to manage our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. The inability to recruit, or loss of services of, certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations and prospects.

We expect to expand our research, development, delivery, manufacturing, commercialization, regulatory, and future sales and marketing capabilities over time, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We may fail to manage our growth effectively. As of September 30, 2023, we had 223 full-time employees, of which 74 have M.D. or Ph.D. degrees. Within our workforce, 187 employees are engaged in research and development and 36 are engaged in business development, finance, legal, and general management and administration. In connection with the growth and advancement of our pipeline and becoming a public company, we expect to increase the number of our employees and the scope of our operations, particularly in the areas of research and clinical development, regulatory affairs and, if any of our future product candidates receive regulatory approval, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

As a growing biotechnology company, we are actively developing our platform technology and pursuing development of future product candidates in many therapeutic areas and across a wide range of diseases. Successfully developing product candidates for and fully understanding the regulatory and manufacturing pathways to all of these therapeutic areas and disease states requires a significant depth of talent, resources and corporate processes in order to allow simultaneous execution across multiple areas. We will need to transition from a company with a research focus to a company capable of conducting clinical trials and ultimately supporting commercial activities if any of our product candidates are approved. We may not be successful in such a transition. Due to our limited resources, we may not be able to effectively manage this simultaneous execution and the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, legal or regulatory compliance failures, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our potential product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to compete effectively and commercialize any product candidates we may develop will depend in part on our ability to effectively manage the future development and expansion of our company, and may prevent us from achieving or maintaining profitability. We cannot assure you that we will be able to compete effectively in the future against existing or new competitors, and our failure to do so could harm our business, financial condition, and results of operations.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved, or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for biologics or modifications to approved biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business.

Risks Related to Our Intellectual Property

Our commercial success depends on our ability to obtain, maintain, enforce, and otherwise protect our intellectual property and proprietary technology, and if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products and product candidates similar to ours and our ability to successfully develop and commercialize our genome editing systems may be adversely affected.

Our commercial success depends, in large part, on our ability to obtain and maintain intellectual property rights protection through patents, trademarks, and trade secrets in the United States and other countries with respect to our proprietary genome editing systems. If we do not adequately protect our intellectual property rights, competitors or other third parties may be able to erode, negate or preempt any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we have filed patent applications and may file other patent applications in the United States or abroad related to our genome editing systems that are important to our business; we may also license or purchase patents or patent applications filed by others. The patent application process is expensive, time-consuming and complex. We may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner.

We may not be able to obtain patents on certain inventions if those inventions are publicly disclosed prior to our filing a patent application covering them. We enter into nondisclosure and confidentiality agreements with parties who have access to confidential information, including confidential information regarding inventions not yet disclosed in patent applications. We cannot guarantee that any of these parties will not breach these confidentiality agreements and publicly disclose any of our inventions before a patent application is filed covering such inventions. If such confidential information is publicly disclosed, we may not be able to successfully patent it and consequently, we may not be able to prevent third parties from using such inventions.

If the scope of the patent protection we obtain is not sufficiently broad, we may not be able to prevent others from developing and commercializing technology and products similar or identical to ours. The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of our pending owned patent applications that mature into issued patents will include claims with a scope sufficient to protect our proprietary genome editing systems or otherwise provide any competitive advantage. Other parties have developed or may develop technologies that may be related or competitive with our approach, and may have

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filed or may file patent applications and may have been issued or may be issued patents with claims that overlap or conflict with our patent portfolio, either by claiming the same compounds, formulations or methods or by claiming subject matter that could dominate our patent position. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new genome editing systems, patents protecting such genome editing systems might expire before or shortly after such genome editing systems are commercialized. As a result, our patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar or identical to ours.

Even if they are unchallenged, our owned patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our patent portfolio by developing similar or alternative genome editing systems in a non-infringing manner. For example, a third party may develop a genome editing system that provides benefits similar to our genome editing systems but falls outside the scope of our patent protection or license rights. If the patent protection provided by the patent and patent applications we hold or pursue with respect to our genome editing systems is not sufficiently broad to impede such competition, our ability to successfully commercialize our product genome editing systems could be negatively affected, which would harm our business.

We, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position.

It is possible that defects of form in the preparation or filing of our patent portfolio may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, or licensees whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patent portfolio, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the U.S. Patent and Trademark Office ("USPTO") and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and patent applications. We rely on our outside counsel or our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent position of biotechnology and pharmaceutical companies carries uncertainty. In addition, the determination of patent rights with respect to genome editing technologies commonly involves complex legal and factual questions, which are dependent upon the current legal and intellectual property context, extant legal precedent and interpretations of the law by individuals. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are characterized by uncertainty.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for

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patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patent portfolio, or that we were the first to file for patent protection of such inventions. If third parties have filed prior patent applications on inventions claimed in our patent portfolio that were filed on or before March 15, 2013, an interference proceeding in the United States can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by our patent portfolio. If third parties have filed such prior applications after March 15, 2013, a derivation proceeding in the United States can be initiated by such third parties to determine whether our invention was derived from theirs.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents may be challenged in the courts or patent offices in the United States and abroad. There is no assurance that all the potentially relevant prior art relating to our patent portfolio has been found. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patent portfolio, or that we were the first to file for patent protection of such inventions. If such prior art exists, it may be used to invalidate a patent, or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party submission of prior art to the USPTO, or to other patent offices around the world. Alternately or additionally, we may become involved in post-grant review procedures, oppositions, derivation proceedings, ex parte reexaminations, inter partes review, supplemental examinations, or interference proceedings or challenges before the USPTO or in district court in the United States, or similar proceedings in various foreign jurisdictions, including both national and regional, challenging patents or patent applications in which we have rights, including patents on which we rely to protect our business. An adverse determination in any such challenges may result in loss of the patent or claims in the patent portfolio being narrowed, invalidated or held unenforceable, in whole or in part, or in denial of the patent application or loss or reduction in the scope of one or more claims of the patent portfolio, any of which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products.

Pending and future patent applications may not result in patents being issued that protect our business, in whole or in part, or which effectively prevent others from commercializing competitive products. Competitors may also be able to design around our patents. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, patent laws in various jurisdictions, including jurisdiction covering significant commercial markets, such as the European Patent Office, China, and Japan, restrict the patentability of methods of treatment of the human body more than United States law does. If these developments were to occur, they could have a material adverse effect on our ability to generate revenue.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our genome editing systems by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance, whether intentional or not, can result in abandonment or lapse of a patent or patent

- application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
 - Company-owned or in-licensed patents that have been issued or may be issued in the future may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
 - our competitors, many of whom have substantially greater resources and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell our genome editing systems;
 - there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
 - countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing products; and
 - countries other than the U.S. may, under certain circumstances, force us to grant a license under our patents to a competitor, thus allowing the competitor to compete with us in that jurisdiction or forcing us to lower the price of our drug in that jurisdiction.

Issued patents that we have or may obtain or license may not provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors do not infringe our patents. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

We maintain certain information as company trade secrets. This information may relate to inventions that are not patentable or not optimally protected with patents. We use commercially acceptable practices to protect this information, including, for example, limiting access to the information and requiring passwords for our computers. Additionally, we execute confidentiality agreements with any third parties to whom we may provide access to the information and with our employees, consultants, scientific advisors, collaborators, vendors, contractors, and advisors. We cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. It is possible that technology relevant to our business will be independently developed by a person who is not a party to such a confidentiality or invention assignment agreement. If any of our trade secrets were to be independently developed by a competitor or other third party, we would have no right to prevent such competitor or third party, or those to whom they communicate such independently developed information, from using that information to compete with us. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by contract manufacturers, consultants, collaborators, vendors, advisors, former employees and current employees. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Furthermore, if the parties to our confidentiality agreements

breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a consequence of such breaches or violations. Our trade secrets could otherwise become known or be independently discovered by our competitors. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets, our business, financial condition, results of operation and prospects may be materially and adversely harmed.

It is difficult and costly to protect our intellectual property and our proprietary technologies, and we may not be able to ensure their protection.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for our proprietary genome editing systems, as well as on successfully defending these patents against potential third-party challenges. Our ability to protect our genome editing systems from unauthorized making, using, selling, offering to sell or importing by third parties is dependent on the extent to which we have rights under valid and enforceable patents that cover these activities.

The patent positions of pharmaceutical, biotechnology and other life sciences companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved and have in recent years been the subject of much litigation. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Over the past decade, U.S. federal courts have increasingly invalidated pharmaceutical and biotechnology patents during litigation often based on changing interpretations of patent law. Further, the determination that a patent application or patent claim meets all the requirements for patentability is a subjective determination based on the application of law and jurisprudence. The ultimate determination by the USPTO or by a court or other trier of fact in the United States, or corresponding foreign national patent offices or courts, on whether a claim meets all requirements of patentability cannot be assured. Although we have conducted searches for third-party publications, patents and other information that may affect the patentability of claims in our patent portfolio, we cannot be certain that all relevant information has been identified. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our own patent portfolio.

We cannot provide assurances that any of our patent applications will be found to be patentable, including over our own prior art publications or patent literature, or will issue as patents. Neither can we make assurances as to the scope of any claims that may issue from our pending and future patent applications nor to the outcome of any proceedings by any potential third parties that could challenge the patentability, validity or enforceability of our patent portfolio in the United States or foreign jurisdictions. Any such challenge, if successful, could limit patent protection for our genome editing systems and/or materially harm our business.

In addition to challenges during litigation, third parties can challenge the validity of our patents in the United States using post-grant review and inter partes review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent filed March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. A petition for inter partes review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of invalidity, whereas inter partes review proceedings can only raise an invalidity challenge based on published prior art and patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally

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considered easier for a competitor or third party to have a U.S. patent invalidated in a USPTO post-grant review or inter partes review proceeding than invalidated in a litigation in a U.S. federal court. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we will be successful in defending the patent, which may result in a loss of the challenged patent right to us.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we may not be able to generate sufficient data to support full patent applications that protect the entire breadth of developments in one or more of our programs;
- it is possible that one or more of our pending patent applications will not become an issued patent or, if issued, that the patent(s) claims will have sufficient scope to protect our technology, provide us with commercially viable patent protection or provide us with any competitive advantages;
- if our pending applications issue as patents, they may be challenged by third parties as invalid or unenforceable under United States or foreign laws;
- we may not successfully commercialize our genome editing systems, if approved, before our relevant patents expire;
- we may not be the first to make the inventions covered by our patent portfolio; or
- we may not develop additional proprietary technologies or genome editing systems that are separately patentable.

In addition, to the extent that we are unable to obtain and maintain patent protection for our genome editing systems, or in the event that such patent protection expires, it may no longer be cost-effective to extend our portfolio by pursuing additional development of any of our genome editing systems for follow-on indications.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. The patent term of a U.S. patent may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new genome editing systems, patents protecting such genome editing systems might expire before or shortly after such genome editing systems are commercialized.

In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a Patent Term Extension (“PTE”) of up to five years beyond the normal expiration of the patent to compensate patent owners for loss of enforceable patent term due to the lengthy regulatory approval process. A PTE grant cannot extend the remaining term of a patent beyond a total of 14 years from the date of the product approval. Further, PTE may only be applied once per product, and only with respect to an approved indication—in other words, only one patent (for example, covering the product itself, an approved use of said product, or a method of manufacturing said product) can be extended by PTE. We anticipate applying for PTE in the United States. Similar extensions may be available in other countries where we are prosecuting patents and we likewise anticipate applying for such extensions.

The granting of such patent term extensions is not guaranteed and is subject to numerous requirements. We might not be granted an extension because of, for example, failure to apply within applicable periods, failure to apply prior to the expiration of relevant patents or otherwise failure to satisfy any of the numerous applicable requirements. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. Moreover, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to obtain approval of competing products following our patent expiration by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have a material adverse effect on our ability to generate revenue.

Changes in the interpretation of patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

The United States Congress is responsible for passing laws establishing patentability standards. As with any laws, implementation is left to federal agencies and the federal courts based on their interpretations of the laws. Interpretation of patent standards can vary significantly within the USPTO, and across the various federal courts, including the U.S. Supreme Court. Recently, the Supreme Court has ruled on several patent cases, generally limiting the types of inventions that can be patented. Further, there are open questions regarding interpretation of patentability standards that the Supreme Court has yet to decisively address. Absent clear guidance from the Supreme Court, the USPTO has become increasingly conservative in its interpretation of patent laws and standards.

In addition to increasing uncertainty with regard to our ability to obtain patents in the future, the legal landscape in the U.S. has created uncertainty with respect to the value of patents. Depending on any actions by Congress, and future decisions by the lower federal courts and the U.S. Supreme Court, along with interpretations by the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

The U.S. Supreme Court has ruled on several patent cases in recent years; these cases often narrow the scope of patent protection available to inventions in the biotechnology and pharmaceutical spaces. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc.* ("*Myriad*"), the Supreme Court ruled that a "naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," and invalidated Myriad Genetics' claims on the isolated BRCA1 and BRCA2 genes. Certain claims of our patent portfolio relate to genome editing systems. While we believe that our proprietary genome editing systems involve significant human intervention, components of the system, such as the isolated nucleases with no modifications, are derived from naturally-occurring products. To the extent that such claims are deemed to be directed to natural products, or to lack an inventive concept above and beyond an isolated natural product, a court may decide the claims are directed to patent-ineligible subject matter and are invalid. The application of *Myriad* to biotechnology inventions has continued to develop and may continue to change over time. Subsequent rulings in cases or guidance or procedures issued by the USPTO relating to patent eligibility may have a negative impact on our business.

In *Amgen Inc. v. Sanofi* ("*Amgen*"), the U.S. Supreme Court held that certain of Amgen's patent claims defined a class of antibodies by their function of binding to a particular antigen. The U.S. Supreme Court further wrote that because the patent claims defined the claimed class of antibodies only by their function of binding to a particular antigen, a skilled artisan would have to use significant trial and error to identify and make all of the molecules in that class. The U.S. Supreme Court ultimately held that Amgen failed to properly enable its patent

claims. Certain claims of our patent portfolio relate to broad classes of gene editors. To the extent that a court finds that the skilled artisan would need significant trial and error to identify all the gene editors in that class, the court may find the claims invalid under *Amgen*. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Further, a new court system recently became operational in the European Union. The Unified Patent Court ("UPC") began accepting patent cases on June 1, 2023. The UPC is a common patent court with jurisdiction over patent infringement and revocation proceedings effective for multiple member states of the European Union. The broad geographic reach of the UPC could enable third parties to seek revocation of any of our European patents in a single proceeding at the UPC rather than through multiple proceedings in each of the individual European Union member states in which the European patent is validated. Under the UPC, a successful revocation proceeding for a European Patent under the UPC would result in loss of patent protection in those European Union countries. Accordingly, a single proceeding under the UPC could result in the partial or complete loss of patent protection in numerous European Union countries. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations. Moreover, the controlling laws and regulations of the UPC will develop over time and we cannot predict what the outcomes of cases tried before the UPC will be. The case law of the UPC may adversely affect our ability to enforce or defend the validity of our European patents. Patent owners have the option to opt-out their European Patents from the jurisdiction of the UPC, defaulting to pre-UPC enforcement mechanisms. We have decided to opt out certain European patents and patent applications from the UPC. However, if certain formalities and requirements are not met, our European patents and patent applications could be subject to the jurisdiction of the UPC. We cannot be certain that our European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC.

We may not be able to seek or obtain patent protection throughout the world or enforce such patent protection once obtained.

Filing, prosecuting, enforcing, and defending patents protecting our genome editing systems in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe or from selling or importing products made from our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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Proceedings to enforce our patent rights, whether successful or not, could result in substantial costs and divert our efforts and resources from other aspects of our business. Further, such proceedings could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly; put our pending patent applications at risk of not issuing; and provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products, if approved. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

In order to protect our competitive position around our future product candidates, we may become involved in lawsuits to enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful and which may result in our patents being found invalid or unenforceable.

Competitors may seek to commercialize competitive products to our genome editing systems. In order to protect our competitive position, we may become involved in lawsuits asserting infringement of our patents, or misappropriation or other violations of other of our intellectual property rights. Litigation is expensive and time consuming and would likely divert the time and attention of our management and scientific personnel. There can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

If we file a patent infringement lawsuit against a perceived infringer, such a lawsuit could provoke the defendant to counterclaim that we infringe their patents and/or that our patents are invalid and/or unenforceable. In patent litigation in the United States, it is commonplace for a defendant to counterclaim alleging invalidity and/or unenforceability. In any patent litigation there is a risk that a court will decide that the asserted patents are invalid or unenforceable, in whole or in part, and that we do not have the right to stop the defendant from using the invention at issue. With respect to a counterclaim of invalidity, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. If any of our patents are found invalid or unenforceable, or construed narrowly, our ability to stop the other party from launching a competitive product would be materially impaired. Further, such adverse outcomes could limit our ability to assert those patents against future competitors. Loss of patent protection would have a material adverse impact on our business.

Even if we establish infringement of any of our patents by a competitive product, a court may decide not to grant an injunction against further infringing activity, thus allowing the competitive product to continue to be marketed by the competitor. It is difficult to obtain an injunction in U.S. litigation and a court could decide that the competitor should instead pay us a "reasonable royalty" as determined by the court, and/or other monetary damages. A reasonable royalty or other monetary damages may or may not be an adequate remedy. Loss of exclusivity and/or competition from a related product would have a material adverse impact on our business.

Litigation often involves significant amounts of public disclosures. Such disclosures could have a materially adverse impact on our competitive position or our stock prices. During any litigation we would be required to produce voluminous records related to our patents and our research and development activities in a process called discovery. The discovery process may result in the disclosure of some of our confidential information. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the price of our common shares.

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Litigation is inherently expensive, and the outcome is often uncertain. Any litigation likely would substantially increase our operating losses and reduce our resources available for development activities. Further, we may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. As a result, we may conclude that even if a competitor is infringing any of our patents, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

If in the future, we in-license any patent rights, we may not have the right to file a lawsuit for infringement and may have to rely on a licensor to enforce these rights for us. If we are not able to directly assert our licensed patent rights against infringers or if a licensor does not vigorously prosecute any infringement claims on our behalf, we may have difficulty competing in certain markets where such potential infringers conduct their business, and our commercialization efforts may suffer as a result.

Concurrently with an infringement litigation, third parties may also be able to challenge the validity of our patents before administrative bodies in the United States or abroad. Such mechanisms include re-examination, post grant review and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our products, potentially negatively impacting any concurrent litigation.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our genome editing systems.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our genome editing systems without infringing, misappropriating or otherwise violating the intellectual property and other proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe, misappropriate or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds, methods of manufacturing compounds and/or methods of use for the treatment of the disease indications for which we are developing our genome editing systems. If any third-party patents or patent applications are found to cover our genome editing systems, or their methods of use or manufacture, we may not be free to manufacture or market such genome editing systems as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our genome editing systems, including patent infringement lawsuits in the U.S. or abroad. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the composition, use or manufacture of our genome editing systems. Third parties may assert infringement claims against us based on existing patents that they own or in-license or patents that may grant to them (or which they may in-license) in the future, regardless of the merit of such patents or infringement claims. If our defenses to such assertions of infringement were unsuccessful, we could be liable for a court-determined reasonable royalty on our existing sales and further damages to the patent owner (or licensee), such as lost profits. Such royalties and damages could be significant. If we are found to have willfully infringed the claims of a third party's patent, the third party could be awarded treble damages and attorney's fees. Further, unless we obtain a license to such patent, we may be precluded from commercializing the infringing genome editing system. Any of the aforementioned could have a material adverse effect on our business, financial condition, results of operations and prospects.

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While we perform periodic searches for relevant patents and patent applications with respect to our genome editing systems, including Cas proteins and therapeutic applications, we cannot guarantee the completeness or thoroughness of any of our patent searches or analyses including, but not limited to, the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, nor can we be certain that we have identified each and every patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of any of our genome editing systems in any jurisdiction. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that any of our genome editing systems may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on intellectual property rights that exist now or arise in the future. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use or manufacture. The scope of protection afforded by a patent is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that the relevant product or methods of using the product either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources, and we may not have sufficient resources to bring these actions to a successful conclusion.

Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing genome editing systems. Our genome editing systems make use of CRISPR-based technology, which is a field that is highly active for patent filings and complex litigation. As of June 2019, it was reported that approximately 2072 patent families worldwide related to CRISPR genome editing inventions and their uses. That number has continued to increase. The extensive patent filings related to CRISPR make it difficult for us to assess the full extent of relevant patents and pending applications that may cover our genome editing systems and their use or manufacture. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our genome editing systems. We are aware of multiple patents and patent applications directed to CRISPR technologies, Cas molecules, and their uses in genome editing. For example, we are aware of patent portfolios related to CRISPR/Cas genome editing systems that are owned or co-owned by Sigma Aldrich, Stanford University and Agilent Technologies, the Broad Institute and/or Harvard University and/or the Massachusetts Institute of Technology ("MIT"), and Targetgene Biotechnologies. We are also aware of patent portfolios related to base editing systems that are owned or co-owned by Beam Therapeutics, the Broad Institute and/or Harvard University and/or MIT, the University of California, Duke University, Kobe University, the Max Planck Institute, Wageningen University, and Bioray Laboratories. We are also aware of patent portfolios related to CRISPR associated transposase/retro-transposase ("CAST") systems that are owned or co-owned by the Broad Institute, Arbor Biotechnologies, and the University of Rochester.

Intellectual property litigation is common in the biotechnology space and multiple parties have engaged in litigation to protect and enforce their CRISPR/Cas related patent estates. For example, patents and patent applications directed to catalytically-active Cas9 systems have been the subject of extensive adversarial patent office proceedings. These proceedings include U.S. Patent and Trademark Office Patent Trial and Appeal Board

("PTAB") proceedings involving the Broad Institute and the University of California regarding the priority of inventions with respect to certain U.S. patents and patent applications each owns directed to catalytically-active Cas9. Our genome editing technologies do not use catalytically-active Cas9 and we are not aware of any third-party patents or patent applications that we believe cover our Cas-related genome editing system and proprietary technology. However, we may not have identified all relevant third-party patents and patent applications. Therefore, there can be no assurance that third parties will not assert patents against us in the future or that our patents and patent applications will not be challenged. Any litigation brought against us or our patents or patent applications, even if meritless, could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product. If we were required to obtain a license to continue to manufacture or market the affected product, we may be required to pay substantial royalties or grant cross-licenses to our patents. Even if we were able to obtain a license, it could be nonexclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. We cannot assure you that any such license will be available on acceptable terms, if at all. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other intellectual property rights. Further, the outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of any adverse party. This is especially true in intellectual property cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree. Furthermore, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing a product or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Others may challenge inventorship or claim an ownership interest in our intellectual property which could expose it to litigation and have a significant adverse effect on its prospects.

Determinations of inventorship can be subjective. While we undertake to accurately identify correct inventorship of inventions made on our behalf by our employees, consultants and contractors, an employee, consultant or contractor may disagree with our determination of inventorship and assert a claim of inventorship. Any disagreement over inventorship could result in our being forced to defend our determination of inventorship in a legal action which could result in substantial costs and be a distraction to our senior management and scientific personnel.

While we typically require employees, consultants and contractors who may develop intellectual property on our behalf to execute agreements assigning such intellectual property to us, we may be unsuccessful in obtaining

execution of assignment agreements with each party who in fact develops intellectual property that we regard as our own. Moreover, even when we obtain agreements assigning intellectual property to us, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached. In either case, we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Furthermore, individuals executing agreements with us may have preexisting or competing obligations to a third party, such as an academic institution, and thus an agreement with us may be ineffective in perfecting ownership of inventions developed by that individual. If we are unsuccessful in obtaining assignment agreements from an employee, consultant or contractor who develops intellectual property on our behalf, the employee, consultant or contractor may later claim ownership of the invention. Any disagreement over ownership of intellectual property could result in our losing ownership, or exclusive ownership, of the contested intellectual property, paying monetary damages and/or being enjoined from clinical testing, manufacturing and marketing of the affected product candidate(s). Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property or claiming ownership of what we regard as our own intellectual property.

Many of our current and former employees and our licensors' current and former employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including some which may be competitors or potential competitors. Although we take commercially reasonable steps to ensure that our employees do not use the proprietary information, know-how or trade secrets of others in their work for us, including incorporating such intellectual property into our genome editing systems, we may be subject to claims that we or these employees have misappropriated the intellectual property of a third party.

If we or any of our employees are accused of misappropriating the proprietary information, know-how or trade secrets of a third party, we may be forced to defend such claims in litigation. If we are found to have misappropriated the intellectual property rights of a third party, we may be forced to pay monetary damages, sustain reputational damage, lose key personnel, or lose valuable intellectual property rights. Further, it may become necessary for us to obtain a license from such third party to commercialize any of our genome editing systems. Such a license may not be available on commercially reasonable terms or at all. Any of the aforementioned could materially affect the commercialization of any of our genome editing systems. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

We consider proprietary trade secrets or confidential know-how and unpatented know-how to be important to our business. We may rely on trade secrets or confidential know-how to protect our technology, especially where patent protection is believed by us to be of limited value. We expect to rely on third parties for future manufacturing of our genome editing systems, and any future genome editing systems. We also expect to collaborate with third parties on the development of our genome editing systems and any future genome editing systems. As a result of the aforementioned collaborations, we must, at times, share trade secrets with our collaborators. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements.

Trade secrets or confidential know-how can be difficult to maintain as confidential. To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements and, if applicable, material

transfer agreements, consulting agreements or other similar agreements with us prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. The need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time consuming and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

We may need to acquire or license additional intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development of our genome editing systems. It may be necessary for us to use the patented or proprietary technology of one or more third parties to commercialize our current and future product candidates.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development. If we are unable to acquire such intellectual property outright, or obtain licenses to such intellectual property from such third parties when needed or on commercially reasonable terms, our ability to commercialize our genome editing systems, if approved, would likely be delayed or we may have to abandon development of that product genome editing systems or program and our business and financial condition could suffer.

If we in-license additional genome editing systems in the future, we might become dependent on proprietary rights from third parties with respect to those genome editing systems. Any termination of such licenses could result in the loss of significant rights and would cause material adverse harm to our ability to develop and commercialize any genome editing systems subject to such licenses. Even if we are able to in-license any such necessary intellectual property, it could be on nonexclusive terms, including with respect to the use, field or territory of the licensed intellectual property, thereby giving our competitors and other third parties access to the same intellectual property licensed to us. In-licensing IP rights could require us to make substantial licensing and royalty payments. Patents licensed to us could be put at risk of being invalidated or interpreted narrowly in litigation filed by or against our licensors or another licensee or in administrative proceedings. If any in-licensed patents are invalidated or held unenforceable, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products.

We may not have the right to control the prosecution, maintenance, enforcement or defense of patents and patent applications that we license from third parties. In such cases, we would be reliant on the licensor to take

any necessary actions. We cannot be certain that such licensor would act with our best interests in mind, or in compliance with applicable laws and regulations, or that their actions would result in valid and enforceable patents. For example, it is possible that a licensor's actions in enforcing and/or defending a patent licensed by use may be less vigorous than had we conducted them ourselves. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- our financial or other obligations under the license agreement;
- whether and the extent to which our technology and processes infringe intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of licensed technology in relation to our development and commercialization of our genome editing systems and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected genome editing systems.

The risks described elsewhere pertaining to our intellectual property rights also apply to the intellectual property rights that we may own or in-license now or in the future, and any failure by us or our licensors to obtain, maintain, defend and enforce these rights could have an adverse effect on our business. In some cases we may not have control over the prosecution, maintenance or enforcement of the patents that we license, and may not have sufficient ability to provide input into the patent prosecution, maintenance and defense process with respect to such patents, and potential future licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain, defend and enforce the licensed patents.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our trademarks of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time-consuming, particularly for a company of our size. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks

or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use for our products in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a usable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Intellectual property rights do not necessarily address all potential threats to our business.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make products that are competitive to our genome editing systems or any of our future genome editing systems but that are not covered by the claims of our patent portfolio;
- others may independently develop similar or alternative technologies or otherwise circumvent any of our technologies without infringing our patent portfolio;
- we or any of our collaborators might not have been the first to invent the inventions covered by our patent portfolio;
- we or any of our collaborators might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- it is possible that our pending patent applications or those that we may file in the future will not lead to issued patents;
- others may have access to the same intellectual property rights licensed to us on a non-exclusive basis in the future;
- issued patents that we own may not provide us with any competitive advantage, or may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership of our patent portfolio may be challenged by third parties;
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business;

- patent enforcement is expensive and time-consuming and difficult to predict; thus, we may not be able to enforce any of our patents against a competitor; and
- we may choose not to file a patent application for certain inventions, instead choosing to rely on trade secret protection, and a third party may subsequently file a patent covering such intellectual property.

Risks Related to the Offering, our Common Stock, and Operating as a Public Company

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of \$ _____ per share, representing the difference between the assumed initial public offering price of \$ _____ per share, the estimated midpoint of the price range set forth on the cover page of this prospectus, and our pro forma as adjusted net tangible book value per share as of _____, 2023 after giving effect to this offering. To the extent the underwriters exercise their option to purchase additional shares or our restricted common stock issued in the Reorganization vests, you will incur further dilution. For a further description of the dilution you will experience immediately after this offering, see "Dilution."

The market price of our common stock may be volatile, which could result in substantial losses for investors purchasing shares in this offering.

The initial public offering price for our common stock was determined through negotiations with the underwriters. This initial public offering price may vary from the market price of our common stock after the offering. As a result, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by those factors discussed in this "Risk Factors" section and many others, some of which may include:

- the success of existing or new competitive product candidates or technologies;
- the timing and results of preclinical studies and clinical trials for any product candidates we may develop;
- failure or discontinuation of any of our development and research programs;
- results of any preclinical studies, clinical trials or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- developments or changing views regarding the use of genetic therapies, including those that involve genome editing;
- commencement or termination of collaborations for our product development and research programs;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs or product candidates that we may develop;
- the results of our efforts to develop product candidates;

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- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts, if any, that cover our stock;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- expiration of market stand-off or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including COVID-19 pandemic, the ongoing geopolitical conflict in Ukraine and the Israel-Hamas war, tensions in U.S.-China relations, rising interest rates and inflation; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock market in general and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. In particular, in relation to uncertainty around inflation and the U.S. Federal Reserve’s measures to slow inflation, the stock market has been exceptionally volatile. Market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our stock shortly following this offering. Following periods of such volatility in the market price of a company’s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future.

Securities litigation could result in substantial costs and divert management’s attention and resources from our business.

We have wide discretion in the use of the net proceeds from this offering and may not use them effectively.

We cannot specify with certainty the particular uses of the net proceeds we will receive from this offering. Our management will have wide discretion in the application of the net proceeds, including for any of the purposes described in “Use of Proceeds.” Accordingly, you will have to rely upon the judgment of our management with respect to the use of the proceeds, with only limited information concerning management’s specific intentions. Our management may spend a portion or all of the net proceeds from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business, financial condition, results of operations and prospects. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002 (“SOX”), the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose

various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company. Our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to SOX Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC after we become a public company. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We do not know whether a market will develop for our common stock or what the market price of our common stock will be, and, as a result, it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. Although we have applied to list our common stock on the Nasdaq Global Select Market, an active trading market for our shares may never develop or be sustained following this offering. If a market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Future sales of our common stock in the public market could cause our stock price to fall.

Our stock price could decline as a result of sales of a large number of shares of our common stock after this offering or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Upon completion of this offering, _____ shares of our common stock will be outstanding (or _____ shares of common stock will be outstanding assuming exercise in full of the underwriters' option to purchase additional shares), based on our shares outstanding as of _____, 2024. All shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act of 1933, as amended (the "Securities Act"), unless held by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The resale of the remaining _____, or approximately _____% of our outstanding shares after this offering, is currently prohibited or otherwise restricted as a result of securities law provisions, market standoff agreements entered into by our stockholders with us, profits interests agreements entered into by our employees with us, unit purchase agreement lock-ups, or lock-up agreements entered into by our stockholders with the underwriters. However, subject to applicable securities law restrictions and excluding shares of restricted common stock that will remain unvested, these shares will be able to be sold in the public market beginning 180 days after the date of this prospectus. Shares of unvested restricted common stock that were issued and outstanding as of the date of this prospectus will become available for sale immediately upon the vesting of such shares, as applicable, and the expiration of any applicable market stand-off or lock-up agreements. Shares issued upon the exercise of stock options pursuant to future awards that may be granted under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market stand-off and lock-up agreements and Rule 144 and Rule 701 under the Securities Act. For more information see the section entitled "Shares Eligible for Future Sale" included elsewhere in this prospectus.

Upon completion of this offering, the holders of approximately _____ shares, or approximately _____% of our common stock, will have rights, subject to some conditions, to require us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register the offer and sale of all shares of common stock that we may issue under our equity compensation plans. Once we register the offer and sale of shares for the holders of registration rights and shares to be issued under our equity incentive plans, they can be freely sold in the public market upon issuance, subject to the lock-up agreements described in the section entitled "Underwriting" included elsewhere in this prospectus.

In addition, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

We are an "emerging growth company" and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"), and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of SOX Section 404, not being required to comply with any requirement for a supplement to the auditor's report providing

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additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. In this prospectus, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption, and, therefore, while we are an emerging growth company we will not be subject to the new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies. As a result of this election, our financial statements may not be comparable to those of other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Insiders will continue to have substantial influence over us after this offering, which could limit your ability to affect the outcome of key transactions, including a change of control.

After this offering, our directors and executive officers and their affiliates will beneficially own shares representing approximately % percent of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

We do not expect to pay any dividends for the foreseeable future. Investors in this offering may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements

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in accordance with generally accepted accounting principles. In connection with this offering, we intend to begin the process of documenting, reviewing and improving our internal controls and procedures for compliance with SOX Section 404, which will require annual management assessment of the effectiveness of our internal control over financial reporting starting with our second filing of an Annual Report on Form 10-K.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy or consequent inability to produce accurate financial statements on a timely basis could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis cause investors to lose confidence in the accuracy and completeness of our financial reports and could cause the market price of our common stock to decline significantly.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon the closing of this offering, we will become subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the facts that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Our amended and restated bylaws that will become effective upon the effectiveness of our registration statement designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our amended and restated bylaws that will become effective upon the effectiveness of our registration statement, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of or based on a breach of a fiduciary duty owed by any director, officer or other employee of ours to us or our stockholders; (iii) any action asserting a claim pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or (iv) any action asserting a claim governed by the internal affairs doctrine (the "Delaware Forum Provision"). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Our amended and restated bylaws further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, the Exchange Act, the respective rules and regulations promulgated thereunder or the Federal Forum Provision. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and

the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the effectiveness of our registration statement and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the effectiveness of our registration statement and Delaware law contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. Our amended and restated certificate of incorporation, which will become effective immediately prior to the closing of this offering, and amended and restated bylaws, which will become effective upon the effectiveness of the registration statement of which this prospectus is a part, include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may be removed only for cause;
- specify that no stockholder is permitted to cumulate votes at any election of directors;

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- expressly authorized our board of directors to make, alter, amend or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock.

In addition, because we are incorporated in the State of Delaware, we are governed by the provisions of Section 203 of the DGCL, which prohibits a person who owns in excess of 15 percent of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 percent of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

Adverse developments affecting the financial services industry could adversely affect our current and projected business operations and our financial condition and results of operations.

Adverse developments that affect financial institutions, such as events involving liquidity that are rumored or actual, have in the past and may in the future lead to bank failures and market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank ("SVB") was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. Similarly, on March 12, 2023, Signature Bank was also swept into receivership. The U.S. Department of Treasury, the Federal Reserve Board (the "Federal Reserve"), and the FDIC released a statement that indicated that all depositors of SVB would have access to all of their funds, including funds held in uninsured deposit accounts, after only one business day of closure. The U.S. Department of Treasury, FDIC and Federal Reserve have announced a program to provide up to \$25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. There is no guarantee, however, that the U.S. Department of Treasury, FDIC and Federal Reserve will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

At this time, we hold substantially all of our cash on deposit at SVB (which has been assumed by First Citizens) and we have not experienced any adverse impact to our current and projected business operations, financial condition or results of operations as a result of the closure of SVB or any other banks. We plan to diversify our cash deposit holdings between multiple financial institutions. However, uncertainty remains over liquidity concerns in the broader financial services industry, and our business, our business partners, or industry as a whole may be adversely impacted in ways that we cannot predict at this time. If, for example, other banks and financial institutions enter receivership or become insolvent in the future in response to financial conditions affecting the banking system and financial markets, our ability to access our existing cash, cash equivalents and available-for-sale marketable securities may be threatened.

Although we expect to assess our banking relationships as we believe necessary or appropriate, our access to cash in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect the financial institutions with which we have banking relationships, and in turn, us.

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These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could also include factors involving financial markets or the financial services industry generally. The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets; or termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, widespread investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

In addition, one or more of our critical vendors, third party manufacturers, or other business partners could be adversely affected by any of the liquidity or other risks that are described above, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. Any business partner bankruptcy or insolvency, or any breach or default by a business partner, or the loss of any significant supplier relationships, could result in material adverse impacts on our current and/or projected business operations and financial condition.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations," and "Business," contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- the initiation, timing, progress and results of our research and development programs, preclinical studies and future clinical trials;
- our ability to demonstrate, and the timing of, preclinical proof-of-concept *in vivo* and *ex vivo* for multiple programs;
- our ability to advance any product candidates that we may identify and successfully complete any clinical studies, including the manufacture of any such product candidates;
- our ability to quickly leverage programs within our initial target indications and to progress additional programs to further develop our pipeline;
- the timing of our IND applications submissions;
- the implementation of our strategic plans for our business, programs and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our genome editing technology and platform;
- developments related to our competitors and our industry;
- our ability to leverage the clinical, regulatory, and manufacturing advancements made by genome editing programs to accelerate our clinical trials and approval of product candidates;
- our ability to identify and enter into future license agreements and collaborations;
- developments related to our genome editing technology and platform;
- regulatory developments in the United States and foreign countries;
- our ability to attract and retain key scientific and management personnel; and
- our use of proceeds from this offering, estimates of our expenses, capital requirements, and needs for additional financing.

In some cases, you can identify forward-looking statements by terminology such as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section entitled "Risk Factors" and elsewhere in this prospectus. If one or more of

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these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement, of which this prospectus forms a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section entitled "Risk Factors" and elsewhere in this prospectus.

REORGANIZATION

Prior to the effectiveness of this registration statement, we intend to engage in a series of transactions pursuant to which Metagenomi Technologies, LLC, the sole stockholder and holding company parent of Metagenomi, Inc., will merge with and into Metagenomi, Inc., and Metagenomi, Inc. will continue to exist as the surviving corporation. Throughout this prospectus, we refer to these transactions and the related transactions enumerated below collectively as the "Reorganization." To consummate the Reorganization, we will file a certificate of merger and amended and restated certificate of incorporation with the Secretary of State of the State of Delaware. In connection with the Reorganization:

- holders of Metagenomi Technologies, LLC's outstanding Series A-1 redeemable convertible preferred units ("Series A-1 preferred units") will receive _____ share of Series A-1 redeemable convertible preferred stock ("Series A-1 preferred stock") of Metagenomi, Inc. for each Series A-1 preferred unit held immediately prior to the Reorganization, with an aggregate of _____ shares of our Series A-1 redeemable convertible preferred stock issued in the Reorganization;
- holders of Metagenomi Technologies, LLC's outstanding Series A-2 redeemable convertible preferred units ("Series A-2 preferred units") will receive _____ share of Series A-2 redeemable convertible preferred stock ("Series A-2 preferred stock") of Metagenomi, Inc. for each Series A-2 preferred unit held immediately prior to the Reorganization, with an aggregate of _____ shares of our Series A-2 redeemable convertible preferred stock issued in the Reorganization;
- holders of Metagenomi Technologies, LLC's outstanding Series A-3 redeemable convertible preferred units ("Series A-3 preferred units") will receive _____ share of Series A-3 redeemable convertible preferred stock ("Series A-3 preferred stock") of Metagenomi, Inc. for each Series A-3 preferred unit held immediately prior to the Reorganization, with an aggregate of _____ shares of our Series A-3 redeemable convertible preferred stock issued in the Reorganization;
- holders of Metagenomi Technologies, LLC's outstanding Series A-4 redeemable convertible preferred units ("Series A-4 preferred units") will receive _____ share of Series A-4 redeemable convertible preferred stock ("Series A-4 preferred stock") of Metagenomi, Inc. for each Series A-4 preferred unit held immediately prior to the Reorganization, with an aggregate of _____ shares of our Series A-4 redeemable convertible preferred stock issued in the Reorganization;
- holders of Metagenomi Technologies, LLC's outstanding Series A-5 redeemable convertible preferred units ("Series A-5 preferred units") will receive _____ share of Series A-5 redeemable convertible preferred stock ("Series A-5 preferred stock") of Metagenomi, Inc. for each Series A-5 preferred unit held immediately prior to the Reorganization, with an aggregate of _____ shares of our Series A-5 redeemable convertible preferred stock issued in the Reorganization;
- holders of Metagenomi Technologies, LLC's outstanding Series B redeemable convertible preferred units ("Series B preferred units") will receive _____ share of Series B redeemable convertible preferred stock ("Series B preferred stock") of Metagenomi, Inc. for each Series B preferred unit held immediately prior to the Reorganization, with an aggregate of _____ shares of our Series B redeemable convertible preferred stock issued in the Reorganization;
- holders of Metagenomi Technologies, LLC's outstanding Series B-1 redeemable convertible preferred units ("Series B-1 preferred units") will receive _____ share of Series B-1 redeemable convertible preferred stock ("Series B-1 preferred stock") of Metagenomi, Inc. for each Series B-1 preferred unit held immediately prior to the Reorganization, with an aggregate of _____ shares of our Series B-1 redeemable convertible preferred stock issued in the Reorganization;

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- holders of Metagenomi Technologies, LLC's outstanding common units will receive _____ shares of common stock of Metagenomi, Inc. for each common unit held immediately prior to the Reorganization, with an aggregate of _____ shares of our common stock (which includes _____ shares of unvested restricted common stock) issued in the Reorganization; and
- holders of Metagenomi Technologies, LLC's outstanding profits interests will receive _____ shares of common stock of Metagenomi, Inc. for each profits interest held immediately prior to the Reorganization, with an aggregate of _____ shares of our common stock issued (which includes _____ shares of unvested restricted common stock) in the Reorganization. Vesting terms of outstanding profits interests will not change.

Metagenomi, Inc.'s Series A-1 preferred stock, Series A-2 preferred stock, Series A-3 preferred stock, Series A-4 preferred stock, Series A-5 preferred stock, and Series B preferred stock and Series B-1 preferred stock will be designated as preferred stock under Metagenomi, Inc.'s amended and restated certificate of incorporation. All outstanding shares of our redeemable convertible preferred stock will be convertible into shares of common stock on a one-for-_____ basis.

In connection with the Reorganization, by operation of law, Metagenomi, Inc. will acquire all assets of Metagenomi Technologies, LLC, and assume all of its liabilities and obligations. The purpose of the Reorganization is to reorganize our corporate structure so that Metagenomi, Inc. will continue as a corporation and the existing investors of Metagenomi Technologies, LLC will own Metagenomi, Inc. capital stock rather than members' equity interests in Metagenomi Technologies, LLC. The Reorganization generally is intended to not result in a taxable event to Metagenomi, Inc. for U.S. income tax purposes. Except as context otherwise requires, all information included in this prospectus is presented giving effect to the Reorganization.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of shares of our common stock in this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise in full their option to purchase additional shares, assuming an initial public offering price of \$ per share, the estimated midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

A \$1.00 increase (decrease) in the assumed initial public offering price of \$ per share, the estimated midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us from this offering by \$ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) net proceeds to us from this offering by \$ million, assuming no change in the assumed initial public offering price per share, the estimated midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the offering price or the number of shares by these amounts would have a material effect on our intended uses of the net proceeds from this offering, although it may impact the amount of time prior to which we may need to seek additional capital.

As of September 30, 2023, we had cash and cash equivalents and available-for-sale marketable securities of \$292.9 million. We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents and available-for-sale marketable securities, as follows:

- approximately million for continued research and development of our therapeutic portfolio, including preclinical studies and advancement through potential preclinical proof-of-concept;
- approximately million for IND-enabling studies and potential initiation of clinical studies for certain of our current programs;
- approximately million to advance our gene editing platform discovery and early-stage research for other potential programs;
- approximately million to advance manufacturing capabilities to support early stage clinical development; and
- the remainder for general corporate purposes.

Based on our current plans, we believe our existing cash and cash equivalents and available-for-sale marketable securities, together with the net proceeds from this offering, will be sufficient to fund our operations and capital expenditure requirements into .

All of our programs are currently in preclinical stage of development. The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our research and development, the status of and results from pre-clinical studies or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates or strategic opportunities that become available to us, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We expect the net proceeds from this offering, together with our existing cash and cash equivalents, and available-for-sale marketable securities, will not be sufficient for us to advance any of our programs through regulatory approval, and we will need to raise additional capital to complete the development and potential commercialization of any of our programs.

Pending our use of proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing financial instruments and U.S. government securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our members' capital. We currently intend to retain any future earnings to fund the development and expansion of our business, and therefore we do not anticipate paying cash dividends on our common stock in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our results of operations, financial condition, capital requirements and other factors deemed relevant by our board of directors.

CAPITALIZATION

The following table sets forth our cash, cash equivalents, available-for-sale marketable securities and our capitalization as of September 30, 2023:

- on an actual basis;
- on a pro forma basis to give effect to (i) the Reorganization, (ii) the conversion of _____ shares of our redeemable convertible preferred stock, issued in connection with the Reorganization in exchange for redeemable convertible preferred units outstanding as of September 30, 2023, in connection with the Reorganization, into an equivalent number of shares of our common stock, immediately prior to the completion of this offering and (iii) the filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the completion of this offering, in each case as if such events had occurred on September 30, 2023; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of _____ shares of our common stock in this offering at an assumed initial public offering price of \$ _____ per share, which is the estimated midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information below is illustrative only, and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read the information in this table together with our consolidated financial statements and the related notes included elsewhere in this prospectus and "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus.

	As of September 30, 2023		
	Actual	Pro forma	Pro forma as adjusted
	(in thousands, except share and per share data)		
Cash and cash equivalents	\$ 101,897	\$	\$
Available-for-sale marketable securities	191,030		
Total cash, cash equivalents and available-for-sale marketable securities	\$ 292,927		
Redeemable convertible preferred units; no par value; 41,813,375 units authorized, 41,813,375 units issued and outstanding, actual; no units authorized issued and outstanding, pro forma and pro forma as adjusted	350,758	—	—
Redeemable Convertible preferred stock; \$ _____ par value; no shares authorized, issued and outstanding, actual; _____ shares authorized and no shares issued and outstanding, pro forma; and no shares authorized, issued and outstanding, pro forma as adjusted	—	—	—
Members'/Stockholders' equity (deficit):			
Profits interests, no par value; 14,604,165 units authorized, 9,556,687 units issued and outstanding, actual; no units authorized, issued and outstanding, pro forma and pro forma as adjusted	6,962	—	—
Common units, no par value; 66,000,000 units authorized, 5,947,500 units issued and outstanding, actual; no units authorized, issued and outstanding, pro forma and pro forma as adjusted	26	—	—
Preferred stock, \$ _____ par value; no shares authorized, issued or outstanding, actual and pro forma; _____ shares authorized and no shares issued or outstanding, pro forma as adjusted	—	—	—
Common stock, \$ _____ par value; no shares authorized, issued and outstanding, actual; _____ shares authorized, _____ shares issued and outstanding, pro forma; _____ shares authorized, _____ shares issued and outstanding, pro forma as adjusted	—	—	—
Additional paid-in capital	—	—	—
Accumulated other comprehensive loss	(359)	—	—
Accumulated deficit	(125,650)	—	—
Total members'/stockholders' equity (deficit)	(119,021)	—	—
Total capitalization	\$ 231,737	\$	\$

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Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ per share, which is the estimated midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total stockholders' equity (deficit) and total capitalization by \$ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total stockholders' equity (deficit) and total capitalization by \$ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the information in this table together with our consolidated financial statements and the related notes included elsewhere in this prospectus and "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus.

The number of shares of our common stock outstanding after this offering assumes the Reorganization takes place immediately prior to the effectiveness of this registration statement and is based on shares of our common stock (including shares of unvested restricted common stock) issued in exchange for common units and profits interests outstanding as of September 30, 2023, and after giving effect to the conversion of shares of our redeemable convertible preferred stock, issued in connection with the Reorganization in exchange for redeemable convertible preferred units outstanding as of September 30, 2023, into an equivalent number of shares of our common stock immediately prior to the completion of this offering.

The number of shares of common stock to be outstanding after this offering excludes:

- shares of common stock reserved for future issuance under our 2024 Stock Option and Incentive Plan (the "2024 Plan"), which will become effective on the date immediately prior to execution of the underwriting agreement related to this offering; and
- shares of common stock reserved for future issuance under our 2024 Employee Stock Purchase Plan (the "ESPP"), which will become effective on the date immediately prior to the execution of the underwriting agreement related to this offering.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of September 30, 2023 was \$(123.4) million, or \$(20.75) per our common unit. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and the carrying values of our redeemable convertible preferred units, which is not included within members' deficit. Our historical net tangible book value (deficit) per unit represents historical net tangible book value (deficit) divided by 5,947,500 of our common units outstanding as of September 30, 2023.

Our pro forma net tangible book value as of September 30, 2023 was \$ million, or \$ per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to (i) the Reorganization, (ii) the conversion of shares of our redeemable convertible preferred stock, issued in connection with the Reorganization in exchange for redeemable convertible preferred units into an equivalent number of shares of our common stock immediately prior to the completion of this offering, and (iii) the filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the completion of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of September 30, 2023, after giving effect to the pro forma adjustments described above.

After giving further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of \$ per share, the estimated midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of September 30, 2023 would have been \$ million, or \$ per share. This amount represents an immediate increase in pro forma as adjusted net tangible book value of \$ per share to our existing stockholders and immediate dilution in pro forma as adjusted net tangible book value of \$ per share to new investors purchasing common stock in this offering.

Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis (without giving effect to any exercise by the underwriters of their option to purchase additional shares):

Assumed initial public offering price per share	\$
Historical net tangible book value (deficit) per common unit as of September 30, 2023	\$ (20.75)
Increase per share attributable to the pro forma adjustments described above	<u> </u>
Pro forma net tangible book value per share as of September 30, 2023	<u> </u>
Increase in pro forma as adjusted net tangible book value per share attributable to new investors participating in this offering	<u> </u>
Pro forma as adjusted net tangible book value per share immediately after this offering	<u> </u>
Dilution per share to new investors participating in this offering	<u><u> </u></u>

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The dilution information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ per share, which is the estimated midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) our pro forma as adjusted net tangible book value per share after this offering by \$ and dilution per share to new investors purchasing common stock in this offering by \$, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase our pro forma as adjusted net tangible book value per share after this offering by \$ and decrease dilution per share to new investors purchasing common stock in this offering by \$, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each decrease of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease our pro forma as adjusted net tangible book value per share after this offering by \$ and increase dilution per share to new investors purchasing common stock in this offering by \$, assuming no change in the assumed initial public offering price and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares in full, our pro forma as adjusted net tangible book value per share after this offering would be \$, representing an immediate increase in pro forma as adjusted net tangible book value per share of \$ to existing stockholders and immediate dilution in pro forma as adjusted net tangible book value per share of \$ to new investors purchasing common stock in this offering, based on the assumed initial public offering price of \$ per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The following table summarizes on the pro forma as adjusted basis described above, the total number of shares of common stock purchased from us on an as converted to common stock basis, the total consideration paid or to be paid, and the average price per share paid or to be paid by existing members/stockholders and by new investors in this offering at an assumed initial public offering price of \$ per share, which is the estimated midpoint of the estimated price range set forth on the cover of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. As the table shows, new investors purchasing common stock in this offering will pay an average price per share substantially higher than our existing members/ stockholders paid.

	Units/Shares Purchased		Total Consideration		Average Price Per Unit/Share
	Number	Percent	Amount	Percent	
Existing members/stockholders	47,760,875		\$351,637,285		\$7.36
Investors participating in this offering					
Total		100%	\$	100%	

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to percent of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors purchasing common stock in this offering would be increased to percent of the total number of shares of our common stock outstanding after this offering.

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The discussion and tables above assume the Reorganization takes place prior to the effectiveness of this registration statement and are based on _____ shares of our common stock (including _____ shares of unvested restricted common stock) issued in exchange for common units and profits interests outstanding as of September 30, 2023, and after giving effect to the conversion of _____ shares of our redeemable convertible preferred stock, issued in connection with the Reorganization, in exchange for redeemable convertible preferred units outstanding as of September 30, 2023, into an equivalent number of shares of our common stock immediately prior to the completion of this offering.

The number of shares of common stock to be outstanding after this offering excludes:

- _____ shares of common stock reserved for future issuance under the 2024 Plan; and
- _____ shares of common stock reserved for future issuance under the ESPP.

To the extent that new stock options are issued, or we issue additional shares of common stock in the future, there will be further dilution to new investors. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our audited consolidated financial statements and unaudited condensed consolidated financial statements and the related notes appearing elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section of this prospectus. Our historical results are not necessarily indicative of the results that may be expected for any period in the future.

Overview

We are a precision genetic medicines company committed to developing curative therapeutics for patients using our proprietary, comprehensive metagenomics-derived genome editing toolbox. Genetic diseases are caused by a diverse set of mutations that have been largely inaccessible by genome engineering approaches to date. Genetic mutations are seen in a variety of forms, including deletions, insertions, single-base-pair changes and sequence repeats, and are found throughout the genome and across a variety of different cell types, tissues, and organ systems. Additionally, many diseases lack a genetic origin but have the potential to be effectively and permanently addressed through genome editing. We are harnessing the power of metagenomics, the study of genetic material recovered from the natural environment, to unlock four billion years of microbial evolution to discover and develop a suite of novel editing tools capable of correcting any type of genetic mutation found anywhere in the genome. Our comprehensive genome editing toolbox includes programmable nucleases, base editors, and RNA and DNA-mediated integration systems (including prime editing systems and clustered regularly interspaced short palindromic repeat ("CRISPR")-associated transposases ("CASTs")). We believe our diverse and modular toolbox positions us to access the entire genome and select the optimal tool to unlock the full potential of genome editing for patients.

Since our inception, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, research and development activities, building our intellectual property portfolio and providing general and administrative support for these operations. We have historically financed our operations primarily through issuing redeemable convertible preferred units and convertible promissory notes and entering into collaboration agreements, which generate collaboration revenue.

We have incurred significant operating losses since inception and we expect to continue to incur substantial losses for the foreseeable future. Our net losses were \$21.4 million and \$43.6 million for the years ended December 31, 2021 and 2022, respectively. Our net losses were \$29.0 million and \$49.0 million for the nine months ended September 30, 2022 and 2023, respectively. As of September 30, 2023, we had an accumulated deficit of \$125.7 million. We anticipate that our expenses and operating losses will increase substantially for the foreseeable future as we:

- advance our current research activities and further develop our platform;
- develop, maintain, expand, and protect our intellectual property portfolio;
- continue preclinical development and initiate clinical trials for any product candidates we may identify;
- seek regulatory approval for any product candidates for which we successfully complete clinical trials;

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- establish our manufacturing capabilities, including internal manufacturing facilities and contracting with other vendors;
- ultimately, commercialize any future product candidates for which we receive regulatory approval, requiring significant marketing, sales, and distribution infrastructure expenses;
- hire additional research and development, clinical, commercial, general and administrative personnel;
- acquire or in-license product candidates, intellectual property and technologies;
- establish and maintain collaborations;
- add operational, financial and management information systems and personnel; or
- incur additional legal, audit, accounting, compliance, insurance, investor relations and other expenses to operate as a public company that we did not incur as a private company.

We will not generate revenue from product sales unless and until we successfully initiate and complete clinical development and obtain regulatory approval for one or more product candidates. If we obtain regulatory approval for any product candidate and do not enter into a commercialization partnership, we expect to incur significant expenses related to developing our commercialization capability to support product sales, manufacturing, marketing, and distribution. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances, and marketing, distribution or licensing arrangements with third parties. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, reduce or eliminate the development and commercialization of our platform or delay our pursuit of potential in-licenses or acquisitions.

As of September 30, 2023, we had cash, cash equivalents and available-for-sale marketable securities of \$292.9 million. We believe that the anticipated net proceeds from this offering, together with our existing cash, cash equivalents and available-for-sale marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements through . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "Liquidity and Capital Resources" and "Risk Factors—Risks Related To Our Financial Position and Need for Additional Capital."

Macroeconomic Trends

Unfavorable conditions in the economy in the United States and abroad may negatively affect the growth of our business and our results of operations. For example, macroeconomic events, including, rising inflation, tensions in U.S.-China relations, the COVID-19 pandemic, the U.S. Federal Reserve raising interest rates, recent and potential future disruptions in access to bank deposits and lending commitments due to bank failures and the effects of the ongoing geopolitical conflict in Ukraine and the Israel-Hamas war, have led to economic uncertainty and volatility globally. The effect of macroeconomic conditions may not be fully reflected in our results of operations until future periods. To date, the macroeconomic trends discussed above have not had a material adverse impact on our business, financial condition or results of operations. If, however, economic uncertainty increases or the global economy worsens, our business, financial condition and results of operations may be harmed. For further discussion of the potential impacts of macroeconomic events on our business, financial condition, and operating results, refer to the section titled "Risk Factors" included elsewhere in this prospectus.

Collaboration and License Agreements

Moderna Strategic Collaboration and License Agreement

On October 29, 2021, the effective date, we entered into a Strategic Collaboration and License Agreement (the "Moderna Agreement") with Moderna. We will collaborate with Moderna on the research and development of *in vivo* genome editing therapies directed at certain targets and the commercialization of such genome editing therapies. The collaboration provides Moderna with exclusive access to our technology platform during the research period in (1) the field of *in vivo* gene editing technology for a therapeutic, ameliorative or prophylactic application by way of knock-out through InDel formation or base editing or insertion of an exogenous DNA template (such field, "DT Field") and (2) the field of *in vivo* gene editing technology for a therapeutic, ameliorative or prophylactic application outside the use of (a) DNA donor templates and (b) no exogenous template at all but including (c) correction by base editing (such field, "RT Field"). We formed a joint steering committee, a joint research subcommittee and a joint patent subcommittee to oversee the collaboration activities.

Under the terms of the Moderna Agreement, we and Moderna will collaborate on one or more programs in the RT Field (the "Moderna RT program") and two programs in the DT Field (the "Moderna DT program" and the "DT Co-Co program").

With respect to the Moderna RT and Moderna DT programs, we will collaborate on the research and development of product candidates under the approved research plans. The initial research term of the Moderna RT program is four years, which may be extended by Moderna for an additional three years upon written notice and a payment of extension fees. The initial research term of the Moderna DT program is four years. We granted to Moderna an option to obtain an exclusive license to develop, manufacture and commercialize up to ten Moderna RT program candidates and up to two Moderna DT program candidates at any time during the research term and prior to filing of an IND application with the FDA or any similar application filed with a regulatory authority in a country other than the United States ("U.S."), subject to Moderna's payment of an option exercise fee of \$10.0 million per target.

With respect to the DT Co-Co program, we will work together with Moderna on the co-development and commercialization of products and share costs and profits equally. We maintain commercialization rights in the U.S. (subject to Moderna's right to appoint up to 50% of the U.S. sales force for the DT Co-Co program), while Moderna maintains these rights in countries other than the U.S. The initial research term for the DT Co-Co program is four years, and each party has a right to opt-out of the DT Co-Co program at any time, at which point the other party has the right to solely continue the development and commercialization activities. If there is no development candidate nomination by the end of the initial research term, the DT Co-Co program will expire, unless we have mutually agreed to continue the program.

During the year ended December 31, 2021, we received a non-refundable upfront payment of \$40.0 million and a \$5.0 million payment for the first year of research costs. Concurrent with the Moderna Collaboration Agreement, Moderna also provided \$30.0 million in cash in the form of a convertible promissory note (see Note 9 in our audited consolidated financial statements included elsewhere in this prospectus) pursuant to a convertible promissory note agreement dated October 29, 2021 (the "Moderna Convertible Promissory Note Agreement"). The convertible promissory note was converted into shares of Series B redeemable convertible preferred units in January 2022. Moderna will reimburse us up to \$5.0 million in annual research and development costs related to the Moderna DT and Moderna RT programs, or up to the agreed amount of expenses per the budget. As of September 30, 2023, we have received a total of \$49.6 million under the Moderna Collaboration Agreement, not including cost-sharing payments under the DT Co-Co program.

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For the Moderna RT and Moderna DT programs, we are eligible to receive (i) technology milestone fees related to the achievement of certain preclinical research objectives of up to \$75.0 million, (ii) development and regulatory milestones of up to \$100.0 million per target, (iii) sales milestones of up to \$200.0 million per target, and (iv) royalties ranging from a mid-single digit to a low-teens percentage of annual net sales of a licensed product. Any profits and losses from the co-development and commercialization of the DT Co-Co program are shared equally between us and Moderna. With respect to the DT Co-Co program for which the opt-out party has exercised its opt-out right, the continuing party will pay to the opt-out party, certain development, regulatory and sales milestone payments that will not exceed an aggregate \$239.0 million per DT Co-Co target, and opt-out royalties ranging from a high-single digit to a low-teens percentage of annual net sales of a licensed product.

The term of the Moderna Agreement will continue on a licensed product-by-licensed product and country-by-country basis, until the expiration of the applicable royalty term. The royalty term commences on the first commercial sale of a licensed product and terminates on the latest of: (a) the expiration or abandonment of the last valid claim of a patent within the licensed Moderna DT or RT technology; (b) 10 years after the first commercial sale of a licensed product; and (c) expiration of the regulatory exclusivity. Upon the expiration of the term of a licensed product in the Moderna DT or Moderna RT program, the licenses granted to Moderna will survive and become perpetual, fully paid and royalty-free. Each party may terminate the Moderna Agreement on a program-by-program basis upon written notice to the other party for an uncured material breach or insolvency. We may terminate the Moderna Agreement upon written notice to Moderna for a patent challenge. Additionally, Moderna may terminate the agreement at its convenience with respect to Moderna DT or Moderna RT programs for any reason upon at least: (a) 60 days' prior written notice if a first commercial sale has not occurred for the products in such program, or (b) 180 days' prior written notice if a first commercial sale of a product in such program has occurred.

We concluded that the Moderna DT and Moderna RT programs are in the scope of ASC 606. We determined that the licenses granted to Moderna, and its participation in the joint steering committee are not capable of being distinct from the preclinical research and development services and therefore concluded that there are two performance obligations: (1) the Moderna RT program and (2) the Moderna DT program. We also concluded that the option to obtain an exclusive license and options to extend Moderna RT program term do not include significant incremental discounts, and as such, the options do not provide material rights.

We concluded the DT Co-Co program research activities are within the scope of ASC 808, as we and Moderna are both active participants in the research, development and commercialization activities, are exposed to significant risks and rewards that are dependent on the success of the DT Co-Co program activities and share costs and profits equally. We determined that the guidance in ASC 730, *Research and Development*, was appropriate to apply to the DT Co-Co program research activities by analogy, based on the nature of the cost sharing provisions of the agreement. We concluded that DT Co-Co program is one unit of accounting, as the co-exclusive license is not distinct from the research and development and the participation in joint steering committee activities. We recognize payments to or from Moderna related to the DT Co-Co program cost sharing research activities as an increase to or reduction of research and development expenses, respectively.

We concluded that the Moderna Collaboration Agreement and the Moderna Convertible Promissory Note Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. We estimated the contract consideration to be \$90.0 million, which consisted of: 1) the non-refundable upfront collaboration payment of \$40.0 million received in 2021, 2) \$30.0 million in cash received in 2021 in exchange for the convertible promissory note and 3) the estimated cost reimbursements for Moderna DT and Moderna RT programs of \$20.0 million. We constrained future milestones, as we assessed that it is probable that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in future

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periods. During the year ended December 31, 2021, we recorded \$30.0 million of the contract consideration for the convertible promissory note based on the fair value (see Note 9 in our audited consolidated financial statements included elsewhere in this prospectus) and allocated the transaction price of \$60.0 million to each of the following programs on a relative standalone selling price basis: 1) \$49.5 million to the Moderna RT program, 2) \$5.5 million to the Moderna DT program, and 3) \$5.0 million to the DT Co-Co program.

The variable consideration is reevaluated at each reporting period and as changes in circumstances occur. We recognize revenue for each of the Moderna DT and Moderna RT programs as collaboration revenue based on the measure of progress using an estimated cost-based input method each reporting period. We also amortize the allocation consideration for the DT Co-Co program of \$5.0 million as a credit to research and development expenses during the discovery and lead optimization phases for the DT Co-Co program.

We recognized collaboration revenue of \$0.2 million and \$14.5 million in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2021 and 2022, respectively. We recognized collaboration revenue of \$10.7 million and \$14.2 million in the condensed consolidated statements of operations and comprehensive loss for the nine months ended September 30, 2022 and 2023, respectively. As of September 30, 2023, the Company recorded \$1.5 million in accounts receivable on the condensed consolidated balance sheet, related to services performed. As of December 31, 2022 and September 30, 2023, deferred revenue related to the Moderna Agreement was \$30.2 million and \$17.2 million, respectively. Collaboration revenue recognized during the nine months ended September 30, 2022 and 2023 included \$10.7 million and \$14.2 million that was included in deferred revenue as of December 31, 2021 and 2022, respectively. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligations was approximately \$27.8 million as of September 30, 2023, which we expect to recognize as revenue over the next two-to-three years.

We recognized \$0.2 million and \$0.3 million in credits to research and development expenses related to cost sharing allocation and amortization of the collaboration advance, respectively, within research and development expenses in the consolidated statement of operations and comprehensive loss during the year ended December 31, 2021. We recognized \$0.9 million and \$3.5 million in credits to research and development expenses related to cost sharing allocation and amortization of the collaboration advance, respectively, during the year ended December 31, 2022. We recognized \$0.5 million and \$2.7 million in credits to research and development expenses related to cost sharing allocation and amortization of the collaboration advance, respectively, within research and development expenses in the condensed consolidated statement of operations and comprehensive loss during the nine months ended September 30, 2022. We recognized \$0.3 million and \$0.5 million in credits to research and development expenses related to cost sharing allocation and amortization of the collaboration advance during the nine months ended September 30, 2023, respectively. As of December 31, 2022, the collaboration advance balance was \$1.1 million, partially offset by the cost-sharing receivable balance of \$0.4 million, which was presented as a collaboration advance on our condensed consolidated balance sheet. As of September 30, 2023, the collaboration advance balance was \$0.7 million, partially offset by the cost-sharing receivable balance of \$0.2 million, which was presented as a collaboration advance on our condensed consolidated balance sheet.

For additional information regarding the Moderna Agreement, please see the section titled "Business—Our License and Collaboration Agreements."

Affini-T Development, Option and License Agreement

On June 14, 2022, the effective date, we entered into a Development, Option and License Agreement (the "Affini-T Agreement") with Affini-T. Pursuant to the Affini-T Agreement, we and Affini-T have agreed to identify,

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develop or optimize certain reagents using our proprietary technology for Affini-T to use such reagents to develop and commercialize gene edited TCR-based therapeutic products exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with any engineered primary TCR alpha/beta T cells and non-exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with certain other engineered immune cells worldwide. A joint steering committee was established by both parties to assign alliance managers and project leaders to oversee the collaboration activities.

Pursuant to the Affini-T Agreement, we granted Affini-T options to receive, on a pre-specified target-by-pre-specified target basis, for up to six pre-specified targets, either (i) an exclusive, royalty-bearing, sublicensable worldwide license under all of our applicable intellectual property to research, develop, manufacture, use, commercialize and otherwise exploit any TCR-based therapy, preventative treatment, or diagnostic for humans that is directed to such pre-specified target, contains or comprises Primary TCR alpha/beta T Cells and is derived from *ex vivo* application of our reagent (the "Exclusive Option") or (ii) a non-exclusive, royalty-bearing, sublicensable worldwide license under all our applicable intellectual property to research, develop, manufacture, use commercialize and otherwise exploit any TCR-based therapy, preventative treatment, or diagnostic for humans that is directed to such pre-specified target, contains or comprises TCR natural killer ("NK") cells derived from iPSC immune cells or TCR T cells derived from donor-derived or iPSC immune cells. Affini-T can exercise its options for either an exclusive license or a non-exclusive license, or both, for each pre-specified target by providing written notice prior to the earlier of (x) the end of the Affini-T Agreement term or (y) 90 days following the filing of an IND for a licensed product directed to a pre-specified target, subject to the payment of certain fees per each option exercised. After the option exercise, Affini-T has agreed to use commercially reasonable efforts to conduct all development and commercialization activities for a licensed product, and development and commercialization of all licensed products will be at Affini-T's sole cost and expense.

In connection with the Affini-T Agreement, we received upfront equity consideration of 719,920 shares of Affini-T's common stock with an estimated fair value of \$1.3 million in June 2022. The fair value of Affini-T's shares of common stock was estimated by our management, considering the most recent third-party valuation. Affini-T has also agreed to reimburse us for expenses incurred while performing research activities under the research plans. As of September 30, 2023, we received a total of \$3.2 million from Affini-T related to reimbursable expenses. Additionally, we are eligible to receive (i) 933,650 shares of Affini-T's common stock upon the achievement of a regulatory milestone, which is the earlier of a submission of a drug master file to the FDA or an acceptance of an IND filing for a licensed product by the FDA, (ii) up to \$18.8 million in future developmental milestone payments depending on the completion of or the number of patients dosed in, the relevant human clinical trial, or the initiation of a pivotal trial, and \$40.6 million in future regulatory approval milestone payments, which include regulatory approvals in the U.S. and other markets for licensed products directed to a pre-specified target if options for both exclusive and non-exclusive licenses are exercised with respect to such target, (iii) up to \$250.0 million in sales-based milestones for aggregate sales of all licensed products directed to a given pre-specified target and (iv) royalties ranging from a low-single digit to high-single digit percentage of worldwide annual net sales of licensed products.

The initial term of the Affini-T Agreement is five years from the effective date. If Affini-T exercises an Exclusive Option with respect to any pre-specified target during the initial term, the initial term will be extended by an additional five years. Following the expiration of the extended term, if any, the agreement will continue on a target-by-target basis and expire with respect to such target upon the expiration of the royalty term for all licensed products directed to such target. The Affini-T Agreement may be terminated during the term by either party for an uncured material breach by, or bankruptcy of, the other party. Additionally, Affini-T may terminate the Affini-T Agreement for convenience, in its entirety, on a research plan-by-research plan basis, on a target-by-target basis or on a licensed product-by-licensed product basis, by providing prior written notice.

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We concluded that the Affini-T Agreement is in the scope of ASC 606 and that there is one performance obligation to perform research activities under the Affini-T Agreement. Exclusive and non-exclusive licenses are optional contingent purchases that do not include significant incremental discounts, and therefore do not provide a material right.

At the effective date, the transaction price consisted of the upfront equity consideration with an estimated fair value of \$1.3 million and estimated research reimbursement costs. Research reimbursement costs represent variable consideration, and our management estimates what portion to include in total consideration at the end of each reporting period. Other payments under the Affini-T Agreement, including additional equity consideration and development and regulatory milestones, also represent variable consideration, and are constrained to the extent that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in future periods. As of December 31, 2022 and September 30, 2023, additional equity consideration and future development and regulatory milestone payments were excluded from the estimated total transaction price as they were considered constrained. The transaction price is reevaluated in each reporting period and as changes in circumstances occur. We recognize revenue each reporting period based on the measure of progress using an estimated cost-based input method.

We recognized \$2.6 million in collaboration revenue in the consolidated statements of operations and comprehensive loss during the year ended December 31, 2022. We recognized \$0.9 million and \$3.7 million in collaboration revenue in the condensed consolidated statements of operations and comprehensive loss during the nine months ended September 30, 2022 and 2023, respectively. As of December 31, 2022, we recorded \$1.3 million in contract assets on the consolidated balance sheet, related to services performed but not invoiced. There was no contract asset related to services performed as of September 30, 2023. As of September 30, 2023, we recorded \$2.4 million in accounts receivable on the condensed consolidated balance sheet, related to services performed. As of December 31, 2022 and September 30, 2023, deferred revenue related to the Affini-T Agreement was zero and \$0.6 million, respectively. In June 2023, the joint steering committee approved the budget for estimated research reimbursement costs for the Affini-T Agreement, which resulted in a \$2.4 million reduction to variable consideration. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligation was approximately \$2.1 million as of September 30, 2023, which we expect to recognize as revenue over the next four-to-five years.

For additional information regarding the Affini-T Agreement, please see the section titled “Business—Our License and Collaboration Agreements.”

Ionis Collaboration and License Agreement

On November 10, 2022, the effective date, we entered into a Collaboration and License Agreement (the “Ionis Agreement”) with Ionis to collaborate on drug discovery and exploratory research activities to advance new medicines using gene editing strategies, with the goal of discovering novel medicines. Pursuant to the terms of the Ionis Agreement, we granted Ionis and its affiliates a worldwide exclusive, royalty-bearing license, with the right to grant sublicenses, to use all licensed systems and licensed products in the field of *in vivo* gene editing for all therapeutic, prophylactic, palliative, and analgesic uses in humans. In connection with the Ionis Agreement, we also have the right to exercise an exclusive option to co-develop and co-commercialize certain products under a drug discovery program. A joint steering committee was established by both parties to coordinate, oversee, and monitor the research and drug discovery activities under the Ionis Agreement.

We will collaborate to discover therapeutic products under a drug discovery program and develop a drug discovery plan for each target, selected by Ionis. The target selection is divided into two waves: up to four targets in Wave 1 and up to four targets in Wave 2. For each drug discovery program, once the parties identify a

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development candidate that is suitable for further development, Ionis will be responsible for the development and commercialization of products resulting from such program. Per the terms of the Ionis Agreement, at any time prior to the designation of a development candidate for a drug discovery program and for any reason, Ionis may replace the collaboration target, provided such target has not previously been substituted out. Ionis may substitute (i) up to two Wave 1 targets and (ii) up to two Wave 2 targets.

The drug discovery activities for a program commence on the selection of a target and expire upon the earlier of (a) completion of all drug discovery activities for such program, (b) the fifth anniversary of the effective date and (c) selection of a development candidate for such drug discovery program. If one or more Wave 2 targets become collaboration targets as a result of the parties achieving enabled delivery and less than two years are remaining in the drug discovery term, then the term will be extended to the earlier of (i) the time that we complete all of our activities under the applicable drug discovery plan and (ii) the seventh anniversary of the effective date, subject to our consent.

We will also conduct an exploratory research program, and will jointly optimize gRNA and select delivery technologies and other activities. The exploratory research activities commence on the effective date and expire upon the earlier of (a) completion of all exploratory research activities established in the exploratory research plan, and (b) the fifth anniversary of the effective date.

We have the exclusive option to co-develop and co-commercialize the licensed products under a drug discovery program (the "Co-Co Option") with Ionis. The Co-Co Option may be exercised for (a) the initial Wave 1 target ("Target 1"), (b) no more than one of the other three discovery programs for the Wave 1 targets, and (c) no more than two drug discovery programs for the Wave 2 targets that become collaboration targets. If we exercise the Co-Co Option for a particular drug discovery program, that drug discovery program will automatically be deemed a "Co-Co Program", all corresponding licensed products be deemed "Co-Co Products," we will be obligated to pay Ionis an option exercise fee, and we and Ionis will enter into a separate co-development and co-commercialization agreement. The Co-Co Option exercise fee will equal 50% of Ionis' internal costs and out-of-pocket costs incurred in the conduct of the drug discovery activities prior to the exercise of the Co-Co Option and be reduced by 50% of our corresponding costs incurred. Future development and commercialization costs will be shared equally. We may elect to reduce our cost-share percentage anywhere between 50% and 25% on a go-forward basis, provided we will continue to bear 50% of the costs of any clinical trials ongoing at the time of the election through the completion of the clinical trials. We will manufacture all licensed systems and certain components of the applicable licensed products that are needed by Ionis for use in its development activities and all of our manufactured components needed by Ionis for use in its commercialization activities. We will provide the manufactured components at a price that represents the cost of goods plus 15%.

Pursuant to the terms of the Ionis Agreement, we have also been granted an option to obtain a non-exclusive, royalty-bearing license, with the right to grant sublicenses, for certain Ionis' background technology to use in up to eight therapeutic products discovered by us in the field of *in vivo* gene editing and directed to a Collaboration Target (each such product, a "Metagenomi Product" and each such option an "Ionis IP Option"), but subject to encumbrance checks with respect to particular targets. A Collaboration Target is a target that is selected by Ionis, and, with respect to us, is not the subject of discussions with a third party, is not the subject of a contractual grant of rights to a third party nor the subject of an internal research and development program. If we exercise our Ionis IP Option, we will pay to Ionis up to several million dollars per Metagenomi Product upon achievement of certain clinical and regulatory milestones. We are also obligated to pay Ionis royalties in an amount equal to a low single-digit royalty on the net sales of the applicable Metagenomi Product on product-by-product and country-by-country basis.

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In November 2022, we received an \$80.0 million upfront payment from Ionis for the Wave 1 drug discovery research collaboration and selected Target 1. Ionis selected its second target ("Target 2") in Wave 1 in December 2022 and its third target ("Target 3") in Wave 1 in November 2023. In November 2023, we agreed to extend the period during which we expect Ionis will select its fourth target ("Target 4") in Wave 1 by an additional three months from the 12-month anniversary of the effective date, as permitted under the arrangement. Ionis has an option to select up to four Wave 2 targets at any time during the drug discovery term, if (a) an IND for any licensed product directed to a Wave 1 target is filed with the applicable regulatory authority or (b) the parties achieve enabled delivery for a non-liver target under the exploratory research activities, by providing written notice and by paying a Wave 2 target selection fee of \$15.0 million or \$30.0 million, depending on and per the selected target.

Ionis is obligated to reimburse us for all internal costs and out-of-pocket costs incurred in the performance of the exploratory research activities, up to an aggregate of \$10.0 million, which is payable in quarterly installments of \$0.5 million during the exploratory research term. As of September 30, 2023, we received a total of \$1.5 million related to the reimbursable expenses. We are also eligible to receive (a) up to \$29.0 million in future development milestone payments for each licensed product; (b) up to \$60.0 million in future regulatory milestone payments for each licensed product; (c) up to \$250.0 million in sales-based milestones for each licensed product; and (d) royalties on annual net sales of licensed products from a mid-single-digit to low-teens percentage, subject to customary reductions.

The term of the Ionis Agreement will continue (i) with respect to the drug discovery programs, until the expiration of all applicable royalty terms for a licensed product, (ii) with respect to the Co-Co Programs, until the parties cease all exploitation for the Co-Co Products that are the subject to such Co-Co Program, and (iii) with respect to the Metagenomi Products, until the expiration of the royalty term for a Metagenomi Product. The royalty term ends on the latest of the following two dates: (i) the expiration of (A) the last claim of any issued and unexpired patent, or (B) a claim within a patent application that has not been pending for more than seven years from the earliest date to which the claim or applicable patent application is entitled to claim priority and which claim has not been revoked, cancelled, withdrawn, held invalid, or abandoned, or (ii) 12 years following the first commercial sale of a licensed product.

The Ionis Agreement may be terminated during the term by either party for an uncured material breach or bankruptcy by the other party. Additionally, Ionis may terminate the Ionis Agreement for convenience and without penalty, in its entirety or on a licensed product-by-licensed product basis, by providing 90 days' written notice.

We concluded that the Ionis Agreement is in the scope of ASC 606 at the effective date and until we exercise our Co-Co Option for any drug discovery program, which was determined to not be probable at the effective date and as of December 31, 2022 and September 30, 2023. We also concluded that exclusive licenses and participation in a joint steering committee are not distinct from discovery research services and should thus be combined into one performance obligation (the "discovery program"). We also concluded that exploratory research services are a separate and distinct performance obligation (the "exploratory program"). As the Ionis options for Wave 2 targets are optional purchases and do not have significant incremental discounts, as such, the options do not provide material rights.

We allocated the total estimated transaction price of \$90.0 million, which consisted of an \$80.0 million upfront payment received in November 2022 and a \$10.0 million reimbursement for research costs, into two performance obligations, and was determined based on their estimated standalone selling prices. We concluded that future development and commercial supply agreements are at market terms, as the terms were consistent with industry standards as of the effective date. We constrain future milestone payments under the arrangement to the extent that the inclusion of such variable consideration could result in a significant reversal

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of cumulative revenue in future periods. We constrained all development and regulatory milestone payments at the effective date and as of December 31, 2022 and September 30, 2023. We are recognizing revenue of \$80.0 million related to the discovery program and of \$10.0 million related to exploratory program over the research terms using an estimated cost-based input method as a measure of progress for each obligation.

We recognized \$0.1 million in collaboration revenue in the consolidated statements of operations and comprehensive loss during the year ended December 31, 2022. We recognized \$14.4 million in collaboration revenue in the condensed consolidated statements of operations and comprehensive loss during the nine months ended September 30, 2023, which was included in deferred revenue as of December 31, 2022. As of December 31, 2022 and September 30, 2023, deferred revenue related to the Ionis Agreement was \$79.9 million and \$67.0 million, respectively. The value of the transaction price allocated to the remaining performance obligations was approximately \$75.5 million as of September 30, 2023, which we expect to recognize as revenue over the next four-to-five years.

For additional information regarding the Ionis Agreement, please see the section titled "Business—Our License and Collaboration Agreements."

Amendment to the LLC Agreement

Our LLC Agreement was amended on July 31, 2023 to provide for "catch-up" distributions for profits interests once the applicable catch-up threshold amount for such profits interests was met (the "Amendment to the LLC Agreement").

The LLC Agreement provides each profits interest with a distribution threshold amount, which is determined on the date of issuance and represents the amount that would be distributed if, immediately after issuance, we sold all of our assets at fair market value and distributed the net proceeds in liquidation. A profits interest does not participate in our distributions until an amount equal to its distribution threshold amount has been distributed to our other members with units that either have a lower threshold amount or no threshold amount.

Once the applicable distribution threshold amount has been met for a particular profits interest, such profits interest will participate in our distributions on a pro rata basis until the catch-up threshold amount has been met. Once the catch-up threshold amount has been met, subsequent "catch-up" distributions will be made solely to holders of profits interests until such holders have received an amount equal to the amount such holders would have received had the distribution threshold not existed. Once the profits interest holders have received distributions in an amount equal to what they would have received had the distribution threshold not existed, all subsequent distributions are made on a pro rata basis with common unitholders.

The catch-up threshold amount of \$11.84 per unit reflected the estimated fair value of the common unit as of July 31, 2023, as determined by our board of managers, with input from management, and considering our most recently available third-party valuation of common units. The amendment to the LLC Agreement resulted in a change to the fair value of the profits interests and is accounted for as a modification of the profits interests' awards. We estimated total modification expense of \$10.3 million. We recognized \$1.1 million associated unit-based compensation expense related to vested profits interests as of the modification date, and the remaining \$9.2 million is expected to be recognized over the next 3.3 years, as profits interests continue to vest.

Reorganization

We currently operate as a Delaware limited liability company under the name Metagenomi Technologies, LLC. Prior to the effectiveness of this registration statement, we intend to complete a series of transactions pursuant to which Metagenomi Technologies, LLC will merge with and into its wholly-owned subsidiary, Metagenomi, Inc., a

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Delaware corporation, with Metagenomi, Inc. continuing as the surviving corporation. In connection with the Reorganization (i) all of the outstanding common unitholders of Metagenomi Technologies, LLC will receive shares of common stock of Metagenomi, Inc., (ii) all of the outstanding redeemable convertible preferred unitholders of Metagenomi Technologies, LLC will receive shares of redeemable convertible preferred stock of Metagenomi, Inc. and (iii) all of the outstanding holders of profits interests in Metagenomi Technologies, LLC will receive shares of common stock or restricted common stock in Metagenomi, Inc. For more information on the Reorganization, see the section titled "Reorganization" included elsewhere in this prospectus.

Components of Results of Operations

Collaboration Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products for the foreseeable future. Our ability to generate product revenues will depend on the successful development and eventual commercialization of any product candidates that we identify. If we fail to complete the development of any future product candidates in a timely manner or to obtain regulatory approval for such product candidates, our ability to generate future revenue and our results of operations and financial position would be materially adversely affected.

To date, all of our revenue consists of collaboration revenue, earned from collaboration agreements with Moderna, Ionis and Affini-T. These agreements may include the following types of promised goods or services: (i) grants of licenses, (ii) performance of research and development services and (iii) participation on joint research and/or development committees. They also may include options to obtain licenses to our intellectual property or to extend the term of the research activities. Our revenues under such collaboration agreements were \$0.2 million and \$17.2 million for the years ended December 31, 2021 and 2022, respectively. Our revenues under collaboration agreements were \$11.6 million and \$32.4 million for the nine months ended September 30, 2022 and 2023, respectively.

For additional information about our revenue recognition policy related to our collaboration agreements, refer to Note 2 in our audited consolidated financial statements included elsewhere in this prospectus.

Operating Expenses

Our operating expenses consist of (i) research and development expenses and (ii) general and administrative expenses.

Research and Development

The largest component of our total operating expenses since our inception has been research and development activities. Research and development expenses consist primarily of compensation and benefits for research and development employees, including unit-based compensation; the costs of acquiring research and development supplies and services; manufacturing process development costs; the research and development expenses that we share with our collaboration partners for co-development programs; other outside services and consulting costs; and allocated facilities, information technology and overhead expenses. Research and development costs are expensed as incurred.

We have not reported program costs since our inception because we have not historically tracked or recorded our research and development expenses on a program-by-program basis. We use our personnel and infrastructure resources across the breadth of our research and development activities, which are directed toward developing our platform.

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We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our platform, including investments in manufacturing, as we advance our programs and conduct clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our platform is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects, the costs of related clinical development costs or when and to what extent we will generate revenue from the commercialization of our platform.

General and Administrative

General and administrative expenses consist primarily of personnel costs, including unit-based compensation expense and other expenses for outside professional services, including legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, consulting and tax services; insurance costs; administrative travel expenses; website development costs; marketing and public relations costs; and facilities, information technology and other allocated overhead costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support development of our platform and our continued research activities. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with being a public company. We also expect our intellectual property expenses to increase as we expand our intellectual property portfolio.

Total Other Income, Net

Total other income, net includes interest income from our investments in available-for-sale marketable securities, grant income, change in fair value of our investments in the Affini-T convertible note, preferred stock and common stock shares related to our investment in Affini-T interest expense on the Moderna convertible note issued in November 2021, which was converted into redeemable convertible preferred units in January 2022.

Provision for Income Taxes

Metagenomi Technologies, LLC is taxed under the provisions of Subchapter K — Partners and Partnerships of the Internal Revenue Code. Under those provisions, Metagenomi Technologies, LLC does not pay federal or state corporate income taxes on its taxable income. Instead, each member includes net operating income or loss for Metagenomi on its individual return.

The wholly owned subsidiary of Metagenomi Technologies, LLC, Metagenomi Inc., is a corporation for tax purposes and is subject to income taxes. We recognized income tax expense for the year ended December 31, 2022 and for the nine months ended September 30, 2022 and 2023 for domestic federal and state income taxes. After giving effect to this offering, Metagenomi, Inc. will continue as the surviving corporation.

As of December 31, 2022, we had net operating loss carryforwards of \$0.02 million and \$8.3 million for federal and state income tax purposes, respectively, available to reduce future taxable income, if any. The federal net operating loss carryforwards do not expire. State net operating loss carryforwards begin expiring in 2037. As of December 31, 2022, we had state research and development credit carryforwards of \$2.8 million, which do not expire. As of December 31, 2022, we had no federal research and development credit carryforwards.

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A valuation allowance is provided for deferred tax assets where the recoverability of the assets is uncertain. The determination to provide a valuation allowance is dependent upon the assessment of whether it is more likely than not that sufficient future taxable income will be generated to utilize the deferred tax assets. Based on the weight of the available evidence, which includes our consolidated entities' historical operating losses and forecast of future losses, we have provided a full valuation allowance against the deferred tax assets resulting from the tax loss and credits carried forward.

Utilization of the net operating loss and credit carryforwards may be subject to a substantial annual limitation due to an ownership change limitation as provided by section 382 of the Internal Revenue Code, as amended, and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization. In the event that we have a change of ownership, utilization of the net operating loss and tax credit carryforwards may be restricted.

Results of Operations

Comparison of the Nine Months Ended September 30, 2022 and 2023

The following table summarizes our results of operations for the nine months ended September 30, 2022 and 2023 (in thousands):

	Nine Months ended September 30,		Change \$
	2022	2023	
Collaboration revenue	\$ 11,605	\$ 32,357	\$ 20,752
Operating expenses:			
Research and development	28,082	69,648	41,566
General and administrative	12,397	21,005	8,608
Total operating expenses	40,479	90,653	50,174
Loss from operations	(28,874)	(58,296)	(29,422)
Other income (expense)			
Interest expense	(98)	—	98
Interest income	1,489	11,836	10,347
Change in fair value of long-term investments	94	2,870	2,776
Other income (expense), net	146	(70)	(216)
Total other income, net	1,631	14,636	13,005
Net loss before provision for income taxes	(27,243)	(43,660)	(16,417)
Provision for income taxes	(1,723)	(5,301)	(3,578)
Net loss	\$ (28,966)	\$ (48,961)	\$ (19,995)

Collaboration Revenue

Our revenue consists of collaboration revenue recognized under our agreements with Moderna, Affini-T and Ionis. We recognize revenue as the performance obligations are satisfied. Collaboration revenue increased by \$20.8 million, from \$11.6 million for the nine months ended September 30, 2022 to \$32.4 million for the nine months ended September 30, 2023. The increase in collaboration revenue for the nine months ended September 30, 2023, was primarily driven by an increase in revenue of \$14.4 million related to the Ionis agreement, which we entered in November 2022. We did not recognize revenue under this agreement during the nine months ended September 30, 2022. Collaboration revenue related to Moderna and Affini-T agreements

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increased by \$6.3 million for the nine months ended September 30, 2023 compared to the nine months ended September 30, 2022, as we performed more services and our collaboration activities progressed.

The collaboration revenue for the nine months ended September 30, 2022 and 2023 included the following (in thousands):

	Nine Months ended September 30,		Change \$
	2022	2023	
Moderna	\$ 10,710	\$ 14,197	\$ 3,487
Affini-T	895	3,744	2,849
lonis	—	14,416	14,416
Total collaboration revenue	\$ 11,605	\$ 32,357	\$ 20,752

Research and Development Expenses

The following table summarizes our research and development expenses for the periods indicated (in thousands):

	Nine Months ended September 30,		Change \$
	2022	2023	
Personnel-related costs	\$ 15,132	\$ 28,099	\$ 12,967
Laboratory materials and supplies	7,302	15,361	8,059
Facilities and overhead costs	4,856	15,431	10,575
Other research and development expenses and consulting costs	792	10,757	9,965
Total research and development expenses	\$ 28,082	\$ 69,648	\$ 41,566

Research and development expenses increased by \$41.6 million, from \$28.1 million for the nine months ended September 30, 2022 to \$69.6 million for the nine months ended September 30, 2023.

Personnel-related costs, including employee payroll and related expenses, increased by \$13.0 million, including a \$1.6 million increase in unit-based compensation expense, as a result of increased headcount in our research and development organization, increase in fair value of common units and recognition of modification expense resulting from the Amendment to the LLC Agreement in July 2023. Laboratory materials and supplies increased by \$8.1 million due to significant expansion of our research and development operations. Facilities and allocated overhead costs, including rent and facilities, depreciation and amortization, repairs and maintenance and information technology-related expenses allocated to research and development increased by \$10.6 million, including a \$5.8 million increase in rent and facilities expenses as we entered into a new lease agreement in November 2022 that commenced in January 2023, and a \$1.9 million increase in depreciation and amortization expense as we continue investing in our manufacturing facility. Other research and development and consulting costs increased by \$10.0 million mainly due to external research and development costs of \$5.9 million and consulting services of \$1.6 million to support our research and pre-clinical development activities.

Other research and development and consulting costs include expenses related to the DT Co-Co program under the Moderna Agreement. Each quarter, a true-up is performed to calculate how much is owed by us or Moderna to equally split the costs incurred during the quarter towards the DT Co-Co program. When Moderna owes a payment to us, we account for this as a reduction of research and development expense. When we owe a

payment to Moderna, we account for this as an addition to research and development expense. For the nine months ended September 30, 2022 and 2023, the total cost true-ups reduced our research and development expenses by \$0.5 million and \$0.3 million, respectively. Additionally, we amortized \$2.7 million and \$0.5 million of the upfront \$5.0 million payment received from Moderna allocated to the DT Co-Co program to offset our share of the DT Co-Co development costs for the nine months ended September 30, 2022 and 2023, respectively.

General and Administrative Expenses

General and administrative expenses increased by \$8.6 million, from \$12.4 million for the nine months ended September 30, 2022 to \$21.0 million for the nine months ended September 30, 2023, as we continued expanding our operations to support our business strategy and the development of therapeutic programs utilizing our metagenomics platform.

Employee payroll and related expenses increased by \$4.5 million, including a \$1.7 million increase in unit-based compensation expense, as a result of increase in headcount of our executives and administrative personnel, increase in fair value of common units and recognition of modification expense resulting from the Amendment to the LLC Agreement in July 2023. Expenses related to professional consulting services increased by \$3.7 million due to increased spending on consulting and outside services to support our growing operations. Other general and administrative expenses, including rent, facilities, insurance, information technology, office supplies, subscriptions and licenses and other miscellaneous expenses, increased by \$0.4 million.

Total Other Income, Net

Total other income, net, increased by \$13.0 million, from \$1.6 million net income for the nine months ended September 30, 2022 to \$14.6 million for the nine months ended September 30, 2023.

Interest income, which includes interest income and amortization of premiums and discounts on our investments in available-for sale marketable securities, increased by \$10.3 million from \$1.5 million for the nine months ended September 30, 2022 to \$11.8 million for the nine months ended September 30, 2023, due to increased investment activity and higher interest rates during the nine months ended September 30, 2023.

The change in fair value of long-term investments increased by \$2.8 million, from \$0.1 million for the nine months ended September 30, 2022 to \$2.9 million for the nine months ended September 30, 2023, as our investment in Affini-T was re-measured at fair value. For more details on our investment in Affini-T, refer to Note 5 in our unaudited condensed consolidated financial statements included elsewhere in this prospectus.

Provision for Income Taxes

We recognized an income tax provision as a result of our taxable income related to upfront payments received under the Moderna and Ionis agreements and the change in the net capitalization of our research and development expenses under the newly enacted Internal Revenue Code Section 174 ("Section 174"), which became effective on January 1, 2022. Section 174 changed the tax treatment of research and experimentation (R&E) expenditures, which requires the capitalization of R&E expenditures over a period of five years for R&E paid or incurred in the United States and 15 years for R&E paid or incurred outside of the United States.

For the nine months ended September 30, 2022 and 2023, we recorded a provision for income taxes of \$1.7 million and \$5.3 million by applying the estimated annual effective tax rate to the year-to-date measure of ordinary income, respectively. The increase in the income tax provision during the nine months ended September 30, 2023 is primarily due to the increase in forecasted research and development spend, which

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results in corresponding increases to Section 174 capitalization, and taxable income related to the Ionis upfront payment which is partially offset by an increase in forecasted research and development credit.

Comparison of the Years Ended December 31, 2021 and 2022

The following table summarizes our results of operations for the years ended December 31, 2021 and 2022 (in thousands):

	Years ended December 31,		Change \$
	2021	2022	
Collaboration revenue	\$ 243	\$ 17,200	\$ 16,957
Operating expenses:			
Research and development	14,478	43,139	28,661
General and administrative	9,712	18,701	8,989
Total operating expenses	24,190	61,840	37,650
Loss from operations	(23,947)	(44,640)	(20,693)
Other income (expense)			
Interest expense	(302)	(98)	204
Interest income	43	3,419	3,376
Change in fair value of long-term investments	2,760	94	(2,666)
Other income, net	4	201	197
Total other income, net	2,505	3,616	1,111
Net loss before provision for income taxes	(21,442)	(41,024)	(19,582)
Provision for income taxes	—	(2,569)	(2,569)
Net loss	\$ (21,442)	\$ (43,593)	\$ (22,151)

Collaboration Revenue

Our revenue consists of collaboration revenue recognized under our agreements with Moderna, Affini-T and Ionis. We recognize revenue as the performance obligations are satisfied. Collaboration revenue increased by \$17.0 million, from \$0.2 million for the year ended December 31, 2021 to \$17.2 million for the year ended December 31, 2022. The increase in collaboration revenue for the year ended December 31, 2022, was primarily driven by a \$14.3 million increase in revenue related to the Moderna Agreement as our research and collaboration activities progressed and a \$2.7 million increase related to the Affini-T and Ionis agreements, which we entered into in June and November 2022, respectively.

The collaboration revenue for the years ended December 31, 2021 and 2022 included the following:

	Years ended December 31,		Change \$
	2021	2022	
Moderna	\$ 243	\$ 14,518	\$ 14,275
Affini-T	—	2,570	2,570
Ionis	—	112	112
Total collaboration revenue	\$ 243	\$ 17,200	\$ 16,957

Research and Development Expenses

The following table summarizes our research and development expenses for the periods indicated (in thousands):

	Years ended December 31,		Change \$
	2021	2022	
Personnel-related costs	\$ 6,962	\$ 22,436	\$ 15,474
Laboratory materials and supplies	3,514	10,518	7,004
Facilities and overhead costs	3,119	7,325	4,206
Other research and development expenses and consulting costs	883	2,860	1,977
Total research and development expense	\$ 14,478	\$ 43,139	\$ 28,661

Research and development expenses increased by \$28.7 million, from \$14.5 million for the year ended December 31, 2021 to \$43.1 million for the year ended December 31, 2022.

Personnel-related costs, including employee payroll and related expenses, increased by \$15.5 million, including a \$0.7 million increase in unit-based compensation expense, as a result of increased headcount in our research and development organization. Laboratory materials and supplies increased by \$7.0 million due to significant expansion of our research and development operations. Facilities and allocated overhead, including rent, repairs and maintenance costs, common facilities and information technology related expenses allocated to research and development increased by \$4.2 million as a result of the expansion of our business operations. Other research and development and consulting costs increased by \$2.0 million due to increases in external consulting services to support our research and pre-clinical development activities.

Other research and development and consulting costs include expenses related to the DT Co-Co program under our collaboration agreement with Moderna. Each quarter, a true-up is performed to calculate how much is owed by us or Moderna to equally split the costs incurred during the quarter towards the DT Co-Co program. When Moderna owes a payment to us, we account for this as a reduction of research and development expense. When we owe a payment to Moderna, we account for this as an addition to research and development expense. For the years ended December 31, 2021 and 2022, the total cost true-ups reduced our research and development expenses by \$0.2 million and \$0.9 million, respectively. Additionally, for the year ended December 31, 2021, \$5.0 million of the upfront payment received under the Moderna Agreement in November 2021 was allocated to the DT Co-Co program, which was presented as a collaboration advance on our consolidated balance sheet. For the years ended December 31, 2021 and 2022, \$0.3 million and \$3.5 million of this upfront payment was amortized, respectively, to offset our share of the DT Co-Co development costs.

General and Administrative Expenses

General and administrative expenses increased by \$9.0 million, from \$9.7 million for the year ended December 31, 2021 to \$18.7 million for the year ended December 31, 2022.

Employee payroll and related expenses increased by \$3.3 million, including a \$0.7 million increase in unit-based compensation expense, as a result of increase in headcount of our executives and administrative personnel. Expenses related to professional consulting services increased by \$4.1 million due to increased spending on consulting and outside services to support our growing operations. Other general and administrative expenses, including insurance, information technology, office supplies, subscriptions and licenses, and other miscellaneous expenses, increased by \$1.6 million as we continued expanding our operations to support our business strategy and the development of therapeutic programs utilizing our metagenomics platform.

Total Other Income, Net

Total other income, net, increased by \$1.1 million, from \$2.5 million net income for the year ended December 31, 2021 to \$3.6 million for the year ended December 31, 2022.

Interest income, which includes interest income and amortization of premiums and discounts on our investment in available-for sale marketable securities, increased by \$3.4 million from \$0.04 million for the year ended December 31, 2021 to \$3.4 million for the year ended December 31, 2022, due to increased investment activity and higher interest rates during the year ended December 31, 2022.

The change in fair value of long-term investments decreased by \$2.7 million, from \$2.8 million for the year ended December 31, 2021 to \$0.1 million for the year ended December 31, 2022, as our investment in the Affini-T convertible promissory note was re-measured at fair value and converted to preferred stock shares of Affini-T in March 2022. For more details on our investment in the Affini-T convertible promissory note, refer to Note 5 in our audited consolidated financial statements included elsewhere in this prospectus.

Provision for Income Taxes

We recognized an income tax provision of \$2.6 million for the year ended December 31, 2022 as a result of our taxable income related to an upfront payment received under the Moderna Agreement and the change in the net capitalization of our research and development expenses under the newly enacted Internal Revenue Code Section 174 ("Section 174"), which became effective on January 1, 2022. Section 174 changed the tax treatment of research and experimentation (R&E) expenditures, which requires the capitalization of R&E expenditures over a period of five years for R&E paid or incurred in the United States and 15 years for R&E paid or incurred outside of the United States. We did not recognize income taxes for the year ended December 31, 2021.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant operating losses. We have historically funded our operations primarily through sales of our redeemable convertible preferred units and convertible promissory notes, which generated approximately \$351.6 million in aggregate gross proceeds. Additionally, through September 30, 2023, we received approximately \$120.0 million upfront cash payments from collaboration and licensing agreements. As of September 30, 2023, we had \$292.9 million in cash, cash equivalents and available-for-sale marketable securities.

Future Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the development of our platform. In addition, upon the completion of this offering, we expect to incur additional costs associated with operating as a public company. The timing and amount of our operating expenditures will depend largely on:

- the timing and progress of research and development, preclinical and clinical development activities;
- the number, scope and duration of clinical trials required for regulatory approval of our future product candidates;
- the costs, timing, and outcome of regulatory review of any of our future product candidates;
- the costs of manufacturing clinical and commercial supplies of our future product candidates;

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- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our future product candidates for which we receive regulatory approval;
- the cost of filing and prosecuting our patent applications, and maintaining and enforcing our patents and other intellectual property rights;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements, and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- any product liability or other lawsuits related to our future product candidates;
- our implementation of various computerized informational systems and efforts to enhance operational systems;
- expenses incurred to attract, hire and retain skilled personnel;
- the costs of operating as a public company;
- our ability to establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payers;
- the extent to which we acquire or invest in businesses, products, and technologies;
- the effect of competing technological and market developments; and
- the impact of the COVID-19 pandemic, as well as other factors, including inflation, economic uncertainty and geopolitical tensions, which may exacerbate the magnitude of the factors discussed above.

As of September 30, 2023, we had \$292.9 million in cash, cash equivalents and available-for-sale marketable securities. We believe that our existing cash, cash equivalents and available-for-sale marketable securities will be sufficient to fund our current operating plan for at least the next 12 months. Based on our current operating plan, we estimate that our existing cash, cash equivalents and available-for-sale marketable securities, together with the estimated net proceeds from this offering, will be sufficient to fund our projected operating expenses and capital expenditure requirements into . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. We expect that we will require additional funding to: continue our current research development activities; develop, maintain, expand and protect our intellectual property portfolio; further develop our platform; and hire additional research, clinical and scientific personnel. If we receive regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize our products.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and marketing, distribution or licensing arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interest for existing investors may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect existing investors' rights as a stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or

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product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

The following table summarizes our sources and uses of cash for the periods presented (in thousands):

	Years ended December 31,		Nine Months ended September 30,	
	2021	2022	2022	2023
Net cash provided by (used in) operating activities	\$ 24,257	\$ 29,724	\$ (38,009)	\$ (70,817)
Net cash used in investing activities	(74,316)	(122,200)	(83,326)	(14,898)
Net cash provided by financing activities	39,922	239,594	144,304	2,346
Net (decrease) increase in cash, cash equivalents and restricted cash	\$ (10,137)	\$ 147,118	\$ 22,969	\$ (83,369)

Cash Flows from Operating Activities

Net cash used in operating activities for the nine months ended September 30, 2022 was \$38.0 million. This was primarily due to our net loss for the period of \$29.0 million, decreased by net non-cash charges of \$3.2 million and increased by a net reduction of \$12.2 million in our net operating assets and liabilities. The net non-cash charges primarily consisted of \$1.4 million in unit-based compensation expense, \$1.0 million in non-cash lease expense and \$1.0 million in depreciation and amortization expense. The net change in our operating assets and liabilities primarily consisted of a \$14.3 million decrease in deferred revenue and collaboration advances as we recognized collaboration revenue under the Moderna and Affini-T agreements and a \$1.4 million increase in prepaid expenses and other current assets, partially offset by a \$2.1 million increase in accrued expenses and other current liabilities, a \$1.0 million increase in income tax payable and a \$0.7 million increase in other non-current liabilities.

Net cash used in operating activities for the nine months ended September 30, 2023 was \$70.8 million. This was primarily due to our net loss of \$49.0 million, decreased by net non-cash charges of \$0.2 million and increased by a net reduction of \$22.1 million in our net operating assets and liabilities. The net non-cash charges consisted of \$4.5 million in unit-based compensation expense, \$3.1 million in non-cash lease expense and \$3.0 million in depreciation and amortization expense, all partially offset by \$6.9 million credit related to amortization of the discounts on available-for-sale marketable securities, \$2.9 million for the change in fair value of our investments in Affini-T and \$0.7 million in amortization of non-cash collaboration revenue related to the Affini-T Agreement. The net change in our operating assets and liabilities primarily consisted of a \$25.0 million decrease in deferred revenue and collaboration advances as we recognized revenue under our collaboration agreements, and a \$3.9 million increase in accounts receivable related to the Affini-T Agreement and the Moderna Agreement, a \$1.0 million decrease in operating lease liabilities due to recurring payments under the existing lease agreements, all partially offset by a \$2.4 million increase in accounts payable due to the timing of payments to our vendors, a \$2.4 million increase in other non-current liabilities, a \$1.3 million decrease in contract assets related to the Affini-T Agreement, a \$0.7 million increase in accrued expenses and other current liabilities, a \$0.6 million increase in income tax payable due to additional tax expense, and a \$0.4 million decrease in prepaid expenses and other current assets.

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Net cash provided by operating activities for the year ended December 31, 2021 was \$24.3 million. This is primarily due to our net loss for the period of \$21.4 million adjusted by net non-cash charges of \$0.6 million and a net change of \$46.3 million in our net operating assets and liabilities. The non-cash charges primarily consisted of \$2.8 million for the change in fair value of our investment in the Affini-T convertible note and \$0.9 million for non-cash lease expense. The changes in our net operating assets and liabilities primarily consisted of a \$44.2 million increase in deferred revenue primarily due to the receipt of an upfront payment under the Moderna Agreement, a \$1.9 million increase in accrued expenses and other current liabilities and a \$0.7 million increase in accounts payable, partially offset by a \$0.5 million increase in prepaid expenses and other current assets.

Net cash provided by operating activities for the year ended December 31, 2022 was \$29.7 million. This was primarily due to our net loss of \$43.6 million, adjusted by net non-cash charges of \$3.8 million and a net change of \$69.5 million in our net operating assets and liabilities. The non-cash charges primarily consisted of \$2.0 million of unit-based compensation expense, \$1.7 million of depreciation expense and \$1.3 million for non-cash lease expense, reduced by \$1.1 million for the amortization of the discount on our investment in available-for-sale marketable securities. The changes in our net operating assets and liabilities primarily consisted of a \$65.7 million increase in deferred revenue primarily due to the receipt of an upfront payment under the Ionis Agreement, a \$4.5 million increase in accrued expenses and other current liabilities, a \$1.5 million increase in income tax payable and a \$1.0 million increase in other non-current liabilities, partially offset by an increase of \$2.5 million in prepaid expenses and other current assets and an increase of \$1.3 million in contract assets.

Cash Flows from Investing Activities

Net cash used in investing activities for the nine months ended September 30, 2022 was \$83.3 million, which consisted of \$136.6 million of purchases of available-for-sale marketable securities and \$10.5 million of purchases of property and equipment, partially offset by \$63.8 million in proceeds from maturities and sales of available-for-sale marketable securities.

Net cash used in investing activities for the nine months ended September 30, 2023 was \$14.9 million, which consisted of \$169.0 million of purchases of available-for-sale marketable securities and \$8.1 million of purchases of property and equipment, partially offset by \$162.2 million in proceeds from maturities and sales of available-for-sale marketable securities.

Net cash used in investing activities for the year ended December 31, 2021 was \$74.3 million, which consisted of \$69.3 million of purchases of available-for-sale marketable securities, \$2.9 million of purchases of property and equipment and \$2.2 million investment in preferred stock of VIToria Biotherapeutics, Inc.

Net cash used in investing activities for the year ended December 31, 2022 was \$122.2 million, which consisted of \$214.9 million of purchases of available-for-sale marketable securities, \$14.0 million of purchases of property and equipment, partially offset by \$106.6 million in proceeds from maturities and sales of available-for-sale marketable securities.

Cash Flows from Financing Activities

Net cash provided by financing activities for the nine months ended September 30, 2022 was \$144.3 million, which consisted of net cash proceeds received from the issuance of Series B redeemable convertible preferred units.

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Net cash provided by financing activities for the nine months ended September 30, 2023 was \$2.3 million, which consisted of \$4.3 million of net cash proceeds from our issuance of Series B-1 redeemable convertible preferred units, partially offset by \$1.9 million payments of initial public offering costs.

Net cash provided by financing activities for the year ended December 31, 2021 was \$39.9 million, which consisted of \$30.0 million net cash proceeds received from the issuance of a convertible note and \$9.9 million net cash proceeds from our issuance of Series A-5 preferred units.

Net cash provided by financing activities for the year ended December 31, 2022 was \$239.6 million, which consisted of net cash proceeds from our issuance of Series B and Series B-1 preferred units.

Contractual Obligations and Commitments

Leases

As of December 31, 2022, our future remaining operating lease payments were \$3.3 million within the next twelve months and \$23.9 million for the remainder of the leases' terms, with respect to leases already commenced as of such date. In addition, we entered into a lease in November 2022 with a lease commencement date in January 2023, for which we are obligated to make lease payments of \$2.9 million in the next twelve months and \$46.2 million through March 2031.

As of September 30, 2023, we leased our office and laboratory space under three lease agreements with a weighted-average remaining lease term of 7.4 years. Remaining lease obligations under our non-cancellable leases were \$72.3 million as of September 30, 2023, including \$1.6 million payable through December 31, 2023 and \$70.7 million for the remainder of the leases' terms.

Refer to Note 10 in our audited consolidated financial statements and Note 8 in our unaudited condensed consolidated financial statements included elsewhere in this prospectus for more information on our lease obligations.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 2 to our consolidated financial statements included elsewhere in this prospectus.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles ("GAAP"). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods.

On an ongoing basis, we evaluate our estimates and judgments, including but not limited to those related to revenue recognition under our collaboration agreements, accrued research and development costs, the fair value of common units and unit-based compensation expense, the valuation of deferred tax assets, and uncertain income tax positions. These estimates and assumptions are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates and assumptions could occur in the future. Our estimates are based on our historical experience and on various other factors that we believe

are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our audited consolidated financial statements and unaudited condensed consolidated financial statements included elsewhere in this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Collaboration Arrangements and Revenue Recognition

We apply judgment to determine whether a collaboration agreement is within the scope of revenue recognition, Accounting Standard Codification Topic 606, *Revenue from Contract with Customers*, or other accounting guidance at the effective date and throughout the term of the agreement. We perform the following five steps in determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of these agreements: 1) identification of the promised goods and services in the contract; 2) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; 3) measurement of the transaction price, including any constraint on variable consideration; 4) allocation of the transaction price to the performance obligations; and 5) recognition of revenue when, or as, we satisfy each performance obligation.

Promises in collaboration agreements may include (i) grants of licenses, (ii) performance of research and development services, and (iii) participation on joint research and/or development committees. They also may include options to obtain licenses to our intellectual property or to extend the term of the research activities. We assess whether each promise is a distinct performance obligation and should be accounted for separately or should be combined with other promises into one performance obligation. Judgment is required to determine whether the license to intellectual property is distinct from the research and development services or participation on steering committees. The event-based milestone payments, royalties and cost reimbursements represent variable consideration. We evaluate the probability that the event-based milestones will be achieved and estimates the amount to be included in the transaction price using the most likely amount method. We include cost reimbursement in the transaction price using the expected value method. Unlike other contingency payments, sales-based milestones and royalties are not included in the transaction price based on estimates at the inception of the contract, but rather, are included when sales or usage occur.

To estimate the transaction price, we include upfront payment and variable consideration, such as research and development milestones, reimbursement for our services, that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. These estimates are re-assessed each reporting period as required.

After we estimate the transaction price, we allocate it to the identified performance obligations based on the standalone selling price ("SSP") of each distinct performance obligation. Judgment is required to determine the SSP. In instances where the SSP is not directly observable, such as when a license or service is not sold separately, the SSP is determined using information that may include market conditions and other observable inputs. When licenses are combined with other promises, we utilize our judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If we conclude over time, we recognize revenue based on the measure of progress

using an estimated cost-based input method each reporting period. In applying the cost-based input method, we measure actual costs incurred relative to budgeted costs to fulfill our performance obligation. These budgeted costs consist of our employee full-time equivalent hours plus allowable external (third-party) costs incurred. Management applies considerable judgment in estimating expected costs as such costs are key inputs when applying the cost-based input method. We recognize revenue based on actual costs incurred as a percentage of total budgeted costs as we complete a performance obligation applied to the transaction price. A significant change in the estimate of expected costs for the remainder of a contract term could have a material impact on revenue recognized, including the possible reversal of previously recognized revenue, at each reporting period, as well as a related impact on contract assets and liabilities.

Accrued Research and Development Expenses

Research and development expenses are recognized as services are performed and as costs occur. Research and development expense accruals are estimated based on the level of services performed, progress of the work orders, including the phase or completion of events, and contracted costs. We make significant judgments and estimates in determining the accrual balance at each reporting period. If the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. To date, there have been no material differences between estimates of such expenses and the amounts actually incurred.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized and recorded in prepaid expenses and other current assets, and then expensed as the related goods are delivered or the services are performed.

Unit-Based Compensation Expense

Unit-based compensation expense related to the profits interests granted to employees, consultants and our board of managers members is measured at the grant date based on the fair value of the profits interests. Compensation expense for those awards is recognized over the requisite service period, which is generally the vesting period. We use the straight-line method to record the expense of awards with service-based vesting conditions. We account for forfeitures as they occur.

Prior to July 31, 2023, we used the Black-Scholes option-pricing model to determine the fair value of profits interests. The following summarizes the inputs used:

Common Unit Fair Value — See the subsection titled “—Determination of Fair Value of Common Units” below.

Expected Volatility — Expected volatility was estimated by studying the volatility of the prices of shares of common stock of comparable public companies for similar terms.

Expected Term — Expected term represents the period that our profits interests were expected to be outstanding and expected exit/liquidation term.

Risk-Free Interest Rate — The risk-free interest rate is based on the U.S. Treasury zero-coupon bonds issued in effect at the time of grant for periods corresponding with the expected term of the option.

Expected Dividend — The Black-Scholes valuation model calls for a single expected dividend yield as an input. To date, we have not declared or paid any dividends.

The grant date fair value of profits interests issued and modified beginning from July 31, 2023 was estimated using the valuation model based on the Probability Weighted Expected Return Method (“PWERM”), which is

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further discussed in the section below "Determination of Fair Value of Common Units". The estimated equity fair value was allocated via the distribution waterfall in accordance with the Amendment to the LLC Agreement to all outstanding redeemable convertible preferred units, common units and profits interests.

We recorded unit-based compensation expense of \$0.4 million and \$2.0 million for the years ended December 31, 2021 and 2022, respectively. We recorded unit-based compensation expense of \$1.4 million and \$4.5 million for the nine months ended September 30, 2022 and 2023, respectively. As of September 30, 2023, there was \$19.3 million of total unrecognized unit-based compensation expense, which we expect to recognize over a remaining weighted-average period of 2.9 years. We expect to continue to grant these awards in the future, and to the extent that we do, our unit-based compensation expense recognized in future periods will likely increase.

The intrinsic value of all outstanding profits interests as of September 30, 2023 was \$ million based on the assumed initial public offering price of \$ per share, which is the estimated midpoint of the price range set forth on the cover page of this prospectus, of which approximately \$ million related to vested profits interests and approximately \$ million related to unvested profits interests.

Profits Units Grants

The following table summarizes by grant date the number of profits interests granted from January 1, 2022, the per unit participating threshold amount and the estimated fair value of the common unit on each grant date:

Grant date	Number of profits interests granted	Threshold amount per unit	Estimated fair value per common unit
April 25, 2022	941,755	\$ 3.20	\$ 3.20
May 26, 2022	1,224,466	\$ 3.20	\$ 3.20
July 12, 2022	78,135	\$ 3.20	\$ 3.20
October 28, 2022	519,000	\$ 3.20	\$ 3.20
March 24, 2023*	462,460	\$ 5.75	\$ 6.93
June 25, 2023*	283,330	\$ 7.40	\$ 9.88
June 26, 2023*	1,247,193	\$ 7.40	\$ 9.92
September 4, 2023*	274,830	\$ 11.84	\$ 12.32

* The fair value per common unit for grants during the 2023 fiscal year was interpolated between the valuation reports' dates in connection with a retrospective fair value assessment for accounting purposes.

Determination of Fair Value of Common Units

As there has been no public market for our common units to date, the estimated fair value of our common units has been determined by our board of managers as of the date of each award grant with input from management, considering our most recently available third-party valuations of common unit, and our board of managers' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation ("the Practice Aid").

For valuations performed prior to December 20, 2022, in accordance with the Practice Aid, we determined the option-pricing method ("OPM") was the most appropriate method for determining the fair value of our common unit based on our stage of development and other relevant factors, which used a market approach to estimate

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our enterprise value. Within the OPM framework, the backsolve method for inferring the total equity value implied by a recent financing transaction involves the construction of an allocation model that takes into account our capital structure and the rights, preferences and privileges of each class of unit then assumes reasonable inputs for the other OPM variables (expected time to liquidity, volatility and risk-free rate). The total equity value is then iterated in the model until the model output value for the equity class sold in a recent financing round equals the price paid in that round. The OPM is generally utilized when specific future liquidity events are difficult to forecast (i.e., the enterprise has many choices and options available), and the enterprise's value depends on how well it follows an uncharted path through the various possible opportunities and challenges. In determining the estimated fair value of the common stock, our board of managers also considered the fact that the stockholders could not freely trade the common stock in the public markets. Accordingly, we applied discounts to reflect the lack of marketability of its common stock based on the weighted-average expected time to liquidity. The estimated fair value of the common stock at each grant date reflected a non-marketability discount partially based on the anticipated likelihood and timing of a future liquidity event.

For valuations performed after December 20, 2022, in accordance with the Practice Aid, we determined the hybrid method was the most appropriate method for determining the fair value of our common unit based on our stage of development and other relevant factors. The hybrid method is a PWERM, where the equity value in one or more scenarios is calculated using an OPM. The PWERM is a scenario-based methodology that estimates the fair value of common unit based upon an analysis of future values for the company, assuming various outcomes. The common unit value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of members' units. The future value of the common unit under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common unit. A discount for lack of marketability of the common unit is then applied to arrive at an indication of value for the common unit. In addition to considering the results of independent third-party valuations, our board of managers considered various objective and subjective factors to determine the thresholds for the profits interests as of each grant date, including:

- the prices at which we sold shares of redeemable convertible preferred units and the superior rights and preferences of the redeemable convertible preferred units relative to our common units at the time of each grant;
- the progress of our research and development programs;
- milestones achieved by us;
- the state of the industry and the economy;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering ("IPO"), or our sale in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

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The assumptions underlying these valuations are highly complex and subjective and represent management's best estimates, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common unit and our unit-based compensation expense could be materially different.

Once a public trading market for our common stock has been established in connection with the completion of this offering, it will no longer be necessary for our board of managers to estimate the fair value of our common unit in connection with our accounting for granted profits interests and other such awards we may grant, as the fair value of our common unit or stock will be determined based on the quoted market price of our common unit or stock.

Income Taxes

We are taxed under the provisions of Subchapter K—Partners and Partnerships of the Internal Revenue Code. Under those provisions, we do not pay federal or state corporate income taxes on our taxable income. Instead, each member includes net operating income or loss for us on its individual tax return.

Metagenomi, Inc., our wholly-owned subsidiary, accounts for income taxes using the asset and liability method. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in our audited consolidated financial statements and unaudited condensed consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the accounting and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets will not be realized. We assess the need for a valuation allowance against our deferred tax assets based on all available evidence, including scheduled reversals of deferred tax liabilities, projected future taxable income, tax planning strategies, results of recent operations, and our historical earnings experience by taxing jurisdiction. Significant judgment is required in making this assessment.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Uncertain tax positions are recorded based upon certain recognition and measurement criteria. Significant judgment is required in making this assessment, and, therefore, we re-evaluate uncertain tax positions and consider various factors, including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, and changes in facts or circumstances related to a tax position. We adjust the amount of the liability to reflect any subsequent changes in the relevant facts and circumstances surrounding the uncertain tax positions.

Off-Balance Sheet Arrangements

During the periods presented we did not have, nor do we currently have, any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Quantitative and Qualitative Disclosures About Market Risks

Interest Rate Risk

The primary objectives of our investment activities are to ensure liquidity and to preserve capital. We are exposed to market risks related to changes in interest rates of our cash equivalents and available-for-sale marketable securities. However, due to the nature of these cash equivalents and available-for-sale marketable securities, we do not believe that a hypothetical 10% increase or decrease in interest rates during any of the

periods presented would have had a material effect on our audited consolidated financial statements and unaudited condensed consolidated financial statements included elsewhere in this prospectus.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and research and development costs. We do not believe that inflation had a material effect on our business, results of operations, or financial condition, or on our audited consolidated financial statements and unaudited condensed consolidated financial statements included elsewhere in this prospectus.

Emerging Growth Company Status

We qualify as an “emerging growth company,” as defined in the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include: (i) being permitted to present only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure in this prospectus; (ii) reduced disclosure about our executive compensation arrangements; (iii) not being required to hold advisory votes on executive compensation or to obtain stockholder approval of any golden parachute arrangements not previously approved; (iv) an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002; and (v) an exemption from compliance with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor’s report on the financial statements.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.235 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. Additionally, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, therefore, while we are an emerging growth company we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies. As a result of this election, our audited consolidated financial statements and unaudited condensed consolidated financial statements may not be comparable to those of other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

BUSINESS

Overview




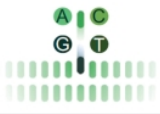

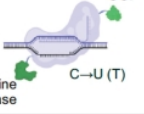

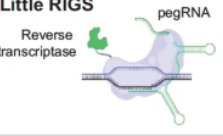

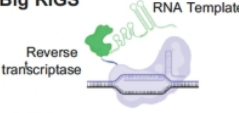

We are a precision genetic medicines company committed to developing curative therapeutics for patients using our proprietary, comprehensive metagenomics-derived genome editing toolbox. Genetic diseases are caused by a diverse set of mutations that have been largely inaccessible by genome engineering approaches to date. Genetic mutations are seen in a variety of forms, including deletions, insertions, single-base-pair changes and sequence repeats, and are found throughout the genome and across a variety of different cell types, tissues, and organ systems. Additionally, many diseases lack a genetic origin but have the potential to be effectively and permanently addressed through genome editing. We are harnessing the power of metagenomics, the study of genetic material recovered from the natural environment, to unlock four billion years of microbial evolution to discover and develop a suite of novel editing tools capable of correcting any type of genetic mutation found anywhere in the genome. Our comprehensive genome editing toolbox includes programmable nucleases, base editors, and RNA and DNA-mediated integration systems (including prime editing systems and clustered regularly interspaced short palindromic repeat ("CRISPR")-associated transposases ("CASTs")). We believe our diverse and modular toolbox positions us to access the entire genome and select the optimal tool to unlock the full potential of genome editing for patients.

The company was founded by pioneers in the field of metagenomics, a powerful science that allows us to tap into the diversity of microbial life on this planet. The metagenomics process starts by collecting samples from microbe-rich ecosystems ranging from simple home gardens to extreme locations such as hydrothermal vents below the ocean. We then extract the DNA from these environmental samples and deeply sequence them to fully reconstruct the genomes of the resident microbes. Each sample may include thousands of distinct genomes from previously unknown organisms revealing novel cellular machinery that we utilize as building blocks for our editing systems. Using high-throughput screening, artificial intelligence ("AI"), and proprietary algorithms, we rapidly mine through billions of novel proteins from our genome-resolved metagenomics database to create genome editing tools. To date, we have analyzed over 460 trillion base pairs of DNA sequencing data, predicted over 7.4 billion proteins, including over 322 million CRISPR-associated ("Cas") proteins, and identified over 1.75 million CRISPRs, which we estimate has resulted in the identification of over 20,000 novel genome editing systems. Simultaneously, we have assembled extensive libraries of millions of nucleases, deaminases, reverse transcriptases ("RTs") and over one thousand CASTs. Our platform enables us to rapidly and effectively find, screen, and select tools with the highest targetability, specificity, and efficiency in order to develop them into genetic medicines. The iterative nature of our process, underpinned by AI, allows us to continuously push the boundaries of innovation.

Our proprietary toolbox of editing systems

We have developed an expansive and modular toolbox of next-generation genome editing systems that will allow us to interact with the human genome in a site-specific manner, where each tool can be matched to specific disease targets. Figure 1 summarizes our diverse and versatile toolbox of different editing capabilities with the potential to address the full spectrum of genetic diseases.

Figure 1. Our Toolbox.

Gene Edit	Tool / System	Examples	Our Advantages
Knockdown / Gene inactivation Knock-in / Gene insertion Exon skipping / Gene modification 	Programmable nucleases, including ultra-small type V and SMART systems	MG Type II & SMART Nucleases  MG Type V Nucleases 	<ul style="list-style-type: none"> • Efficient and precise genome editing systems • Diverse nucleases have extensive genome targeting capabilities • Compact and ultra-small systems will enable delivery via a single AAV • Function as programmable modules for base editing and RIGS
Nucleotide changes 	Base editors, including ultra-small systems	MG ABE Adenine deaminase A→I (G) MG CBE Cytosine deaminase C→U (T) UGI  	<ul style="list-style-type: none"> • Extensive genome targetability enabled by Metagenomi nucleases/nickases • SMART base editors are smallest nickase-based systems characterized to-date, will enable more efficient delivery via a single AAV
Small replacements/corrections (1-100 base pair replacement, insertion, or deletion) 	Prime editing with RNA-mediated integration systems for small corrections ("Little RIGS")	MG Little RIGS Reverse transcriptase pegRNA 	<ul style="list-style-type: none"> • Extensive genome targetability enabled by Metagenomi nucleases/nickases • Ultra-small RTs are highly active and accurate for prime editing
Large insertions (>100 base pair integrations) 	RNA-mediated integration systems for large integrations ("Big RIGS") DNA-mediated integration with CRISPR associated transposases ("CAST")	MG Big RIGS Reverse transcriptase RNA Template  MG CAST DNA Template Transposase 	<ul style="list-style-type: none"> • Potential to accurately and efficiently integrate large transgenes without the need for double-stranded DNA breaks • Potential to address genetic diseases driven by loss of function mutations <p>Big RIGS</p> <ul style="list-style-type: none"> • Potentially extensive genome targetability enabled by Metagenomi nucleases/nickases • RNA-templated integrations • Will enable 'all RNA' delivery of genome editing system and integration template <p>CAST</p> <ul style="list-style-type: none"> • DNA-templated integrations, potentially including templates much larger than what can be accomplished with RIGS

Our programmable nucleases are the backbone of our broad set of genome editing tools. These novel nucleases including type II and type V Cas nucleases, of which some are ultra-small systems that we call Small Arginine-Rich sysTems ("SMART") nucleases, have unique targeting abilities and can be programmed by guide RNAs ("gRNAs") to target and cut at specific locations in any genome sequence. Targeted genomic breaks trigger DNA repair pathways that can be used for genome editing, for example, to integrate a gene at a target site (knock-in) or for gene inactivation (knockdown). Our toolbox contains thousands of CRISPR nucleases with diverse abilities to target different parts of the genome, allowing us to potentially select the ideal nuclease for targeting any given gene in a site-specific manner and overcome a major limitation of first-generation CRISPR/Cas9 systems.

We also modify our nucleases to either nick the genome (i.e., a nickase that cuts one strand of the DNA) or to simply bind to target sites (i.e., a nuclease dead variant). These capabilities (searching, cutting, nicking, and binding) can be leveraged as a chassis by adding on additional effector enzymes to create base editors for single nucleotide changes, RNA-mediated integration systems ("RIGS") for both small and large genomic integrations using "Little RIGS" for prime editing and "Big RIGS" for large integrations. Using modular engineering, we match nickases with deaminases and RTs for base editing and RIGS, respectively. Furthermore, nucleases can be engineered by swapping the search modules of the enzyme to expand the targetability of the chassis, which is critical for site-specific genomic modifications. Given the measured targeting density of our toolbox, we believe that essentially any codon in the human genome could be addressed with our gene editing systems.

Our highly active nucleases have gone through extensive preclinical evaluation for both *in vivo* and *ex vivo* applications, with demonstration of broad potency of these systems across human primary cells, mouse, and nonhuman primate ("NHP") models. Our base editors, RIGS, and CAST systems have demonstrated activity across various cell-based models. In addition to evaluating system activity, we have undertaken detailed characterization of guide-specific on- and off-target effects. We routinely identify guides that have no or minimal verifiable off-target editing, thus overcoming another limitation of first-generation CRISPR/Cas9 systems.

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In addition to overcoming the activity, targetability, and specificity limitations of first-generation systems, our nuclease toolbox was designed to have broad compatibility with viral and nonviral delivery technologies. This compatibility is accomplished by having a variety of nuclease and gRNA structures, which range in terms of their size and biochemistry. For example, small guides for some type V Cas systems streamline manufacturing for delivery by lipid nanoparticle (“LNP”) approaches, and SMART nickases can be used to construct base editors that are small enough to fit within the packaging limitations of adeno-associated viruses (“AAV”). SpCas9, which is currently used in most base editing applications, is roughly three times the size of some of the smallest SMART nickases and cannot be efficiently packaged into a single AAV. Combined, we believe these features will facilitate delivery of our genome editing tools to previously inaccessible tissue types and organ systems.

While nucleases, base editors, and prime editors can precisely address a wide variety of genomic modifications required to treat disease, the fact that many diseases are caused by a multitude of mutations across a gene means that a diverse set of editing tools are required to fully address these patient populations. The integration of a complete and functional gene through targeted genome editing may provide a way in which every patient with a given disease could potentially be treated by a single genetic medicine. Big RIGS and CASTs are novel genome editing systems that are under development to achieve what has been a major challenge for the genome editing field — large, targeted genomic integrations. Initial preclinical readouts conducted in mammalian cells indicate that these systems could potentially have a major impact on how diseases caused by loss-of-function mutations, the most common cause of genetic diseases, can be addressed through genome editing.

Therapeutic translation roadmap and initial programs

We are taking a stepwise approach deploying our genome editing toolbox to develop potentially curative therapies for patients. Our lead programs are selected to both address important diseases and to establish new standards in targetability, precision, efficiency, and scope of editing capabilities. Figure 2 summarizes the portfolio of programs that we and our partners are advancing, as we aim to match the optimal genome editing tools for each indication. Each of these indications were chosen based on our conviction in the underlying biology, existence of validating preclinical and clinical data, availability of pharmacodynamic and translational tools to assess early proof-of-concept, relevant value supporting outcome measures, and ongoing clinical unmet need. While we do not currently have any approved products and all of our product candidates are preclinical, our lead programs capture an ever-growing set of translational learnings and insights that will inform and accelerate future programs.

Figure 2. Therapeutic Translation.



Hemophilia A—novel, durable , knock-in approach for expression of Factor VIII

Hemophilia A is the most common X-linked inherited bleeding disorder and is caused by mutations in the Factor VIII (“FVIII”) gene leading to loss of functional FVIII protein that impacts the body’s ability to form normal clots in response to injury. FVIII is normally produced in the liver within sinusoidal endothelial cells and is then secreted into the bloodstream where it acts as a cofactor for the catalytic activation of Factor X in the clotting pathway. The lack of functional FVIII disrupts the normal clotting cascade and predisposes patients to increased risk of bleeding, either spontaneously or in response to injury or surgery. Repeated bleeding episodes in joints or soft tissues can lead to progressive joint damage, inflammation, pain, and mobility impairment. Intracranial bleeding is of greatest concern as this can be rapidly fatal or lead to major morbidity.

The standard of care for patients with severe hemophilia A, involves lifelong repeated intravenous (“IV”) infusions of recombinant FVIII preparations prophylactically and in response to bleeding events. The major limitation of this approach is fluctuating FVIII activity levels, with trough values that can still result in breakthrough microscopic and macroscopic bleeding events, particularly within sensitive and previously damaged joints. Additionally, frequent FVIII infusions are inconvenient, which can be associated with suboptimal compliance, and in some patients result in inhibitor formation (antibodies against FVIII) that compromise efficacy. More recently, emicizumab, a bispecific antibody, has been approved for hemophilia A in the United States. Valoctocogene roxaparvovec, the first hemophilia A gene therapy, was conditionally approved for use in Europe in August 2022 and was approved in the United States in June 2023. This genetic medicine delivers a FVIII gene construct to the liver using an AAV vector; however, longitudinal clinical data has demonstrated that FVIII levels drop over time. Importantly, AAV gene therapy is also not a feasible treatment approach for infants or children due to the high degree of liver growth during pre-adulthood that would dilute out the episomal FVIII levels during progressive rounds of liver cell division.

Rather than provide the FVIII gene in an episomal location, which risks dilution from cell division or cell death as well as episomal transcriptional silencing, our approach is to insert a FVIII DNA cassette into a “safe harbor location,” within an intron of the albumin gene that is not expected to have deleterious effects. FVIII expression is then driven off the strength of the native albumin promoter. This approach has previously been demonstrated in preclinical studies to lead to therapeutically relevant expression of a different clotting factor (Factor IX) with negligible impact to systemic circulating albumin levels. Our FVIII knock-in approach is

designed to provide stable expression and clinically relevant circulating levels of FVIII, even at low integration rates because of the strength of the albumin promoter.

We have demonstrated the feasibility of the FVIII gene knock-in approach in mice with several mouse specific guides and different FVIII DNA donor cassettes, with integration of the FVIII gene leading to FVIII mRNA expression and therapeutically relevant levels of FVIII protein in the blood. In an ongoing NHP study we demonstrated integration of a surrogate cynomolgus-FVIII cassette (used to avoid immune response that would occur with a foreign human FVIII protein) and observed therapeutically relevant levels of the cyno-FVIII protein encoded by the integrated cassette in all 3 treated animals that has extended for 4.5 months following a single dose of the AAV-cFVIII virus followed five weeks later by a liver tropic LNP encapsulating the mRNA encoding MG29-1 and guide 2 at a dose of 1mg/kg body weight. We intend to continue measuring FVIII levels in these monkeys up to the 12 month time point to generate a robust data set on durability.

Evaluation of different human FVIII donor DNA cassettes has been completed in mice resulting in the selection of 2 lead cassettes that will be compared in another NHP study, potentially leading to a development candidate selection anticipated in Q2 2024.

In parallel, we are manufacturing mRNA, gRNA, AAV and LNP to support future investigational new drug (“IND”) enabling studies.

Primary Hyperoxaluria, Type 1 (“PH1”)—a durable knockdown of HAO1 for substrate reduction therapy

PH1 is a rare autosomal recessive metabolic disease arising from loss of function mutations in the alanine-glyoxylate aminotransferase (“AGXT”) gene that encodes alanine glyoxylate aminotransferase. This enzyme is found in peroxisomes of the liver where it catalyzes the conversion of glyoxylate to glycine and pyruvate. Lack of functional AGXT leads to an accumulation of glyoxylate substrate, which is then converted to oxalate and excreted in the kidney. The excess urinary oxalate forms an insoluble complex with urinary calcium that leads to the production of calcium oxalate crystal precipitates. This pathologic process results in the formation of repeated calcium oxalate urolithiasis and nephrolithiasis, which in turn leads to obstructive uropathy, inflammation, fibrosis, tubular toxicity, and progressive loss of kidney function. PH1 is a serious disease that causes kidney failure. More than 70% of individuals with PH1 mutations will develop end-stage renal disease, with a median age in young adulthood.

Until recently, the standard of care for treating PH1 was primarily supportive in nature, with hydration and diuretics used to reduce urinary oxalate concentration, pyridoxine (vitamin B6) to enhance residual function of alanine glyoxylate aminotransferase catalytic activity, and hemodialysis once renal function progressed to end stage. More recently, the standard of care has been updated to include treatment with lumasiran, a small interfering RNA (“siRNA”) therapeutic approved in adults and children with PH1 that acts to reduce the levels of urinary oxalate. Using a therapeutic approach known as substrate reduction therapy, lumasiran targets mRNA from a separate gene, HAO1, that encodes glycolate oxidase (“GO”). Lumasiran has been generally well tolerated in clinical studies of adults and children with PH1 but as a siRNA therapy, it requires repeat subcutaneous administration indefinitely in order to maintain its effect. An additional RNAi drug, Nedosiran, which targets LDH, a different enzyme in the same pathway as HAO1, was also given FDA approval for adults and children with PH1 in October 2023.

The goal of our genome editing approach is to durably knock down HAO1 resulting in stable and permanent reduction of oxalate levels to effect a lifelong benefit. We have performed nuclease and guide screening to select an optimal nuclease and gRNA combination. Along with our partner ModernaTX, Inc. (“Moderna”) we have achieved preclinical proof-of-concept in an AGXT knock-out mouse which is an accepted disease model of PH1. We are in the final stages of confirming the candidate to take into NHP studies and expect to have NHP data in 2024 to support final development candidate selection.

Transthyretin Amyloidosis—a single treatment to knockdown TTR gene expression

Transthyretin amyloidosis is a disease of misfolded and aggregated transthyretin (“TTR”) protein that can deposit in tissues causing organ dysfunction, primarily in the heart and/or peripheral nerves. The TTR protein is normally produced in the liver and circulates in a homotetramer (four copies of the same TTR protein bound together) where it serves as a carrier protein for vitamin A and thyroxine. Certain mutations have been identified that can cause TTR homotetramers to fall apart, misfold, and aggregate into insoluble fibrils that deposit in cardiac tissue and peripheral nerves. However, more commonly, the normal aging process is associated with an increased propensity for TTR misfolding and aggregation in the heart without any known genetic sequence variation. These distinctions lead to TTR amyloidosis being characterized as either hereditary transthyretin amyloidosis (“ATTRv”) caused by mutations in TTR, or wild-type ATTR amyloidosis (“ATTRwt”). It is estimated that globally there are approximately 50,000 patients with ATTRv and between 300,000 and 500,000 patients with ATTRwt. Among the larger ATTRwt patient population, the most common presentation is a rapidly progressive, restrictive, and hypertrophic cardiomyopathy due to progressive deposition of insoluble TTR fibrils, which result in thickening of the myocardium and stiffening of the ventricles. These pathologic processes lead to impaired diastolic function and progressive cardiomyopathy that typically leads to progressive heart failure and often death within three to five years from disease onset. Although cardiac manifestations are more common and severe, patients with neurologic manifestations also experience significant morbidity, loss of functionality, and impaired quality of life.

Using our novel nucleases, we aim to provide efficient TTR knockdown and halt further deposition of amyloid fibrils. Previous experience suggests a clinical correlation between the degree of TTR knockdown and potential for benefit in familial forms of the disease, which are expected to translate similarly to wild type forms. The high degree of *in vivo* editing efficiency and specificity of our nuclease platform suggest the potential for a single treatment to knockdown TTR gene expression and remove the requirement for life-long therapy. Along with our partner Ionis Pharmaceuticals, Inc. (“Ionis”), we are currently in advanced stages of nuclease and guide selection, having achieved more than 90% knockdown of human TTR protein in a humanized TTR mouse model, and expect to move into NHP studies in 2024.

Further areas of therapeutic activity and interest

In parallel with our translation efforts in our lead programs using our novel programmable nucleases to knock-in or knockdown gene expression in liver-associated targets, we are developing more complex editing systems for liver associated targets as well as moving beyond the liver. Given that our genome editing toolbox contains small editing systems designed to be amenable to viral vector delivery, and given the progress established in targeting the central nervous system and muscle with established AAV capsids, our first extrahepatic indications will be neurodegenerative and neuromuscular diseases.

Building on our experience delivering our nucleases to the liver via LNP systems, we are extending that experience delivering novel RIGS to the liver to potentially correct ATP7B mutations in Wilson’s disease and PZ mutations in alpha-1-antitrypsin deficiency (“A1AT deficiency”). We are also exploring addressing A1AT deficiency via a base editor approach given the predominant mutation involves a single base pair. Both of these liver diseases have well-defined biology, readily available translational biomarkers for early proof-of-concept, established development pathways based on prior drug approvals, and important unmet medical needs.

Building on our experience with our novel type II and type V programmable nucleases, we are extending that experience by working to deliver these nucleases via AAV to the central nervous system to potentially knock down genetic targets important for both spontaneous and familial amyotrophic lateral sclerosis (SOD1, ATXN2) and Charcot-Marie-Tooth Type 1a (PMP22). In addition, we are working to address a series of mutations

common in Duchenne Muscular Dystrophy with our programmable nucleases through exon skipping approaches. In diseases outside of the liver, we intend to initially leverage known biology and clinical validation achieved with RNA-targeted approaches like antisense and siRNA to advance more potent and definitive one-time genome editing treatments.

Building on our experience with both knock-in gene expression and smaller gene corrections with RIGS, we are progressing our larger RNA- and DNA-mediated integration systems to potentially provide a single curative approach to cystic fibrosis. As opposed to currently-available therapies limited to subsets of patients with individual mutations, we intend to deliver a full copy of a functional cystic fibrosis transmembrane conductance regulator ("CFTR") gene. This approach can similarly be pursued across many other diseases characterized by loss of function mutations.

Our Team

We have assembled a world-class team that is driven by a passion to create potentially curative genetic medicines through the discovery of novel genome editing technologies by harnessing the power of metagenomics. Key members of our executive and leadership team include:

- **Brian C. Thomas, Ph.D., Chief Executive Officer and Founder**, prior to co-founding the company, Dr. Thomas spent more than 20 years in academic research at UC Berkeley helping to pioneer the field of metagenomics. Dr. Thomas has been cited over 16,000 times and listed as an inventor in 28 patent families.
- **Jian Irish, Ph.D., MBA, President and Chief Operating Officer**, has held biopharma executive leadership roles for nearly 20 years at Kite Pharma / Gilead, Sanofi, and Amgen in drug development and global operations, and has helped launch several breakthrough medicines.
- **Pamela Wapnick, MBA, Chief Financial Officer**, has over 20 years of diversified financial leadership experience spanning strategic and operational finance roles at public and private companies including life sciences and biotechnology companies, Diality Inc, Capsida Biotherapeutics, True North Therapeutics and Amgen.
- **Sarah Noonberg, M.D., Ph.D., Chief Medical Officer**, has spent more than 20 years in translational and clinical development leadership roles with a track record of advancing therapeutic programs from discovery to commercialization, including at Medivation and BioMarin.
- **Simon Harnest, Chief Investment Officer and SVP of Strategy**, has held leadership roles in corporate finance and strategy in the life sciences sector, having raised over \$1 billion in public and private capital, including leading Collectis' U.S. IPO and subsequent spin-out and IPO of Calyxt.
- **Luis G. Borges, Ph.D., Chief Scientific Officer**, has over 27 years of experience in the biotechnology industry, including Amgen, Five Prime Therapeutics, Cell Medica, and Century Therapeutics, where he held leadership roles in the research and development of multiple therapeutic candidates.
- **Simren Delaney, Ph.D., LL.M, VP of Legal**, is specialized in Intellectual Property and Patent law, having previously worked at Wilson Sonsini Goodrich & Rosati, and plays an instrumental role in driving the development of the company's growing IP portfolio.
- **Christopher T. Brown, Ph.D., VP of Discovery**, is a former scientist at the Jillian F. Banfield laboratory at UC Berkeley and an expert in using metagenomics to discover novel microbial systems for use in genome editing. Dr. Brown's research has resulted in over 35 publications and over 20 patent family filings.

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- **Michael Conway, MBA, CPA, VP of Finance**, has spent nearly 20 years in finance leadership positions at life science and technology companies, including Adamas Pharmaceuticals, InterMune, and Intel.
- **Alan Brooks, Ph.D., SVP of Preclinical**, has worked on genetic medicines providing scientific leadership in translational research for more than 25 years, including at Casebia Therapeutics and Bayer Healthcare. Dr. Brooks' research has led to 20 publications and numerous patent filings.

Our company is supported by our board of directors, Scientific Advisory Board, and a leading syndicate of investors, with more than 30 funds supporting our Series B preferred unit and Series B-1 preferred unit financings (collectively, the "Series B preferred unit financing").

Our Strategy.

Our goal is to harness the power of our proprietary metagenomics platform to create curative genetic medicines for patients. Key components of our strategy to achieve this goal include:

- **Leverage our leadership position in metagenomics to continually advance and expand innovative genome editing tools.** We expect to build on the diversity and versatility of our toolbox through continuous interrogation of novel microbial genomic information, identification of highly active natural enzymes, design and optimization of genome editing systems, and continuous integration of learnings to accelerate development. In connection with these discoveries, we will continue to strenuously file and protect our intellectual property. Coupled with our trade secret protection around our discovery platform, our broad intellectual property estate creates a significant barrier to entry.
- **Develop and deliver products that make precise modifications to the human genome to cure disease.** We focus on disease areas with well understood disease biology, readily available translational biomarkers for early proof-of-concept, clear development pathways, and important unmet medical need. We are taking a stepwise approach deploying our genome editing toolbox to develop potentially curative therapies for patients. Along with our development efforts using our novel programmable nucleases to knock-in or knockdown gene expression in liver-associated targets, we are leveraging our toolbox to deliver more complex editing systems to targets in and outside the liver. Our approach allows us to systematically incorporate knowledge and insights from our initial development programs, thereby accelerating therapeutic translation across our genome editing technologies.
- **Build a fully integrated genome editing company.** Our team includes experts in discovery, preclinical and clinical development, encompassing all major functions necessary to take a molecule from target identification through registrational clinical trials. To rapidly translate editing technologies into genetic medicines, we strategically invest in automation, characterization, and manufacturing capabilities. This applies not only to process development and manufacturing for clinical trial materials, but also high throughput automated screening and genome sequencing, and state-of-the-art characterization assays. We believe our ability to develop and characterize complex human genome editing components is essential to pursue a successful regulatory pathway for genetic medicine development.
- **Expand therapeutic impact to patients through continued investment in business development and enabling partnerships.** We carefully consider opportunities for business development such as collaborations and partnerships with industry leaders that have unique strengths and we may pursue additional partnership opportunities which complement our technologies, with the objective of accelerating our programs and pushing forward our therapeutic translation efforts. Our existing partnerships with Moderna, Ionis, and Affini-T Therapeutics, Inc. ("Affini-T") demonstrate our thoughtful approach to collaborating with industry pioneers to accelerate and optimize the development of our genetic therapeutic candidates.

- **Maintain our entrepreneurial outlook, scientifically rigorous approach, and culture of tireless commitment to patients.** We are a team of experienced drug discoverers, developers, and company builders who are united by our mission and passion to unlock the full potential of genome editing for patients with high unmet needs. We are dedicated to attracting and retaining top talent and partnerships at the intersection of academia and industry. We are unwavering in our commitment to deliver cutting-edge technology and unlock the long-awaited, transformative potential of genome editing.

Introduction to Genome Editing and Limitations with Current Approaches

Genome editing is a new treatment modality that has the potential to revolutionize healthcare by creating permanent, one-time treatments that address disease at the genomic level. Genome editing involves the alteration of genetic material of a living organism by inserting, replacing, converting, or deleting nucleotides within the DNA. Several approaches and technologies are being studied and developed in order to perform these edits, including:

Nuclease-based genome editing: Several genome editing methods rely on a class of enzymes called nucleases to create double-stranded breaks in DNA at a targeted location to cause gene inactivation, gene insertion, or alter gene splicing. Examples of nucleases include CRISPR associated nucleases, zinc finger nucleases ("ZFNs"), engineered meganucleases, and transcription-activator like effector nucleases ("TALENs"). The discovery and characterization of a particular nuclease, Cas protein 9 from *Streptococcus pyogenes* ("SpCas9"), has been leveraged to develop a number of different therapeutic approaches. Importantly, additional novel and distinct Cas nucleases exist in nature and have the potential to be developed into tools for genome editing. When introduced at target sites in a genome sequence, genomic breaks trigger DNA repair pathways that can be used for genome editing. If a DNA template is provided, the DNA repair machinery may incorporate the sequence at the site of the genomic break, resulting in a site-specific knock-in. If not, the cut will lead to the disruption of a gene sequence and subsequent knock-down of the encoded protein.

Base editing: Base editing is a genome editing approach that relies on using deaminases to chemically convert specific nucleotides in a genome. Deaminases are enzymes that catalyze chemical reactions to remove an amino group. Multiple programmable nuclease platforms, such as CRISPR nucleases, have been harnessed for base editing by using the programmable nature of these enzymes to direct deaminases to specific genomic target sites. In these cases, the nuclease activity is deactivated, thus creating a nicking or nuclease-dead version that does not disrupt the ability of the enzyme to be programmed to target specific genomic sites for editing. There are two primary types of base editors: adenine base editors ("ABEs") and cytosine base editors ("CBEs"). ABEs convert adenine-thymine base pairs to guanine-cytosine base pairs. CBEs target cytosine-guanine and convert them to thymine-adenine.

RNA-mediated integration, including prime editing: RNA-mediated integration systems ("RIGS") are genome editing systems that make programmable genomic modifications that are encoded in RNA templates. Because the modifications are encoded in RNA, these systems have the ability to repair diverse mutations, including insertions, deletions, and all types of point mutations. These systems rely on RTs to convert messages encoded as RNA into DNA. CRISPR systems are used to direct RTs to genomic target sites. Some systems use a nickase to create a target-specific site that primes the activity of the RT and results in the corrected genomic sequence encoded in the RNA to be incorporated into the genome. Prime editing can be accomplished with RIGS, as can large, targeted genomic integrations.

DNA-mediated integration, including CAST: CASTs are a class of genome editing systems that provide directed and programmable genomic integration of large DNA templates. CASTs are naturally occurring systems that have been engineered to accomplish large integrations for genome editing in various cell

types and for therapeutic applications. The systems consist of a catalytically dead Cas effector that can be programmed by gRNAs to target a transposase to integrate large DNA cargos into specific genomic target sites. DNA-templated integrations can be accomplished with other transposase and recombinase systems; however, these systems typically require extensive protein engineering in order to alter their targetability, or need to be used in concert with other genome editing tools such as prime editing systems in order to incorporate targeting motifs into specific genomic sites.

There have been significant advancements in genome editing since the seminal research that led to the discovery of CRISPR SpCas9 and its application in humans. However, there remain key limitations that must be addressed to unlock the full potential of genome editing. We believe the key limitations facing current genome editing platforms are:

- 1) **First-generation technology lacks the ability and flexibility for accomplishing complex genome editing.** The majority of genome editing platforms are limited to a single genome editing approach, such as gene insertions/deletions, single nucleotide changes, or small gene corrections. As a result, they are faced with inherent limitations including the diversity of edits in which they can employ and, as a result, an inability to address a range of diseases. In addition, they lack the flexibility to tailor their genome editing system to a broad range of genomic targets of interest.
- 2) **Lack specificity and control over resulting edits.** Current genome editing platforms have a narrow armamentarium of genome editing systems and therefore limited access to systems capable of high activity and specificity at desired target sites. This lack of control and specificity is often measured by “off-target” edits which can pose a risk for undesirable side effects or unexpected safety findings.
- 3) **Size of current genome editing technologies limits in vivo delivery methods and target organs.** First-generation SpCas9 systems are about 1,300 amino acids (“aa”) in length and as such are not feasible to package into many delivery vectors such as AAV. As such, their delivery is largely limited to LNP systems, which precludes delivery to many tissues outside of the liver.
- 4) **Inability to access certain sequences in the genome.** SpCas9 is only able to target DNA sequences which contain a flanking sequence of “NGG”, restricting the range in genetic targets it can be programmed to locate, and subsequently limiting the ability to address certain underlying mutations that drive disease.
- 5) **Substantial engineering requirements.** Limited access to highly active natural nucleases and effectors drives the need for substantial modifications to make a system operate at therapeutically-relevant levels, resulting in long lead times from discovery to candidate nomination.
- 6) **Narrow terms of license agreement from academic institutions.** The majority of genome editing platforms have been formed as a result of a licensing agreement for specific genome editing systems or technology from academic institutions and are therefore limited to the confines of that technology arrangement. Alternatively, genome editing tools developed by us are built from highly novel components derived from our metagenomics database, and thus are not subject to these constraints.

In order to address these broad challenges with current genome editing approaches, we have leveraged our deep expertise with metagenomics to develop a proprietary discovery platform that is designed to continuously identify novel editing systems and optimize our expansive editing toolbox. Starting at the microbial level, our multifaceted platform enables discovery beyond nucleases, translating highly active natural enzymes into powerful genome editing systems optimized for efficiency and specificity.

Our Metagenomics Platform

We believe genome editing tools with capabilities that go beyond the current technology landscape will be required in order to treat the vast majority of genetic diseases. Our goal is to unlock the full potential of genome editing by developing tools with new capabilities using novel cellular machinery discovered from the natural environment. Our company was founded by Brian C. Thomas and Jillian F. Banfield, pioneers in the field of metagenomics. They recognized the power that naturally evolved microbial systems could have in revolutionizing access to enhanced genome editing technologies to create potentially highly efficacious and curative genetic medicines. Our metagenomics discovery platform is foundational to our business and therapeutic pipeline. This platform enables us to rapidly and effectively find and engineer highly active natural enzymes sourced from nature into genome editing tools that are highly specific, efficient, and have enhanced targetability.

CRISPR systems, having been studied for decades, are known to be ubiquitous in the microbial world. However, it was not until the recent discovery and characterization of CRISPR-SpCas9 that it became possible to use these systems as tools for genome editing. SpCas9 is only a single representative of the CRISPR systems that exist in nature, leaving open the potential to identify and develop new genome editing tools through continued and systematic discovery efforts. The vast majority of microbes, including bacteria, archaea, viruses, fungi, and single-celled eukaryotes, are extremely difficult, and potentially impossible, to study using traditional laboratory methods. We aim to address the limitations of traditional laboratory methods through a process whereby microbes are recovered from the natural environment and studied based on their genetic blueprint-their genome sequences. This approach has supported the ability to characterize the extent of CRISPR biology on the planet, and to expand beyond CRISPR to identify a vast collection of novel enzymes and other cellular machinery.

Samples from diverse climates and geographies have been used to build a metagenomic database that is continuously analyzed via high-throughput screening that utilizes AI and proprietary algorithms to direct our discovery efforts. This continuous genome mining process generates expansive libraries of novel systems, including nucleases, deaminases, RTs, and CAST systems (together, "effector enzymes"), that make up the foundational building blocks necessary to assemble a modular, novel genome editing toolbox that can be harnessed to make precise changes to the human genome to address a variety of important diseases with curative intent. We have simultaneously developed a modular approach to engineering that involves interchanging key components in a high-speed process to translate the discovery of novel nucleases and other effector enzymes into optimized genome editing systems with substantially reduced translation time compared with previously described systems. We estimate that our metagenomics platform and modular engineering process has resulted in the discovery of over 20,000 novel genome editing systems, to which we are seeking coverage through our pending patent portfolio. These systems span hundreds of novel nuclease families and fuel a growing genome editing toolbox.

Mining Our Natural Environment to Create an Expansive Genomics Database

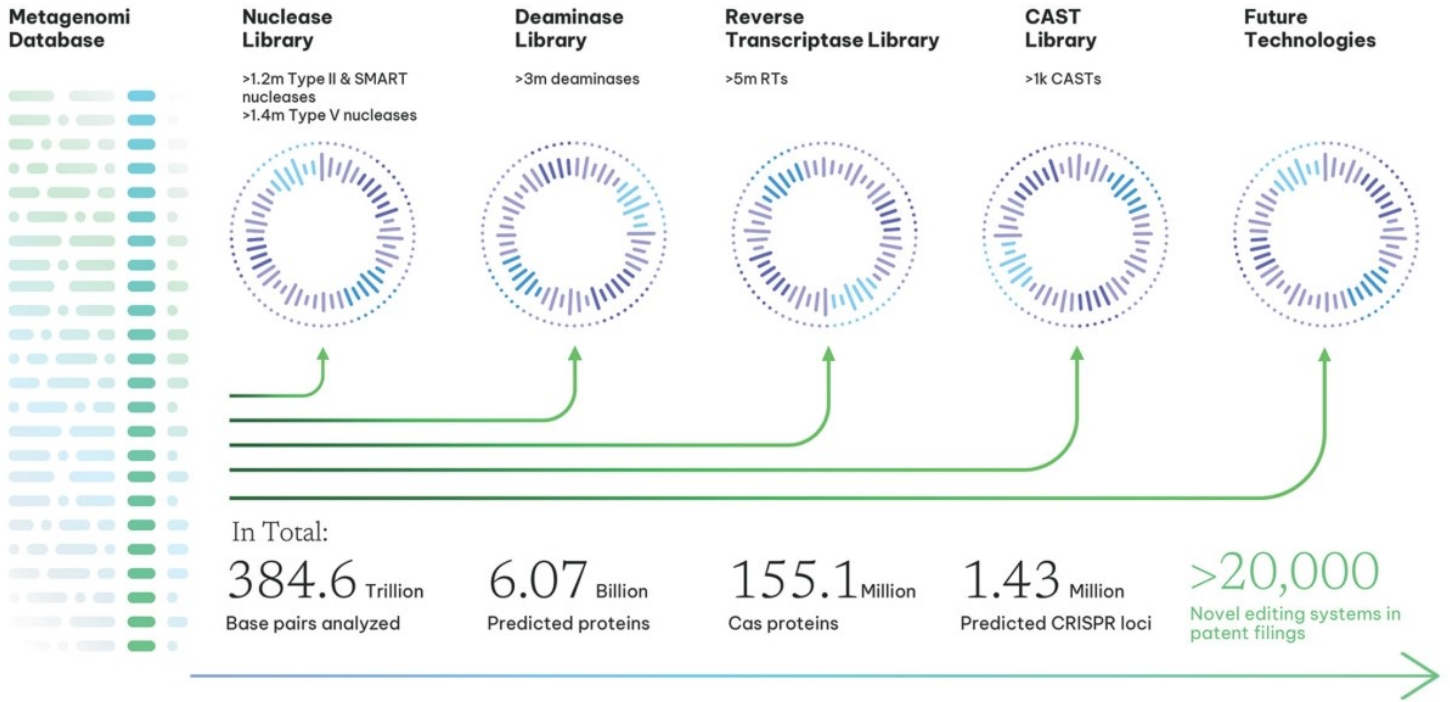
We aim to harness the power of the metagenome by using our continuous genome mining process to assemble a broad, diverse library of novel genome editing nucleases and other effector enzymes. This is accomplished by studying all the DNA from microbial communities at the same time. Our mining process begins with proprietary sampling in which our scientists collect samples from diverse climates and geographies to build a database that spans broad biodiversity including, but not limited to our local natural environments and extreme environments such as from high-altitudes, high-temperatures, and hydrothermal vents below the ocean. Samples collected in a natural environment may contain billions of cells representing tens of thousands of distinct species. Every sample collected from a natural environment is subjected to deep DNA sequencing and bioinformatics analysis to identify and functionally analyze recovered microbial genomes for the discovery of genetic elements of interest.

Through our metagenomics process, DNA is extracted from these environmental samples and sequenced in order to reconstruct the genomes of the resident microbes. The process of DNA extraction and sequencing results in the fragmentation of each individual microbial genome into small sections which are blended into a backdrop of all other sequences present. Due to the clonal replication of the organisms in microbial communities, multiple copies of nearly-identical genome sequences are recovered, and the overlap between these sequences provides the information needed to reconstruct the original genomes. This complex process is only the beginning. Once reconstructed, it is necessary to predict the function of each section of the newly reconstructed genomes. Our platform has facilitated the discovery of vast sequences and functional components that, to our knowledge, have never been published before. These novel components have resulted from the unique selective pressures that microbes face from different environments and that drive immense genomic diversification. The evolutionary process of natural selection provides highly optimized enzymes that require little, if any, protein engineering. The novelty of the genomes recovered from metagenomics requires the de novo prediction of genes, proteins, non-coding RNAs, and other essential features. This is challenging and necessary due to the fact that previously studied 'reference' sequences do not provide enough information to sufficiently guide this process. Considering that these evolutionary processes have been at work for billions of years, there is considerable genetic diversity to mine for the development of highly-optimized genome editing tools. Our industry-leading database of novel microbial genetic sequences provides the basis for our discovery process. To date, our continuous genome mining process has analyzed over 460 trillion base pairs of DNA sequence, an amount of data roughly equivalent to what would be required to sequence hundreds of thousands of human genomes, and resulted in the prediction of over 7.4 billion proteins and over 1.75 million CRISPRs – including over 322 million Cas proteins.

Leveraging AI and High-Throughput Screening to Identify Novel Editing Systems

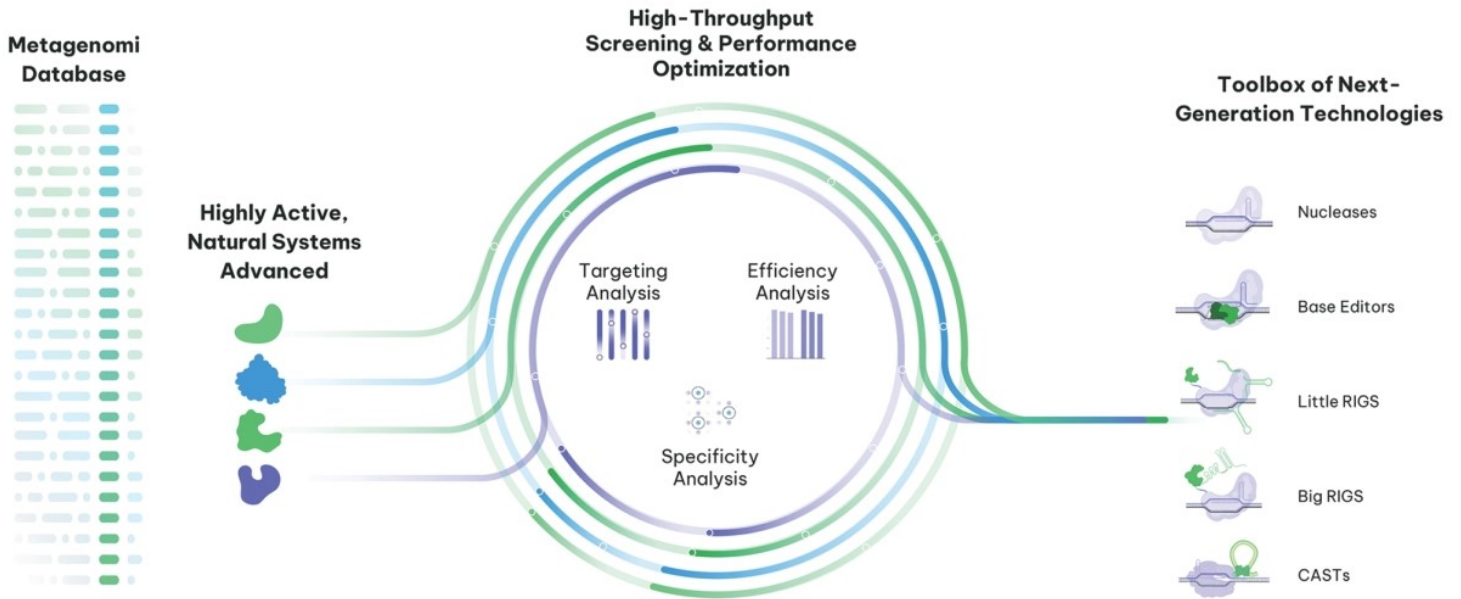
To interrogate our metagenomics database, our platform combines AI, including machine learning, and proprietary algorithms run on expansive cloud computing infrastructure to screen for novel CRISPR nucleases and other effector enzymes at high speed. The screening process consists of high-throughput sequencing that allows us to quickly analyze large amounts of genomic data and subsequently synthesize the identified components, building blocks, into functioning CRISPR nucleases and other effector enzymes that can be interrogated biochemically and in mammalian cells. Once extensively characterized, novel nucleases and other effector enzymes are categorized into our ever-expanding library. Through the metagenomics-driven discovery process we have characterized one of the largest known libraries of novel nucleases, which we estimate includes 20,000 novel genome editing systems from hundreds of nuclease families. We have also assembled a robust library of other effector enzymes to design and engineer the next generation of genome editing systems that are fit for essentially any therapeutic purpose. Our effector enzyme library includes over three million deaminases, over five million RTs, and thousands of CAST systems, as shown in Figure 3 below. The continuous interrogation of an ever-expanding database of programmable nucleases and other enzyme effectors accelerates the pace of learning and insights to feedback into proprietary machine learning algorithms and further separates us from peer companies. As we continue to build upon our metagenomic library, we expect to make additional discoveries of novel genome editing technology and expand our toolbox.

Figure 3. Our Effector Enzyme Library.



From this library, we select our lead nucleases and other effector enzymes through a funnel of stringent performance and safety criteria that involves testing in a series of cell-free, cell-based, and *in vivo* experiments. Ultimately, we prioritize editing systems that exhibit high editing efficiency and precision, and have a compact size that will optimize their delivery. Because most systems added to our genome editing toolbox have different genomic targeting specifications, we believe that our expanding toolbox could enable us to target every base pair in the human genome. This process, highlighted in Figure 4, helps us to identify highly active natural enzymes that require minimal engineering and optimization to translate into potentially curative genetic medicine.

Figure 4. Overview of High-Throughput Screening Process.



Our metagenomics platform and modular engineering process has supported the discovery and development of our broad genome editing toolbox at a rapid pace since our company's founding in 2018. By selecting highly active nucleases from our library, our process requires minimal optimization to develop genome editing systems. We utilize a modular engineering approach to match lead nuclease candidates with an optimal gRNA and targeting domain in order to optimize targeting, specificity, and editing efficiency. Furthermore, additional effector enzymes can be included to modify the function of the system, for example by adding a deaminase to a nickase variant for base editing.

In order to achieve these modifications, we leverage our vast library of editing systems to perform targeting domain swaps between enzymes, substituting domains from less-active enzymes into the backbone of highly-active nucleases. This results in chimeric enzymes that can provide high efficiency editing at gene loci.

The modular engineering process is accelerated using *in silico* screening algorithms to predict the optimal chimera. This predicative, high-speed engineering process allows us to continually iterate across each component of the genome editing system to quickly develop an engineered system that is optimized for various therapeutic applications.

Modular engineering can be used to adjust the targeting of high-performing systems by leveraging the diverse targeting capabilities of diverse Metagenomi nucleases. Given the measured targeting density of our toolbox, we believe that essentially any codon and ultimately every base pair in the human genome could be addressed with our gene editing systems.

Genome editing remains in the early stages of development and our platform allows us to continuously learn, iterate, and optimize our genome editing toolbox in pursuit of curative genome editing medicines. The increasing insights from our modular engineering and target domain swapping are captured and further interrogated and organized by our proprietary AI platform to accelerate the pace of future development and further separate us from our peers. As the genetic medicine field continues to rapidly evolve, our platform positions us to be at the forefront of unlocking the full potential of genome editing through the continuous discovery of new editing systems and the development of the next wave of genetic medicines.

Our Solution: Proprietary Toolbox Derived from Our Metagenomic Approach

Our Platform of Genome Editing Technologies

Gene Edit	Metagenomi ("MG") Tools	Key Attributes
Double-strand DNA break (e.g for knockdown, knock-in, gene activation, and exon skipping)	Type II Nucleases	<ul style="list-style-type: none"> • Extensive targetability (Alexander et al 2023, Lamothe et al 2023) • Can be converted to nickases for base editing and RIGS
	Type V Nucleases	<ul style="list-style-type: none"> • Systems with small gRNAs (Goltsman et al 2020) • Includes ultra-small systems that expand delivery approaches (e.g., AAV)
	SMART Nucleases	<ul style="list-style-type: none"> • Ultra-small systems expand delivery approaches (e.g., AAV) (Goltsman et al 2022) • Can be converted to nickases for base editing and RIGS
Nucleotide changes (i.e. base editing)	ABE and CBE	<ul style="list-style-type: none"> • Engineered from MG nickase and MG deaminase • CBE also include MG uracil glycosylase inhibitor ("UGI") • Base editors engineered from type II have extensive genomic targetability • SMART base editors are smallest nickase-based systems characterized to date
Small changes (1-100 base pair replacement, insertion, or deletion, i.e. prime editing)	Little RIGS	<ul style="list-style-type: none"> • Engineered from MG nickase and MG RT • Ultra-small RTs are highly active and accurate for prime editing • Enabled by extensive targetability and deliverability of MG nickases
Large insertions (>100 base pair integrations)	RNA-templated: Big RIGS	<ul style="list-style-type: none"> • Engineered from MG nickase and MG RT • MG RT are accurate, and can convert >4,000 bp RNA templates into DNA • Programmable integration of large transgenes delivered as RNA
	DNA-templated: CAST and other systems	<ul style="list-style-type: none"> • CASTs are naturally occurring programmable transposase systems • Ability to site-specifically integrate large transgenes delivered as DNA, possibly including templates much larger than 4,000 bp • Potential to addresses any genetic disease driven by loss of function

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All components of our toolbox have been discovered and derived from our proprietary metagenomics library. We have assembled a full suite of differentiated tools that, together, can potentially effectuate any desired gene modification – gene knockdown, gene knock-in and replacements. We believe there is no other single platform enabling the breadth and differentiation of genome editing technologies as our toolbox. All elements of our toolbox are wholly owned, and we have constructed a broad patent estate that protects our intellectual property, and it will continue to expand as we discover, interrogate, and optimize our novel editing systems. As we continue to expand our metagenomic library, we expect to make additional discoveries of novel genome editing technology. The core technologies in our toolbox to date are outlined in the above table.

Key Attributes of Our Proprietary Toolbox

Key advantages of our platform and technologies are:

- 1) **Potential to create a full spectrum of genetic medicines** – Our broad suite of genome editing technologies include: programmable nucleases, base editors, RIGS and CASTs, that, together, can potentially effectuate any desired modification to the genome – gene knock-down, gene knock-in, and replacements. This allows us to address a diverse set of mutations by matching the right tool to a specific target, with limited unintended effects such as off-target editing. As such, we intend to prosecute a genetic medicine therapeutic development strategy across a broad array of diseases and target organs including liver, central nervous system, muscle, kidney, and lung.
- 2) **Potential next generation genome editing systems** – Our scientific underpinnings based in metagenomics provide a continuous engine for discovering and developing potential next generation genome editing systems. For example, RIGS and CAST. As we continue to build upon our metagenomic library we expect to expand our toolbox as we make more discoveries. We have constructed a broad patent estate that protects our intellectual property, and it will continue to expand as we discover, interrogate, and optimize our novel editing systems.
- 3) **Ultra-small nuclease platform to expand in vivo delivery of multiple genome editing systems** – Compact systems create potential advantages for delivery, manufacturing, and dosing. For example, at 429 aa in length, one of our SMART nucleases is a fraction of the size of the industry-standard SpCas9 system, which is 1,300 aa and exceeds the delivery capacity of standard AAV vectors. The ability to package our systems into a single AAV will enable more efficient targeting of organs and diseases beyond what is currently possible with LNP delivery.
- 4) **Designed to edit any target in the human genome** – Our metagenomics library contains hundreds of nucleases with diverse targeting abilities that allow us to address a diverse set of mutations that cause disease, including those found at sites that often cannot be targeted by first-generation nucleases. This allows us to select the ideal nuclease for any target site of interest. Given the measured targeting density of our toolbox, we believe that essentially any codon in the human genome could be addressed with our gene editing systems.
- 5) **Shortened optimization period** – We benefit from a diverse set of highly-active nucleases and effectors which have required little -if any- protein engineering to optimize. These highly active natural enzymes allow us to quickly identify systems for therapeutic development. As a result of not having to heavily engineer systems to be active in human genome editing applications, we are able to move quickly from discovery to candidate nomination for particular genetic disease applications.
- 6) **Ability to target large gene integrations into the genome using our RIGS and CAST systems** – Our novel RIGS and CAST systems allow for programmable, large gene insertions, an outcome which has been a major challenge for the genome editing field. RIGS are a proprietary genome editing system engineered from nickases and RTs, while CAST are systems that exist in nature but have required engineering to allow




for mammalian genome editing. We believe we are the first to demonstrate targeted genomic integration in human cells using compact CAST systems. While CAST have the theoretical capability to integrate very large DNA templates into the genome, RIGS are also being developed in order to achieve targeted, large genomic integrations when all components need to be delivered as RNA, for example when using standard LNP delivery technology.

Specific Components of Our Toolbox

Programmable Nucleases

Overview

Figure 5. Schematic Showing Programmable Nucleases and Their Use for Genome Editing.

Gene Edit	Tool / System	Examples	Advantages	
Knock-down / Gene inactivation Knock-in / Gene insertion Exon skipping / Gene modification 	Programmable nucleases, including ultra-small type V and SMART systems	MG Type II & SMART Nucleases 	MG Type V Nucleases 	<ul style="list-style-type: none"> • Efficient and precise genome editing systems • Diverse nucleases have extensive genome targeting capabilities • Compact and ultra-small systems will enable delivery via a single AAV • Function as programmable modules for base editing and RIGS

We are building a toolbox that includes programmable nucleases that are selected to target any site in the human genome with high precision. Most therapeutic genome editing applications to date use CRISPR/SpCas9 as the programmable nuclease. However, this system has several limitations that prevent its broad use across the thousands of genetic diseases that impact patients. Most importantly, SpCas9 is limited by where it can be targeted in the human genome and in some cases has a lack of specificity that leads to frequent off-target editing. In addition, the size of the SpCas9 enzyme complicates options for delivery using industry-standard methods. We have explored diverse programmable nucleases found in nature in order to identify novel systems that overcome all of these limitations (Figure 5).

The discovery of new CRISPR enzymes with unique functionality and structure may offer the potential to further disrupt genome editing technologies, improving speed, specificity, functionality, and ease of use. CRISPR systems are commonly organized into two classes, six types and an expanding number of subtypes based on functional characteristics and evolutionary relatedness. We focus our attention on CRISPR type II and type V systems, owing to the simplicity of these programmable nucleases. Type II and type V nucleases are RNA-guided enzymes that can be programmed to target specific sequences of DNA, and sometimes RNA. Unlike type II nucleases, type V nucleases are more likely to generate staggered versus blunt-end cuts in double stranded DNA. Nucleases from both of these systems are extensively used in biotechnology, despite limitations that prevent their more widespread use in therapeutic applications. Our type II and type V CRISPR systems are distinct from previously studied CRISPR enzymes (based on their protein sequence, size, and biochemistry), while maintaining the core functionality of being programmable nucleases. Our lead systems have undergone extensive study across multiple mammalian cell types and animal models, demonstrating their utility as genome editing tools in both *in vivo* and *ex vivo* applications.

Throughout our search for novel programmable nucleases, we have identified several new types of ultra-small nucleases that range in size from approximately 450 aa to 1,000 aa, compared with type II and type V nucleases which are typically between 1,000 aa and 1,500 aa in length (for comparison, the most studied SpCas9 enzyme is 1,368 aa). Our newly-discovered, ultra-small nucleases include new types that we collectively refer to as SMART, as well as those that come from novel type V sub-groups. Given their small size, these new systems have the potential to be delivered to additional therapeutic target sites that expand beyond what is possible with first-generation systems. In adapting these novel systems into potential precision genetic

medicines, our programmable nucleases are designed to have the capability to target essentially any therapeutically relevant genomic site with a high level of specificity (i.e. with limited off-target editing), while expanding compatibility with available delivery technologies.

Our Approach

To date, we have identified thousands of novel CRISPR type II, type V and SMART nucleases, including ultra-small systems, expanding the collection of known programmable nucleases by mining our proprietary metagenomics database. Using high-throughput *in vitro* testing, we have validated the activity of hundreds of novel nucleases. This has led to the identification of highly-active natural nucleases while also enabling us to catalog the unique targeting capabilities of each system. We select for natural, un-engineered systems with high activity and specificity. Our best-characterized nucleases have demonstrated activity levels meeting and often greatly exceeding SpCas9 while exhibiting low levels of off-target editing in mammalian cells. Given the measured targeting density of our toolbox, we believe that essentially any codon in the human genome could be addressed with our gene editing systems. The targeting density (frequency of targetable sites in the human genome) of the toolbox greatly increases the likelihood of identifying a highly active and specific nuclease and gRNA combination for any therapeutically relevant genomic target. We can use these programmable nucleases for genome editing, and also as a chassis for developing base editors and RIGS. The diverse biochemistry of these novel systems, including their size and DNA cutting profiles, makes it possible to link editing systems to the particular genomic target, edit type, and delivery technology we believe are required to develop genetic medicines. Additional discovery and characterization of programmable nucleases will further expand the targeting density of our toolbox, improving the overall activity and specificity of lead systems identified for therapeutic development.

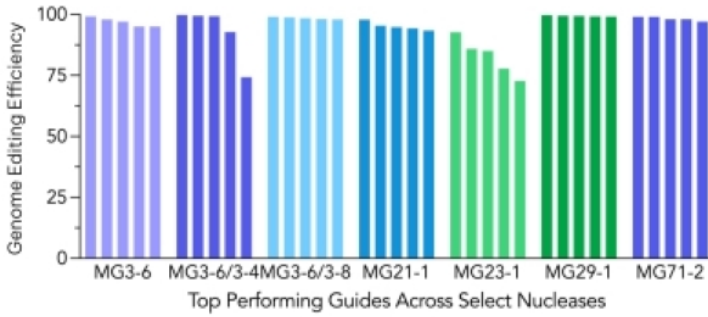
Our best-characterized type II and type V nucleases are suitable for a wide variety of genome editing applications

Nucleases with the activity and specificity required for potential therapeutic genome editing applications are identified through a series of high-throughput screening and characterization steps. Novel protein and gRNAs are first predicted bioinformatically and then validated in both cell-free and mammalian cell screens. These steps validate the activity of a system and provide an accurate measure of targeting and specificity profiles. This approach has been applied to both type II and type V CRISPR nucleases in order to establish an expanding collection of well-characterized systems. In addition to discovery of novel nucleases with distinct targeting capabilities, a modular protein engineering approach is also used in order to create chimeric systems. The chimera approach leverages the high activity of top-performing systems but changes where they can edit by incorporating distinct targeting domains from related systems. Through continuous discovery and refinement, this collection of systems will expand, with the potential to target essentially every site in the human genome, while also creating a chassis to support the accelerated development of base editing, prime editing, and targeted integration systems.

Given the measured targeting density of our toolbox, we believe that essentially any codon in the human genome could be addressed with our gene editing systems.

Figure 6. Our Expanding Nuclease Toolbox is Designed to Enable Extensive Targeting throughout the Human Genome.

Figure 6a. Our nucleases have shown high editing efficiency in mammalian cells.



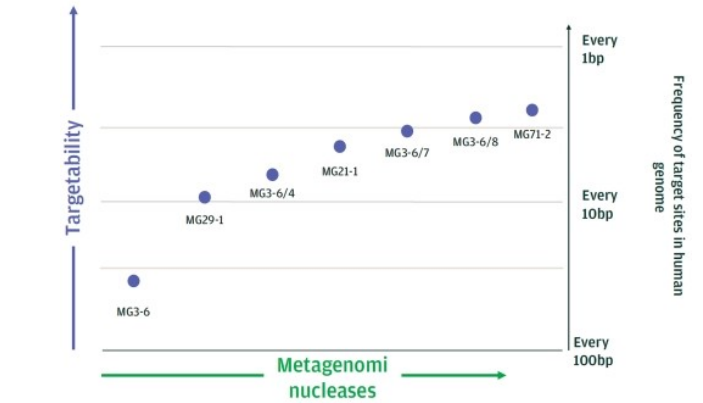
* Editing efficiency was determined based on the frequency of InDels detected by next generation sequencing (NGS) at genomic sites targeted by each nuclease.

* Graph depicts editing efficiency for the top five guides for each of six nucleases.

Our nucleases are capable of highly efficient genome editing in mammalian cells. Systems are tested across a collection of gRNAs designed based on the unique requirements and targeting preferences determined for each system. If a nuclease is routinely capable of editing at near-saturating levels, sometimes up to 99% editing efficiency, the system will go through further characterization and therapeutic development. Figure 6a shows the high editing efficiency of six systems observed in mammalian cells, indicating that they have the potential for broad use in therapeutic development given an ability to rapidly identify high performing guides that require minimal optimization.

Given that each nuclease has distinct genomic targeting capabilities, we are able to determine which sites in the human genome can be addressed by each system. Figure 6b shows how the targeting density of our toolbox increases with each new system. Given the measured targeting density of our toolbox, we believe that essentially any codon in the human genome could be addressed with our gene editing systems. This collection of systems includes both natural enzymes as well as chimeric forms that have been engineered to alter the targetability of the nuclease. For reference, SpCas9 is able to target roughly every ten base pairs in the human genome. The targeting density of the toolbox increases the likelihood of identifying a highly-potent guide for any desired genome edit.

Figure 6b. Given the measured targeting density of our toolbox, we believe that essentially any codon in the human genome could be addressed with our gene editing systems.

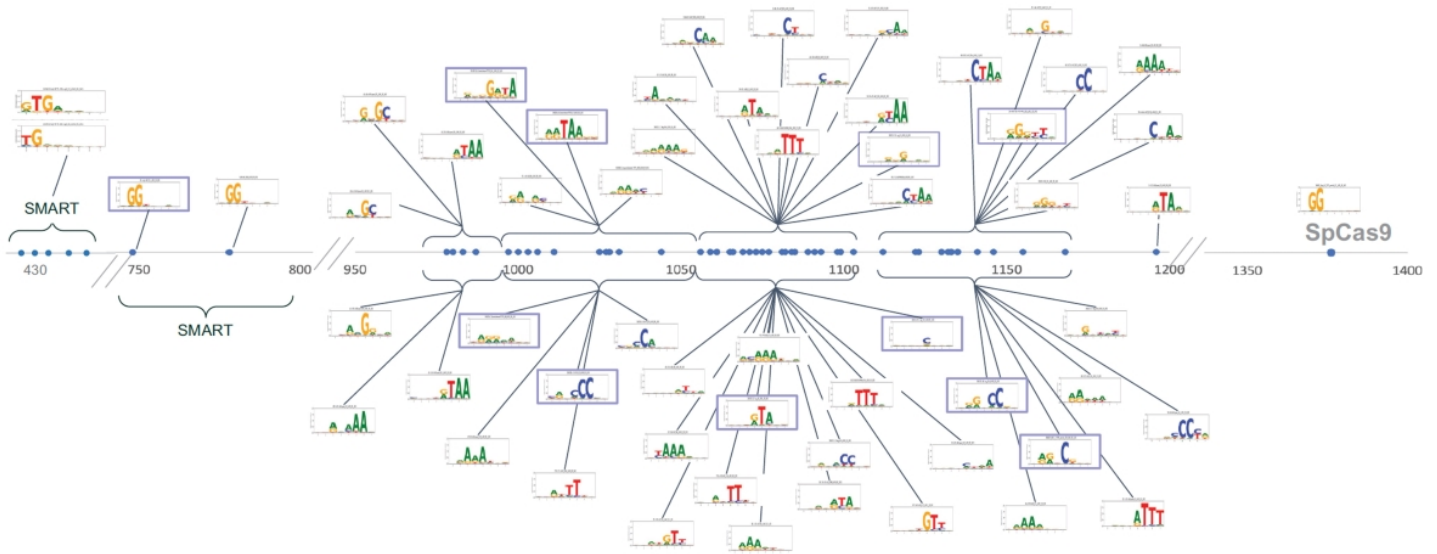


* Graph depicts cumulative targetability.

* Targeting density (targetability) is the average distance between nuclease target sites in the human genome.

Our nuclease toolbox is on track to target anywhere in the human genome

Figure 7. Our Nucleases are Compact with Diverse Targeting Sequence Motifs, Selected to Enable Broad Genome Editing Applications.



* Graph depicts a selection of our nucleases, including their size in aa on the horizontal axis and their corresponding targeting motifs shown as sequence logos (PAM and TAM sequences), compared to SpCas9.

Multiple parameters are considered when screening and promoting nucleases for further development, including the size of the system, activity across various assays and cell types, and targeting. For CRISPR systems, nuclease targeting is limited by a PAM sequence, or protospacer adjacent motif. The PAM is a short DNA sequence motif that must be present next to a target sequence in order for the nuclease to cut at the target site. Other systems have similar requirements that go by different names. For example, some SMART nucleases recognize functionally similar sequences called target-adjacent motifs ("TAMs"). Figure 7 shows the diversity of protein sizes and targeting motifs recognized by our nucleases. The vast diversity of the protein size and targeting motif requirements of our nucleases continues to fuel toolbox development and will enable the identification of additional systems that could make it possible to target nearly every base pair in the human genome.

Our nucleases are highly active across many human cell types which may indicate broad potential utility for human therapeutic applications

Beyond initial nuclease benchmarking conducted in immortalized mammalian cell lines, we have conducted extensive surveys to show that these systems can be used in a variety of primary cells important for preclinical studies (i.e., T cells, natural killer ("NK") cells, B cells, hematopoietic stem cells ("HSCs") and induced pluripotent stem cells ("iPSCs")), as illustrated by Figure 8 below. The versatility of these exemplary systems indicates their potential use in broad therapeutic applications. These benchmarks against SpCas9 also indicate that our systems may have potency advantages in which fewer genome editing reagents will need to be delivered in order to achieve high levels of genome editing.

Figure 8. Our Nucleases Show High Editing Efficiency in Human T Cells, NK Cells, B Cells, HSCs, and iPSCs.

Fig 8.a: Highly efficient editing in T Cells targeting TCR alpha (TRAC)

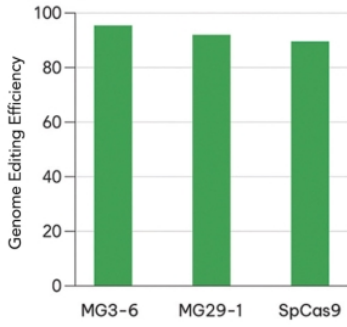


Fig 8.b: Highly efficient editing in Natural Killer (NK) cells, eliminating cell-surface marker CD38

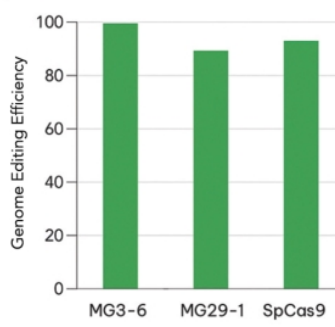


Fig 8.c: Highly efficient editing in B Cells targeting TCR alpha (TRAC)

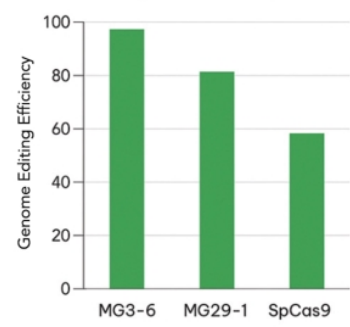


Fig 8.d: Highly efficient editing in HSCs targeting TCR alpha (TRAC)

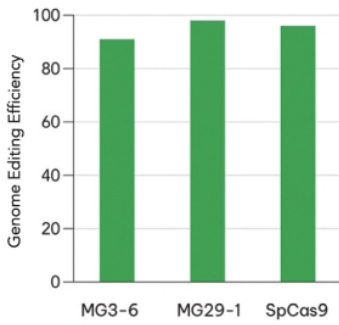
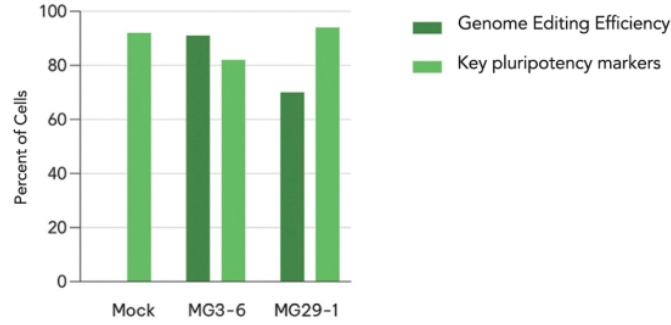


Fig 8.e: MG3-6 edits >90% of iPSCs with retention of Oct4/Sox2 staining (key pluripotency markers) confirming viability of cells post-editing



* Two example nucleases are shown, type II MG3-6 and type V MG29-1.

* Editing efficiency was determined based on the frequency of InDels detected by NGS at genomic sites targeted by each nuclease.

Our nucleases exhibit high specificity when benchmarked in multiple mammalian cell types

Our therapeutic development of genome editing systems require that they exhibit high activity and specificity across multiple cell-based models. We employ a broad set of specificity and off-target assessment methodologies, including *in silico*, biochemical, and cell-based approaches. Figure 9 shows peer-reviewed and published off-target assessments conducted using an unbiased, industry standard, cell-based, oligonucleotide capture method. In Figure 9a we show that two of our nucleases are more specific than SpCas9 when compared across multiple guides, and in Figure 9b we show that we can identify guides with no to minimal detectable off-targets with two lead nucleases tested in both immortalized and primary human cells. This trend has continued, and we are able to identify guides that have minimal or no detectable off-target activity for therapeutic targets. It is expected that the higher specificity of these systems will translate into better safety profiles across various therapeutic genome editing applications.

Figure 9. Our Nucleases are Highly Specific.

Figure 9a. Our nucleases are highly specific in multiple mammalian cell types.

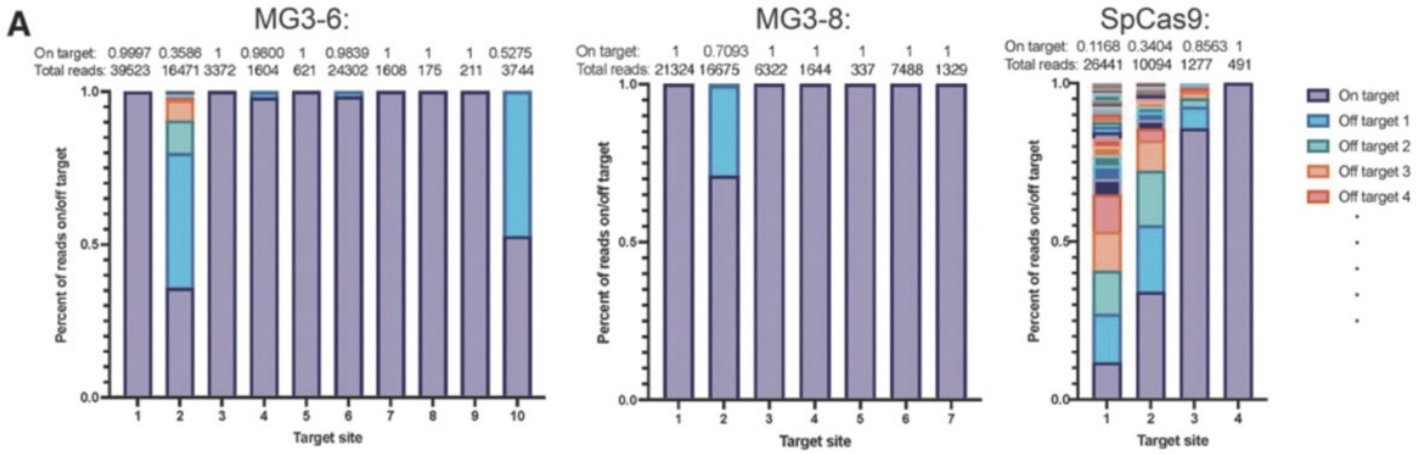
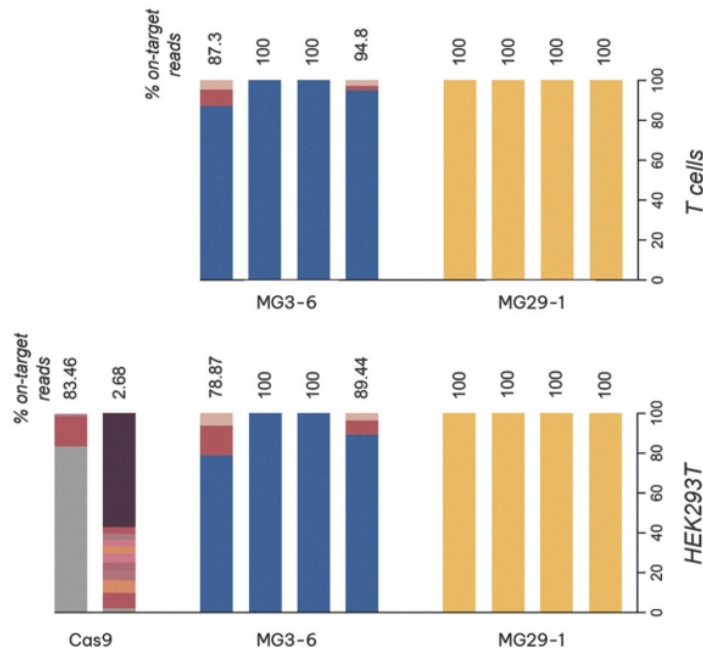


Figure 9b. Our best-characterized nucleases have guides that showed no to minimal detectable off-target edits when assayed in immortalized and primary human cells.



* Figure 9a: Off-target analysis showed that our type II MG3-6 and MG3-8 nucleases have high specificity in multiple mammalian cell types as measured by the number of off-target sites and the fraction of on-target reads. The target sites are the same between the three nucleases, including SpCas9. Off-target experiments were conducted at N = 2, and reads for both replicates were summed for analysis. Double strand break ("DSB") discovery via capture of a double-stranded oligonucleotide in primary T cells using the same MG3-6 and MG29-1 guides from (A, averaged across three biological replicates). Source: Alexander et al 2023 CRISPR Journal

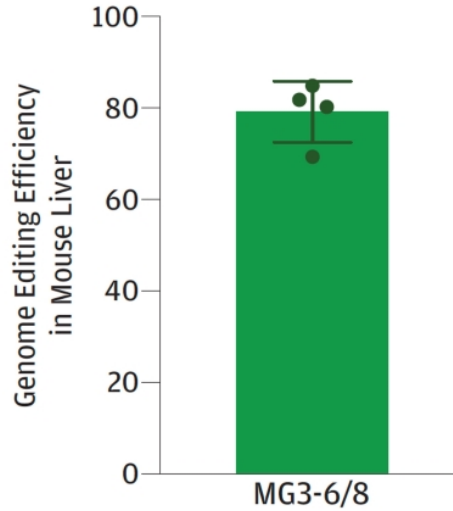
* Figure 9b: DSB discovery via capture of a double-stranded oligonucleotide in HEK293T cells with SpCas9 (on target read in gray), guides MG3-6 TRAC B2, TRAC D2, TRAC 6, and GR 3 (on target in blue), and MG29-1 guides TRAC 9, TRAC 19, TRAC 35, and GR 13 (on target in yellow) across three biological replicates. Source: Lamothe et al 2023 CRISPR Journal

Our nucleases enable highly efficient and specific in vivo genome editing in preclinical evaluations

Type II MG3-6/8 is our chimeric nuclease that has been extensively characterized *in vitro* and *in vivo*. This system is engineered from the MG3-6 chassis, which was discovered from the genome of a commensal, non-pathogenic representative of the human microbiome that showed high editing efficiencies when tested

across multiple mammalian cell types (see Figures 6, 8 and 9 above). The engineering involved changing the PAM interacting domain of the chassis, which enables the enzyme to be targeted to new sites in the human genome. Figure 10 shows that this system is suitable for *in vivo* applications, based on saturating levels of editing achieved in a mouse study with a single administration of nuclease mRNA and guide encapsulated in a LNP with tropism to the liver.

Figure 10. *In Vivo* Editing in Mice with MG3-6/8 Nuclease.



Editing efficiency was determined based on the frequency of InDels detected by NGS at genomic sites targeted by each nuclease.

* Delivery by mRNA and LNP, dosing at 1 mg/kg.

* Mean of 79% genome editing efficiency as measured by the frequency of InDels detected by NGS at the targeted genomic site.

In addition, one of our most highly characterized type V nucleases, MG29-1, demonstrated high activity and specificity during multiple preclinical studies spanning from *in vitro* to NHP. Originating from a bacterial genome found in a deep sea hydrothermal vent, MG29-1 has a smaller protein (1,280 aa) and gRNA (~70 nt) compared with MG3-6 (1,135 aa and ~110 nt) and SpCas9 (1,368 aa and ~100 nt). MG29-1 has demonstrated up to 97% editing in primary mouse hepatocytes in culture (Figure 11a), superior liver editing to an exemplary SpCas9 guide targeting an overlapping genomic site when delivered to mice using a LNP that delivers primarily to the hepatocytes in the liver (Figure 11b), and on average 50% editing in the whole liver of NHP when delivered in a LNP that delivers primarily to the hepatocytes in the liver (Figure 11c, guide 2). Approximately 76% of the genomes in mouse liver are from hepatocytes based upon a published analysis of gene editing in whole liver compared to hepatocytes isolated from the same edited mice. Using this conversion factor of 76% (1/0.76), we achieved 100% editing of hepatocytes with MG3-6/3-8 (Figure 10) and 94% editing of hepatocytes with MG29-1 (Figure 11b).

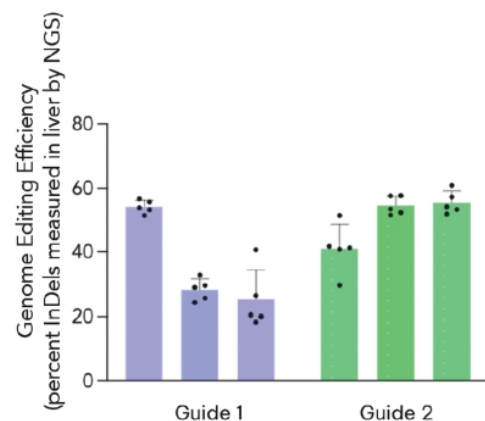
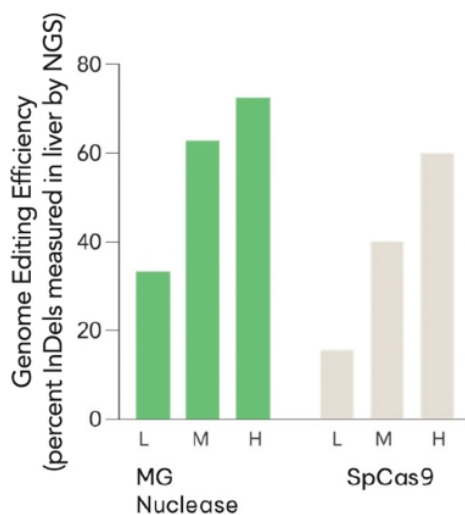
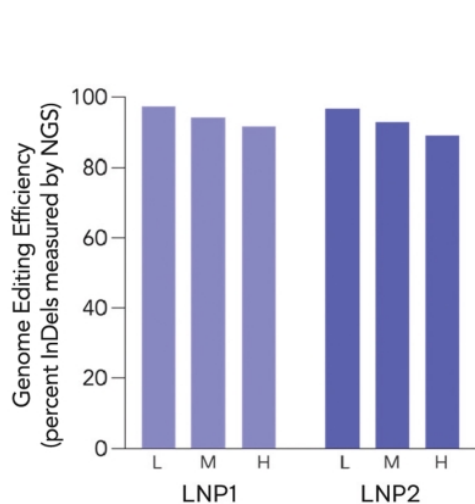
In cynomolgus monkeys, it is estimated that hepatocytes make up 60% of the cells in the liver. Therefore, 50% editing in the whole liver achieved with MG29-1 in NHP (Figure 11c, guide 2) translates to editing of approximately 80% of the hepatocyte genomes which are the therapeutically relevant target cell.

Figure 11. Our Type V MG29-1 Nuclease is a Highly Active Natural Enzyme for *In Vivo* Genome Editing.

Figure 11a. MG29-1 achieved saturating levels of editing in primary mouse hepatocytes.

Figure 11b. MG29-1 has higher potency than SpCas9 when editing mouse liver cell genomes *in vivo*.

Figure 11c. MG29-1 demonstrates successful editing in NHPs.



- * MG29-1 and SpCas9 were delivered by LNP with co-formulated mRNA and gRNA.
- * gRNAs for both MG29-1 and SpCas9 have overlapping target sites.
- * mRNAs for both nucleases use the same overall design and were codon optimized with the same algorithm.
- * The SpCas9 gRNA incorporated extensive optimizations published in the literature.
- * InDels were analyzed by NGS four days after IV infusion.
- * L, M, H, refer to low, medium and high doses.

* 50% whole liver editing = 80% hepatocytes editing.

We use multiple unbiased, industry standard methods to identify putative off-target edits, which are then investigated using sensitive targeted sequencing. To date no detectable off-target editing has been observed for the MG29-1 lead guide for two of our therapeutic programs at therapeutically relevant doses, which is consistent with MG29-1 being a highly efficient, specific and programmable nuclease suitable for broad *in vivo* genome editing applications. Beyond MG29-1, the multitude of nucleases in our toolbox enables us to screen an extensive guide library for any genomic locus of interest. For exemplary lead guides that have been examined for off-target editing we observe minimal or no detectable off-target editing.

Our ultra-small nucleases are efficient genome editors that unlock additional delivery modalities

Delivery of genome editing payloads is often restricted by the size limitations of the delivery vehicle. Therefore, we leverage our metagenomics database to find new nucleases that are significantly smaller than current systems. After searching through billions of predicted proteins from bioinformatically reconstructed microbial genomes, we uncovered several distinct types of ultra-small nucleases. Our lead ultra-small nucleases are significantly smaller than CRISPR SpCas9, enabling new and improved *in vivo* delivery methods and new possibilities for building base editing systems and prime editors that can be packaged in size-constrained delivery vehicles. Typical CRISPR Cas9 systems are about 1,300 aa in length whereas some of these new systems are just over 450 aa. Compact systems create potential advantages for delivery, manufacturing, and dosing. Furthermore, they can be delivered to organs and tissues currently only accessible by AAV, given that the nucleases are well-within the packaging limitations of these delivery vectors. The smaller size of these nucleases compared to previous systems potentially unlock target indications beyond applications in the liver. Because of their novel biochemistry and divergence from typical type II, we refer to some of these ultra-small nucleases as SMART. In addition, we identified several novel families of ultra-small type V nucleases. Unlike compact type V, and all other previously studied type V, SMART have a dual catalytic domain structure that enables engineering of nickase variants that can be used for base and prime editing.

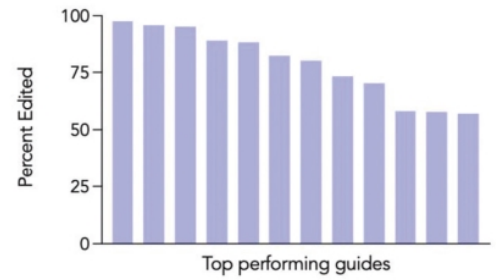
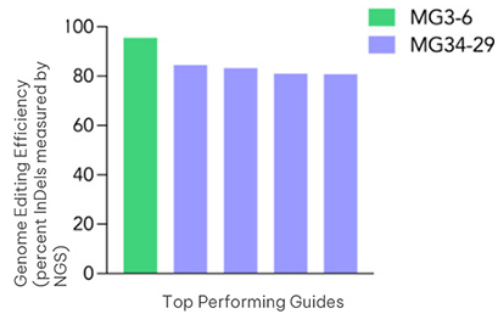
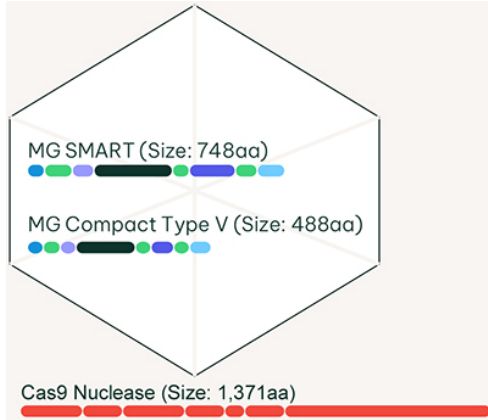
Figure 12 shows that genome editing efficiencies achieved for SMART and compact type V nucleases are comparable to other lead systems. These results show that our ultra-small nucleases are highly efficient genome editing systems that have the potential for extensive therapeutic applications, including for those in which delivery is a limiting factor.

Figure 12. Our Ultra-Small Nucleases are Designed to be Highly Efficient Genome Editing Systems that Are Well-Within the Packaging Limits of AAV Vectors.

Figure 12a. Schematic representation of how our ultra-small nucleases are a fraction of the size of a typical CRISPR SpCas9 nuclease.

Figure 12b. SMART nuclease showed high editing efficiency in mammalian cells, prior to optimization.

Figure 12c. Compact type V nuclease showed high editing efficiency in mammalian cells, prior to optimization.



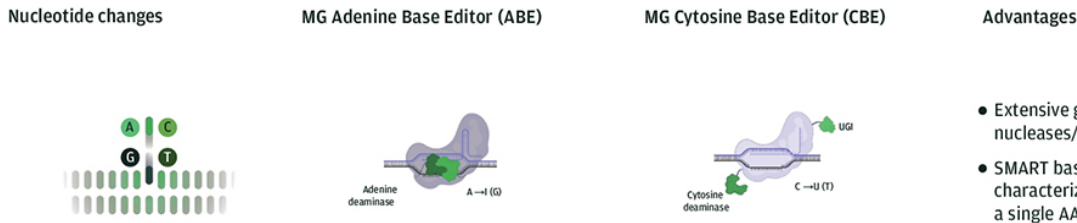
* InDels are measured by NGS.
 * Each bar represents a distinct guide.
 * MG3-6 used as internal control.

* InDels are measured by NGS.
 * Each bar represents a distinct guide.

Base Editors

Overview

Figure 13. Schematic Showing the Two Primary Types of Base Editors under Development.



We leverage our toolbox of programmable nucleases to develop a highly targetable and flexible base editing platform compatible with various delivery technologies. Base editing modifies individual bases in the genome without making double-stranded breaks in the DNA. This approach uses a chemical reaction designed to create precise, predictable, and efficient genetic outcomes at the targeted sequence. These precise changes to individual base pairs in the genome can be used to correct or change genomic sequence in order to address disease. Notably, the most common class of genetic mutations are errors of a single base, known as point mutations. These point mutations, many of which could be addressed with a base editor, represent approximately 58% of all the known genetic errors associated with disease. Furthermore, base editors can be used to precisely knockdown genes by introducing premature stop codons or interrupting gene splice sites.

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There are two types of base editors: ABEs and CBEs. ABEs convert adenine-thymine base pairs to guanine-cytosine base pairs. CBEs target cytosine-guanine and convert them to thymine-adenine. We are developing both ABEs and CBEs, which have been validated across multiple mammalian cell types and *in vivo*, to enable broad use of the base editing approach for addressing disease (Figure 13).

Base editors are composed of a targeting enzyme, typically a programmable nuclease that has been engineered to localize to a specific site in the genome but not cause a dsDNA break, and a deaminase, which is responsible for the chemical conversion of targeted genomic bases. Base editors can be engineered using modified nickase programmable nucleases that have been engineered to nick rather than cut genomic targets (i.e. a nickase variant). The nickase recognizes and binds to specific DNA sequences, determined by a gRNA, enabling deaminases that are fused to the nickase to modify the targeted bases. Typically, the modified bases are found on the single-stranded DNA that is exposed at a target site when the gRNA is bound to one of the strands of DNA. The efficiency of cytosine base editors can be improved by the addition of another enzyme called a UGI. The UGI protects edited bases against DNA repair machinery that would otherwise remove them and revert the edited sequence back to its original form.

Base editing results in one or more mismatched bases in the dsDNA, which are resolved by DNA repair mechanisms in the cell. Nickases are typically used such that the DNA strand opposite to the modified bases is nicked, thus biasing DNA repair pathways to favor the modified strand over the original sequence. The result is a precise change in one or more targeted bases without creating double-stranded breaks or requiring a donor template.

Our Approach

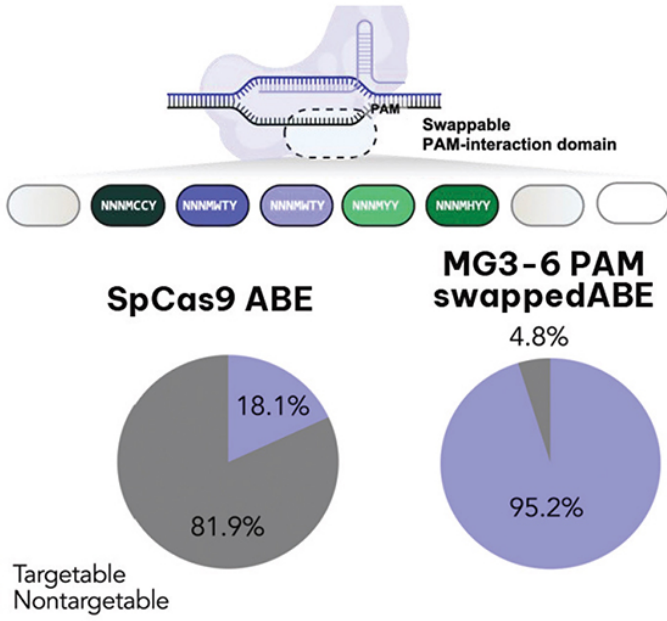
We are leveraging our toolbox of programmable nucleases and our metagenomics discovery platform to develop next generation base editing tools. Our programmable nucleases provide the ability to efficiently and precisely target locations in the genome required in order to potentially create a wide-variety of genetic medicines. In addition, the availability of ultra-small SMART effectors enables us to develop base editors that could be delivered to various target tissues and organs. While established base editing systems using SpCas9 require splitting the system into two AAV vectors for delivery, those developed from SMART are designed to be within the packaging limitations of a single AAV. We have discovered and engineered what we believe to be two of the smallest base editors developed to date, one SMART ABE that is 623 aa in length and another SMART ABE that is 969 aa. These systems provide substantial opportunities for vector optimization compared with SpCas9 ABEs that are 1,588 aa. Furthermore, the flexibility of the modular, chimeric nuclease platform, enables rapid optimization of base editors capable of editing at a multitude of target sites, since engineering and optimization applied to one base editor can rapidly be applied to other systems with the capability of targeting to new genomic sites.

Given that base editors require deaminases, and a UGI in the case of cytosine base editors, substantial enzyme discovery beyond programmable nucleases has been required in order to develop highly efficient base editors that have the potential to overcome the limitations of the current technology. We have mined over three million deaminases in order to identify enzymes with the capability to function as part of base editing systems. In many cases these novel deaminases have required minimal protein engineering to achieve therapeutically-relevant editing efficiencies in multiple studies. The ability of our metagenomics discovery platform to identify novel enzymes with high activity makes it possible to rapidly develop differentiated technology that surpasses first-generation systems.

Our base editors are highly active in mammalian cells across various genomic targets

Figure 14 ABE and CBE Developed from Type II MG3-6 System Have Been Shown to be Highly Active in Mammalian Cells, with Extensive Genome Targetability to Enable Potential *In Vivo* and *Ex Vivo* Therapeutic Development.

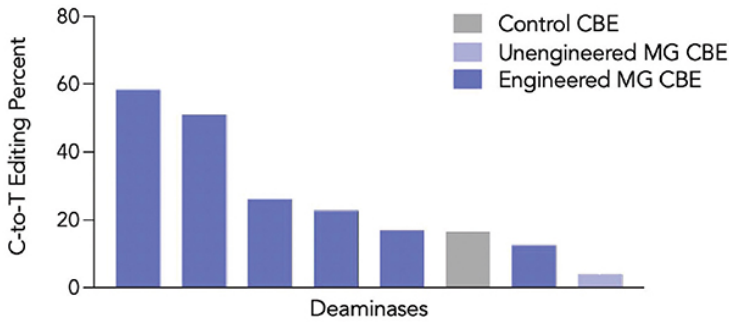
Figure 14a. PAM interacting domain engineering was used to develop a suite of chimeric MG3-6 base editors with extensive genome targetability.



* ABE: SpCas9 = 18% and MG3-6 = 95% targetability.
 * CBE (not shown): SpCas9 = 5% and MG3-6 = 53%.

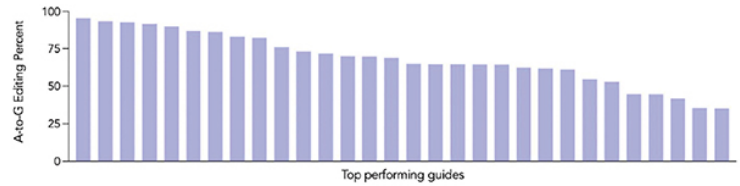
* ABE: SpCas9 = 18% and MG3-6 = 95% targetability.
 * CBE (not shown): SpCas9 = 5% and MG3-6 = 53%.

Figure 14c. CBE screening identified highly active deaminases for C-to-T editing, compared to published control.



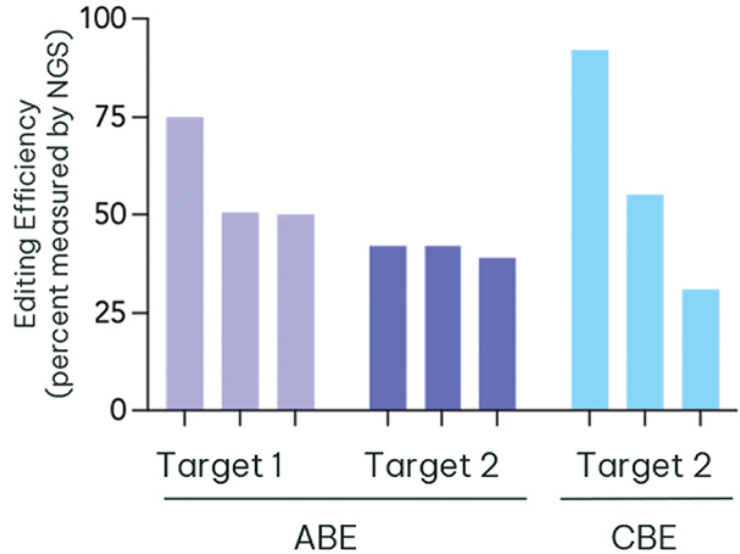
* Unoptimized CBE construct tested in HEK293T cells with plasmid delivery.
 * CBE control uses hyperactive CDA A0A2K5RDN7.

Figure 14b. ABE screening identified guides capable of achieving saturating levels of A-to-G genome editing in mammalian cells.



* Optimized ABE construct tested in Hepa 1-6 cells with mRNA delivery.

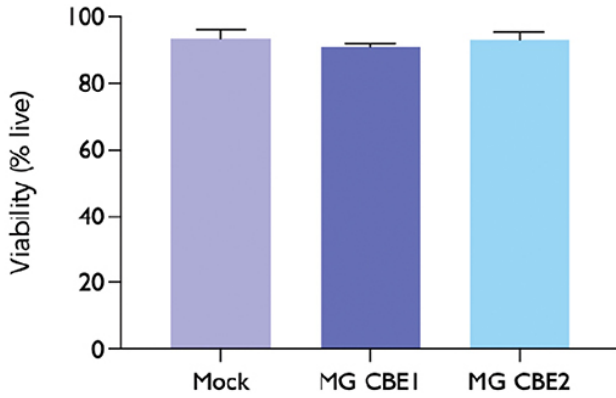
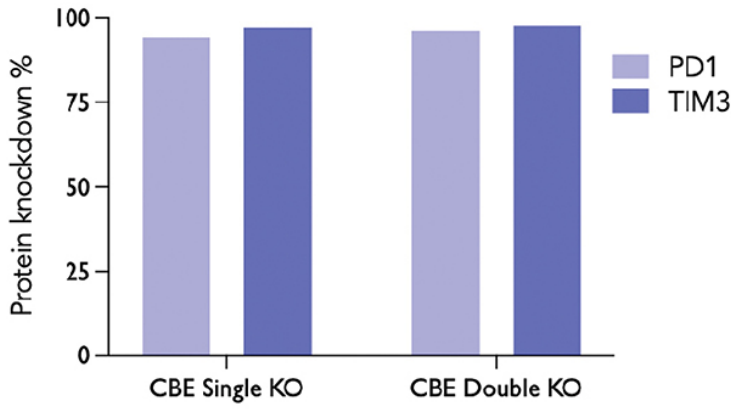
Figure 14d. MG3-6 PAM chimera ABE and CBE achieved efficient editing at splice-sites for enacting therapeutically-relevant knock-out of genes in human cells.



* Top three guides shown for each target and system.

* Constructs tested in HEK293T cells with mRNA delivery for the BE along with chemically synthesized guides.

Figure 14e. MG3-6 CBEs are efficient for multiplexed knock-outs in primary human T cells with no impact on cell viability.



* Top panel shows two guides that were used to knock out two different proteins, either when edited independently or when multiplexed.
 * Experiments were conducted in primary human T cells using mRNA delivery for the BE along with chemically synthesized guides.

Our base editors are highly active and progressing towards *in vivo* therapeutic applications. Both of our ABE and CBE systems have been tested in mammalian cells in order to determine editing efficiency, where a large collection of guides spanning various genomic loci were tested for each system. Figure 14 shows the development of a highly efficient and targetable base editing platform established from the MG3-6 nuclease chassis. Using PAM interacting domain engineering, the theoretical targetability of the ABE and CBE was shown to be significantly greater than that of typical base editors developed from SpCas9. Based on PAM availability the ABE was able to target over 95% of the adenine bases in the human genome, and the CBE was able to target over 50% of the cytosine bases, compared with approximately 18% and 5%, respectively, for SpCas9. Furthermore, over 95% editing efficiency was achieved with both an optimized ABE and CBE construct delivered by mRNA. Initial CBE testing without construct optimization using a less-efficient plasmid delivery approach achieved up to 58% editing efficiency, which was notable because it outperformed an industry-standard control CBE by several fold in the benchmarking experiment shown in Figure 14. We demonstrated that these efficient ABE and CBE systems could be used for creating edits that have the potential to result in protein knockdown, which could be applied for therapeutically relevant editing *in vivo*. Furthermore, we believe the observed CBE multiplexing in primary T cells shows that this platform has the potential to advance *ex vivo* cell therapy development by making it possible to efficiently knock out multiple proteins without impacting cell viability.

Our base editing platform has broad *in vivo* therapeutic potential

Figure 15. Lead ABE System Developed from Type II MG3-6 System Demonstrated High Activity in Primary Cells and in an *in vivo* Mouse Model.

Figure 15a. Our lead ABE system efficiently edited primary mouse hepatocytes at example target sites.

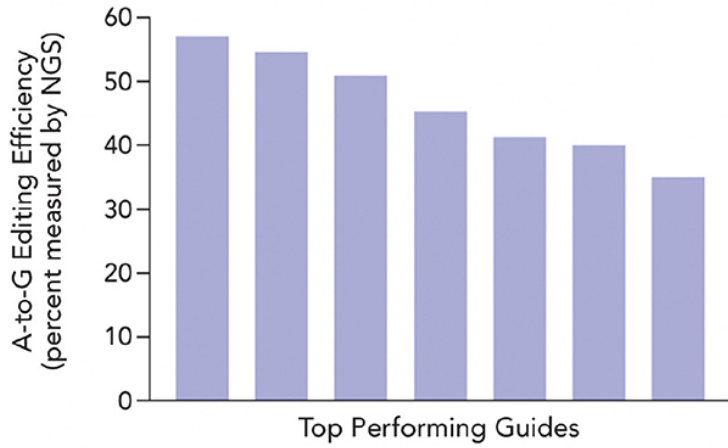
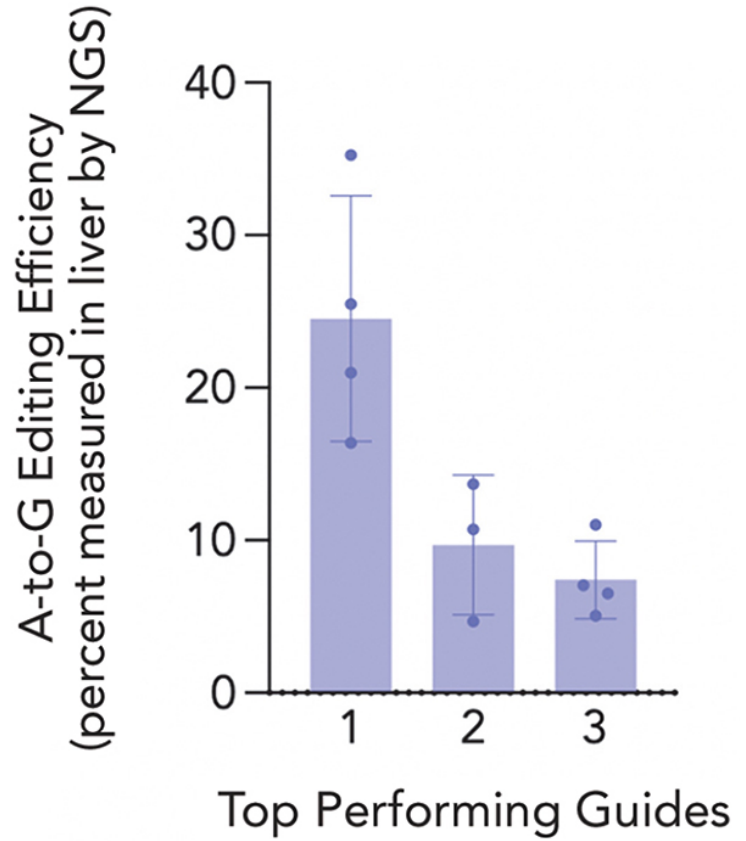


Figure 15b. Our lead ABE system demonstrated activity *in vivo* when delivered to mouse livers by mRNA and LNP.



In order to demonstrate the utility of the MG3-6 ABE platform for *in vivo* base editing, a lead construct design was tested both in primary cells and in mice. Multiple guides were tested in each study, designed to target different genomic loci. Figure 15 shows the results of these evaluations of the ABE platform, where up to 60% editing efficiency was demonstrated in primary hepatocytes and 35% efficiency was achieved across all liver cells in an initial *in vivo* study using mRNA and LNP delivery. Given that approximately 70% of liver cells are hepatocytes, and therefore targetable by the LNP platform, this editing experiment suggests that approximately 50% of all targetable cells were successfully edited. We believe this level of editing, which is comparable to other initial *in vivo* base editing studies, supports the potential to rapidly progress towards therapeutic applications. Given that both the ABE and CBE data shown in Figures 14 and 15 are based on a chimeric MG3-6 nickase, we anticipate that the broad targetability of this system will enable rapid development of multiple potential new therapeutic applications of base editing technology.

Our SMART have been engineered to create ultra-small base editors, expanding the potential deliverability of base editing technology

Figure 16. SMART Can be Engineered into Ultra-Small Base Editors with Naturally High Editing Efficiency and AAV Compatibility.

Figure 16a. Ultra-small SMART base editors are a fraction of the size of a typical Cas9 system, enabling AAV delivery.

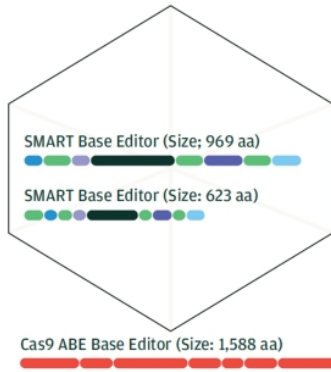
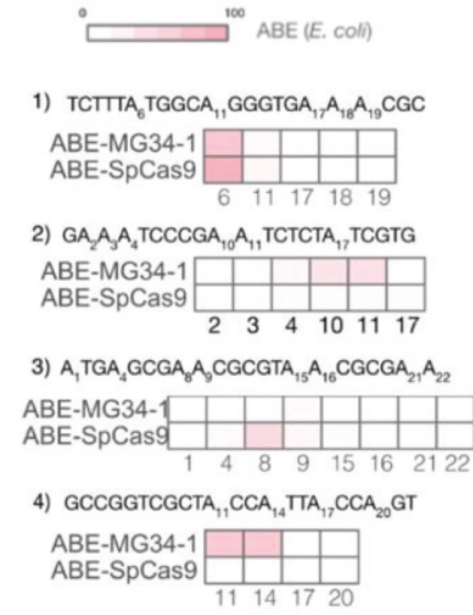
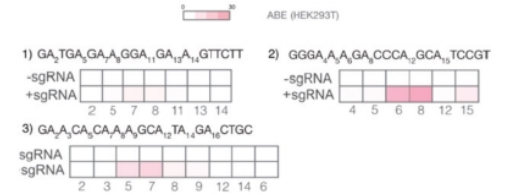


Figure 16b. SMART ABE exhibited a similar editing profile *in vitro* compared to SpCas9.



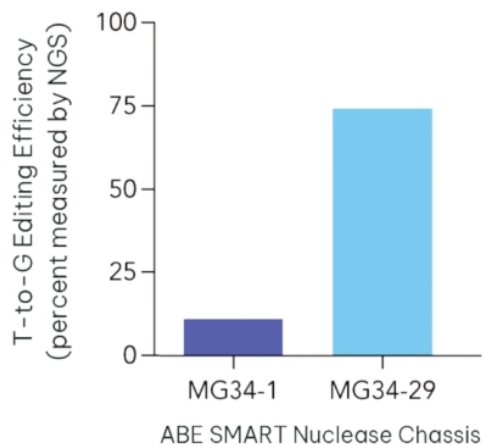
- * SMART ABE-MG34-1 base editing at four genomic targets loci in *E. coli*. vs. reference SpCas9 system.
- * Heatmap values represent the mean of two independent experiments.
- * The target sequence for each locus is shown above the heatmap.
- * Heatmaps represent the percentage of NGS reads supporting an edit at each position.

Figure 16c. SMART ABE were active in mammalian cells.



- * SMART ABE achieved up to 22% base editing efficiency in human cells.
- * Base editing efficiency shown at three genomic targets tested in human HEK293T cells.
- * Heatmap values represent the mean of three independent experiments.

Figure 16d. SMART ABE optimization improved editing efficiency in human cells.



* Top guide shown for each SMART ABE system.

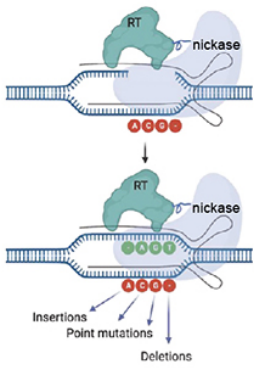
Figure 16 illustrates how our ultra-small SMART nucleases provide an opportunity to develop compact base editors with the potential to improve delivery using existing AAV technology. Our engineered, but unoptimized SMART ABE systems were observed to edit target loci at levels comparable to reference SpCas9 systems, and with up to 22% editing efficiency in mammalian cells. Achieving this level of efficiency with an unoptimized system, comparable to initial base editing readouts achieved with SpCas9, indicates the potential of this novel CRISPR platform. Additional optimization enabled editing in human cells at over 80% efficiency. The SMART ABE highlighted in Figure 16 is one of the smallest nickase-based systems with activity in mammalian cells (969 aa), and at 623 aa another SMART ABE under development is even smaller. Together, these systems provide us with unique opportunities to optimize base editors using the naturally compact, precise, and programmable SMART platform.

RNA-Mediated Integration Systems: RIGS for prime editing and large genomic integrations

Overview

Figure 17. Schematic Showing Application of RIGS for Small Replacements and Large Integrations.

Little RIGS (Prime Editing)

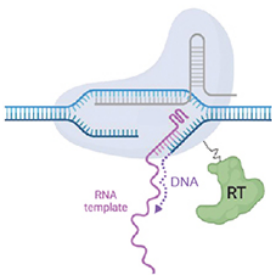


1-100 base pair replacement, insertion, or deletion

Advantages

- Extensive genome targetability enabled by Metagenomi nucleases/nickases
- Ultra-small RTs are highly active and accurate for prime editing

Big RIGS for Large Integrations



100-10,000+ bp integrations

- Potentially extensive genome targetability enabled by Metagenomi nucleases/nickases
- RNA-templated integrations
- Will enable 'all RNA' delivery of genome editing system and integration template

Programmable nucleases, which use dsDNA breaks to trigger DNA repair machinery to enact specific genomic changes, and base editors, which use chemical modifications to convert specific base pairs in the human genome, cannot address all mutations that cause disease. RIGS are being developed in order to encode any type of genomic modification in an RNA template, and thus create any type of genome modification necessary to address a disease (Figure 17). RIGS involve using RTs to convert genomic corrections encoded in RNA into DNA, and are engineered with programmable nucleases or nickases to incorporate newly synthesized DNA messages into the genome at specified target sites. Importantly, any genomic modification can be encoded in the RNA template. Furthermore, the potential for having an all-RNA format for the system, including delivery of the protein components as mRNA, could simplify delivery for some applications. For example, the all-RNA format could enable use of LNPs for delivery of systems to the liver for large, targeted genomic integrations. The enzymatic nature of the genome integration, combined with the ability to deliver the entire system as RNA is of particular importance when considering large integrations, since the delivery of DNA templates at concentrations required for integration mediated by DNA repair machinery can be toxic.

One implementation of RIGS is to use our programmable nickases and RTs for prime editing. Prime editing can repair diverse mutations, including all types of point mutations, deletion mutations, insertion and duplication mutations and insertion-deletion mutations. As with other genome editing approaches, prime editing systems, and RIGS more broadly, create permanent modifications at natural genomic locations, resulting in durable edits that are passed on through cell divisions and that are expressed under natural mechanisms specific to the gene or target of interest. One key aspect of prime editing is the modification of a CRISPR gRNA to create a pegRNA ("prime editing gRNA"). In this design, the typical backbone and targeting components of the gRNA are maintained; however, additional sequence is added to the guide in order to code for a desired genomic correction and to prime a RT to begin synthesizing new DNA sequence. During prime editing a portion of the

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pegRNA containing the genomic modification is copied into DNA at a specific site in the genome sequence. Once the RT has incorporated the new DNA sequence into the target site, DNA repair machinery will finalize the genome edit by removing the corresponding section of the original sequence, synthesizing any required complementary DNA, and ligating the ends of the nicked DNA strands. We have discovered a collection of novel RTs that can be combined with our nickases to perform prime editing in mammalian cells at levels and with accuracy that surpasses industry-standard systems.

Current prime editing and RNA-templated editing approaches are limited by the size of the RNA template that can be incorporated into a genomic site. This limitation is based on multiple aspects of the system design, including 1) the need to encode gRNA and RT template sequences in a single pegRNA, and 2) the processivity and fidelity of the RT. The first constraint can be addressed by creating new system designs in which the gRNA and repair template are encoded in separate RNA molecules, where additional engineering ensures that the templates and RT are able to co-localize to the nucleus, and more specifically, to targeted sites in the genome. Regarding the second point, processivity and fidelity are biochemical characteristics that relate to the ability of an RT to traverse through large and structurally complex RNA templates (processivity) and to do so without introducing errors (fidelity). We have identified and developed novel RTs that we believe surpass the processivity and fidelity requirements for therapeutic delivery of transgenes as RNA templates, for example in order to treat diseases by introducing a complete and correct copy of a gene in order to overcome a loss-of-function mutation. Furthermore, we are engineering these RTs with programmable nucleases and nickases to achieve large, targeted genomic integrations.

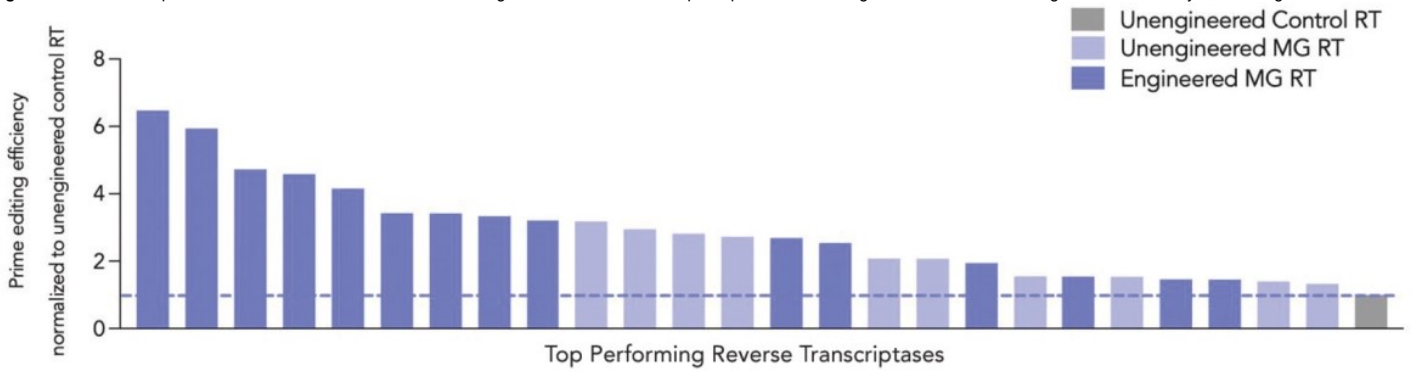
Our Approach

Similar to base editing, development of RIGS leverages our expansive platform of programmable nucleases that can be converted into nickases, including ultra-small SMART, as well as a metagenomics discovery approach that enables the rapid identification of novel RTs that have the specific characteristics necessary for different genome editing applications. The targetability of our toolbox of programmable nucleases will enable essentially any target sites of interest to be addressed, and compatibility with ultra-small SMART effectors could expand the deliverability of RIGS to therapeutically relevant tissues and organs.

Little RIGS describes systems used for prime editing (e.g., for small genomic replacements such as transversions, transitions, insertions, and deletions), while Big RIGS describes systems capable of making large targeted genomic integrations. The mechanisms driving these systems differ from one another, but both are based on using a reverse transcriptase to incorporate genomic corrections encoded in RNA into target sites in the genome identified by a programmable nickase or nuclease. We identified five million RT candidates from novel families in order to find systems for Little and Big RIGS development. RTs found in nature are highly diverse, but typically do not have all the characteristics suited towards being useful in a therapeutic context. Based on measured enzyme characteristics such as fidelity and processivity, RTs are nominated and combined with our programmable nucleases/nickases for either Little and/or Big RIGS engineering. Our Little RIGS are benchmarked against industry-standard prime editing systems in order to rapidly identify top-performing systems. Currently, we believe no genome editing system has been described that is comparable to Big RIGS. Our Big and Little RIGS are undergoing indication-specific optimization. We believe that this combination of discovery and system optimization will enable the rapid development of best genome editing systems that, together, can enact any type of genomic edit.

Our RIGS have shown complex prime editing in mammalian cells

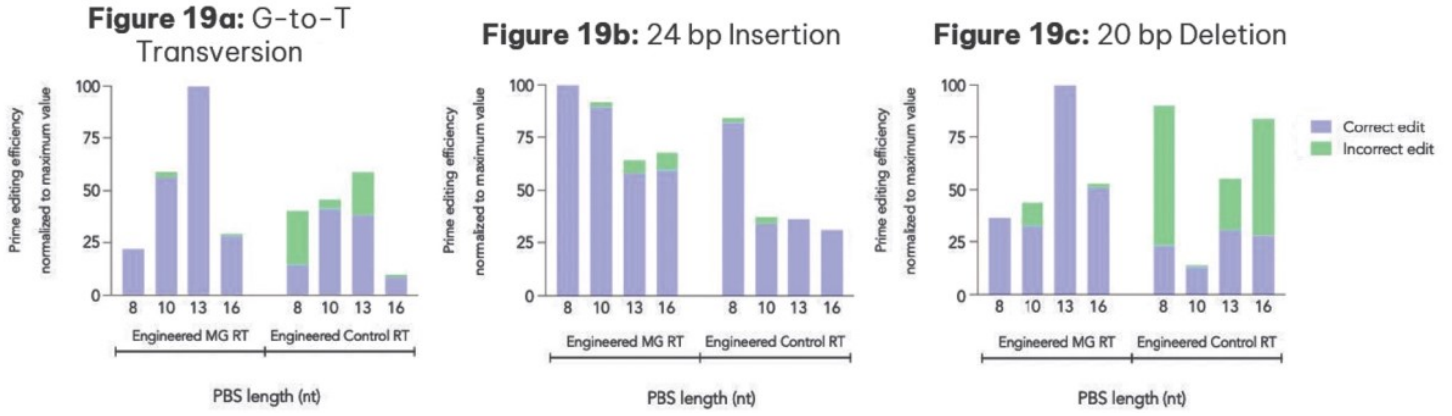
Figure 18. Our RTs Outperformed Benchmarks for G-to-T Prime Editing in Mammalian Cells. Graph Depicts a Broad Range of RTs that Exhibited Higher Natural Activity than Unengineered Prime Editing RT.



- * Unengineered prime editing control RT is from Moloney murine leukemia virus ("MMLV").
- * RTs were cloned into a plasmid backbone that was co-transfected with chemically synthesized pegRNAs designed to edit the genome of human HEK293T cells.
- * Genomic DNA was isolated 72 hours post transfection and target loci were amplified for NGS to evaluate editing outcomes.

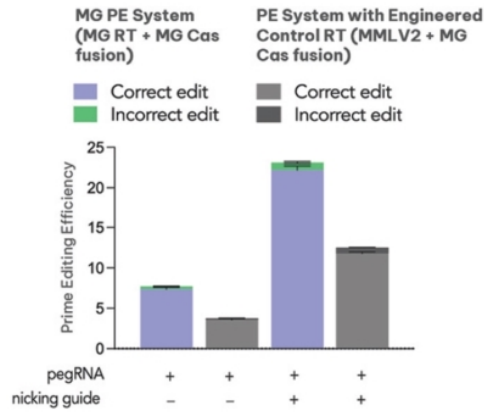
Our RTs are benchmarked against natural and engineered variants of an RT widely used for prime editing in order to identify highly active natural enzymes for further optimization along with our programmable nickases. Figure 18 shows that our natural RTs are more active than a control RT when used for prime editing. In addition, our minimally engineered RTs demonstrated up to 6 times higher activity than the unengineered control RT for a G-to-T change. This indicates that we can potentially optimize gene editing activity quicker than comparable prime editing RTs. Figure 19 shows that a minimally engineered Metagenomi RT has editing efficiencies equivalent to or better than engineered, industry-standard prime editing RT. Notably, this has been achieved with an ultra-small RT that is only 251 aa in length, compared with the 671 aa of the standard prime editing RT. For therapeutic applications, complex corrections must be precise, and the precision of RIGS depends on the unique characteristics of the reverse transcriptase used. Figure 19 also shows that one of our RTs has demonstrated significantly higher editing accuracy compared to the engineered, industry-standard control. In order to measure optimal activity for new systems, multiple primer binding sequence ("PBS") lengths must be tested. In some case, Metagenomi RT are more active across a broader range and with smaller PBS lengths compared with the control, providing more flexibility around pegRNA design. We believe our RIGS are distinguished from typical systems used for prime editing by the high efficiency and accuracy of the RTs, as well as the broad targetability of our programmable nickases.

Figure 19. Our Ultra-Small RTs are Efficient and Accurate Systems for Conducting Complex Genomic Corrections in Human Cells.



- * The engineered prime editing benchmark RT is the MMLV variant used in PE2 prime editing systems.
- * RT were tested with an unoptimized plasmid delivery system that enables high-throughput benchmarking of novel RT to identify leads.
- * Plasmids encoding RT and Cas were co-transfected with chemically synthesized pegRNAs designed to edit the genome of human HEK293T cells.
- * Genomic DNA was isolated 72 hours post transfection and target loci were amplified for NGS to evaluate editing outcomes.

Figure 19d. 5 bp Replacement

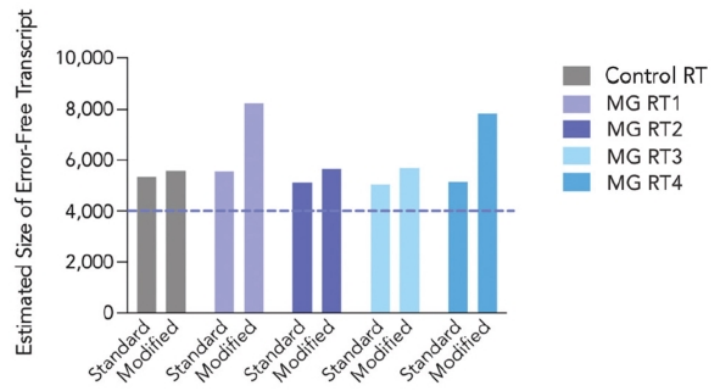
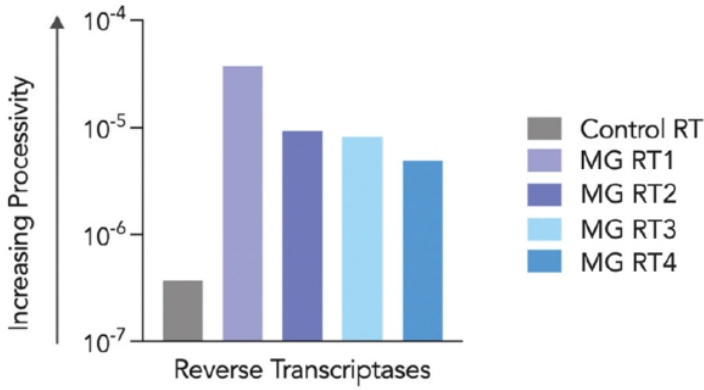


- * The engineered prime editing benchmark RT is the MMLV variant used in PE2 prime editing systems.
- * Our ultra-small MG RT was fused to MG Cas and tested with mRNA delivery and chemically synthesized pegRNAs designed to edit the genome of human HEK293T cells.
- * Co-transfection with chemically synthesized guides designed to program the Cas to create a nick in the vicinity of the edit were included to bias DNA repair towards the edited strand.
- * Genomic DNA was isolated 72 hours post transfection and target loci were amplified for NGS to evaluate editing outcomes.

Our novel RTs are selected to enable the development of Big RIGS for RNA-templated, large, targeted therapeutic transgene integration

Figure 20. Our RTs Have Been Observed to be Active, Processive, and High-Fidelity.

Figure 20a. Our RTs were more processive than RT typically used for prime editing, enabling transcriptions of large gene templates in mammalian cells. **Figure 20b.** Our RTs were more accurate than industry-standard RT.



* Prime editing benchmark RT is MMLV.

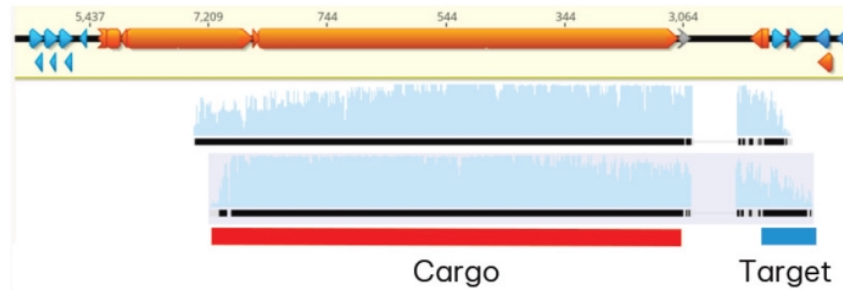
* Processivity was measured by quantitative polymerase chain reaction ("qPCR") quantification of cDNA produced in mammalian cells from 4 kb templates.

* Typically, less than 1% of 4 kb templates are fully transcribed by MMLV.

* Template modifications are N1-methylpseudouridine.

* Fidelity was measured by NGS.

Figure 20c. Our RT can be combined with our Cas to achieve targeted integration of >900 bp in human cells.



* Targeted integration confirmed by Sanger sequencing.

* Our MG RT was combined with MG Cas and tested using mRNA delivery along with chemically synthesized gRNA and the RNA integration template.

* Integration was targeted to an engineered landing pad located in the genome of HEK293T cells.

Our RTs were screened based on their activity and processivity in mammalian cells in order to identify highly active systems capable of reverse transcribing RNA templates over 4,000 base pairs in length (>4 kbp). We chose the 4 kb benchmark as many potential therapeutic targets could be addressed with a genomic integration of this size (current prime editing systems are limited to RNA-templated integration around 100 bp). In Figure 20, our best-characterized RTs were compared with industry standard systems in order to benchmark their activity, processivity, and fidelity. When tested in mammalian cells, our RTs were routinely able to fully transcribe a 4 kbp template into DNA. In Figure 20a, we show that our RTs demonstrated orders of magnitude more processivity than control RT when tested on these large templates, which we believe is a strong indication of being able to convert therapeutically relevant templates delivered as RNA into DNA for genomic integration. Importantly, Figure 20b also shows that on average our RTs transcribed over 4 kbp without introducing errors. Furthermore, template modifications (N1-methylpseudouridine), which could enable delivery of RNA templates

less likely to trigger an immune response, improved fidelity. We are engineering our RTs along with our programmable nucleases and nickases for targeted genomic integration of a donor template delivered as RNA. Initial readouts show that when combined with a CRISPR effector and targeting gRNA, Metagenomi RT are able to incorporate newly synthesized DNA from an RNA template into a target site. In Figure 20c, we report what we believe to be the first-ever targeted integration of >900 bp in human cells with all-RNA delivery. In principle, these systems, which represent a major step forward in the genome editing space, could be delivered entirely as RNA and could enable large, targeted exogenous gene integrations.

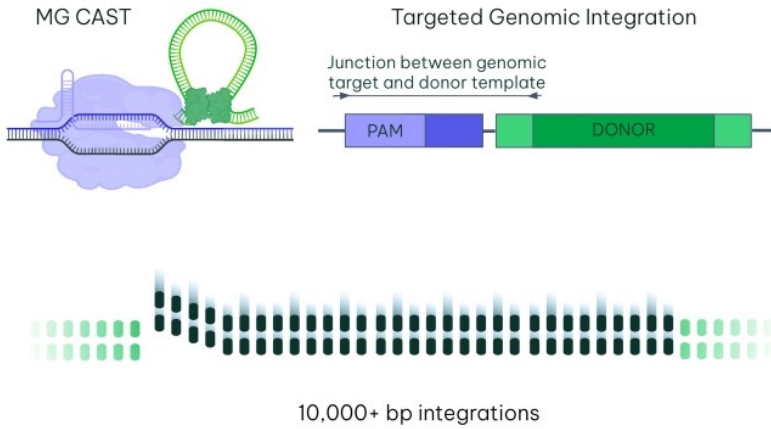
DNA-Mediated Integration Systems: CAST and other approaches to achieving large genomic integrations

Overview

Figure 21. Schematic Showing Application of CAST for Large, Targeted Genomic Integrations.

CASTs for Large Integrations

Advantages



- DNA-templated integrations, potentially including templates much larger than what can be accomplished with RIGS

Genome editing approaches based on nucleases, base editing, and prime editing are capable of precisely modifying the genome to address disease. However, for therapeutic approaches that necessitate expression of an exogenous gene or complete gene correction, large integration approaches are needed. Many individual diseases are associated with a wide variety of genetic mutations and thus may require an entire healthy gene to counteract each of the many different underlying causes. For example, there are over 1,800 mutations in the CFTR gene associated with cystic fibrosis. While in theory most of these mutations could be addressed using distinct and mutation-specific base or prime editing systems, this would require the optimization and translation of a large number of genome editing therapies. Alternatively, integration of a complete and correct copy of the CFTR gene could potentially cure patients with varying mutations in a one-and-done treatment. Directed DNA integration has largely been considered the ultimate goal of corrective genome editing, where enzymatic systems with this capability could provide safe and sustained therapeutic protein expression. By developing DNA-mediated integration systems and RIGS, we are at the forefront of creating a new class of genome editing therapeutics.

Many efforts over the past decades have sought to achieve direct DNA integration in order to develop treatments that work across diverse tissues, cell types, and genetic variants. Established transposase and lentiviral systems are efficient at inserting large DNA cargos into the human genome but result in non-specific and sometimes hyperactive integrations that have led to severe adverse events during clinical trials. Furthermore, recombinases have gained attention recently as a possible solution, given that they are able to incorporate large (>10 kbp) genomic cargos in a non-random, site-specific manner in mammalian cells. However, these systems typically require additional genome editing tools, such as prime editing systems, in order to first install recognition sites into the genome. These recognition sites are required by the recombinase and thus control where the enzyme can incorporate new genomic material.

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CASTs are a new technology that is exciting because of their programmable, site-specific, and enzymatic integration capabilities. While these systems have been challenging to translate for mammalian cell and human therapeutic applications, we have had recent breakthrough success by demonstrating that the most compact type of CAST, based on catalytically dead nucleases, are capable of programmable and targeted DNA integration into the genome of human cells. Our CASTs are being developed in order to enable large (>10 kbp), targeted genomic integrations for therapeutic applications. This technology has the potential to address a large collection of complex genetic diseases driven by a loss of function mutation, such as cystic fibrosis.

Our Approach

We are pursuing multiple approaches to achieve targeted, large genomic integrations, including both RNA and DNA templated systems. Unlike RNA-templated systems that undergo a copying mechanism in order to integrate into the genome, DNA templated systems orchestrate the direct mobilization of the template into the genome. This direct integration avoids copying mechanisms that may be inhibited by certain template features, and thus allows for the incorporation of much larger templates compared with RNA-mediated systems. Given that RNA-templated systems may have delivery advantages for some applications, we are developing both technologies to have the broadest potential to address diseases through targeted integration of large transgenes.

The development of our novel CAST systems was made possible by the discovery and engineering of active natural variants from our metagenomic library. CASTs are being developed to achieve accurate and efficient integration of large DNA cargos at a target locus, without depending on dsDNA breaks. CASTs are unique in that they combine the programmability of a CRISPR effector with the enzymatic integration capability of a transposase. We hypothesized that activity in human cells could be accomplished by combining novel system discovery with systematic development designed to tune the systems to the mammalian nuclear environment. We conducted a detailed survey of newly-discovered CAST systems and demonstrated the ability of novel systems for programmable integration of a transgene *in vitro* and in *E. coli*. The high efficiency of our systems enabled us to demonstrate directed transposase activity into single copy, safe harbor loci in the genome of human cells, as shown in Figure 21. Our results will enable the rapid development and optimization of CASTs to address unmet therapeutic and biotechnological needs. We believe we are the first to achieve this milestone using the most compact variety of CASTs.

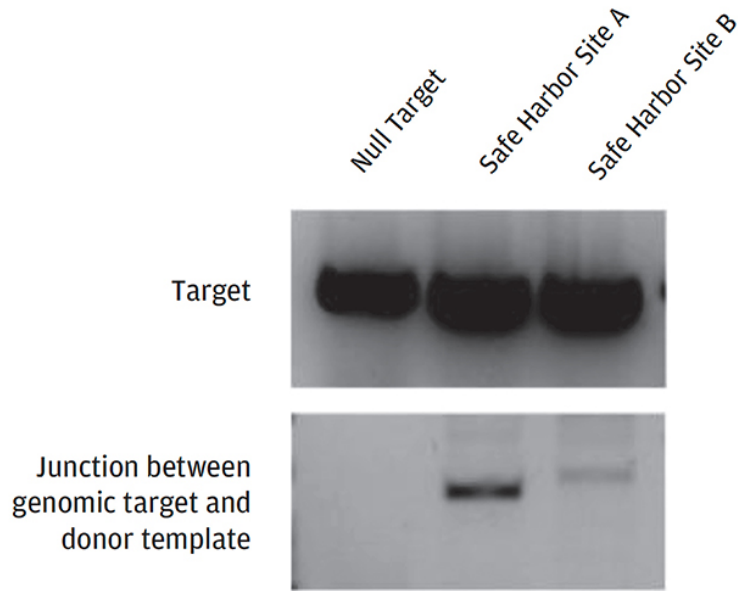
We are also developing systems based on recombinases and other mobile elements that can be used in combination with programmable nucleases, including catalytically dead variants, as well as with Little RIGS in order to affect large, targeted genomic integrations under circumstances where CASTs are not the ideal genome editing technology. Beyond therapeutic use, novel systems with these capabilities could enable synthetic biology, antibody discovery, functional genomics, animal model development, and various other unmet needs in the biotechnology space.

Our novel and engineered CASTs are capable of integrating large DNA cargo at a safe-harbor locus in the human genome

We have shown preclinical proof-of-capability for our CASTs by demonstrating targeted integration of a large DNA template in the genome of mammalian cells. Translation from bacteria to human cell editing required protein engineering to mitigate the complex coordination between multiple protein and nucleotide components. Figure 22 shows polymerase chain reaction ("PCR")-based confirmation achieved by detecting the junction between the donor DNA template and the target sequence in the genome of HEK293T cells. Targeted integration was achieved by delivering the CAST system as an all-in-one plasmid, while the DNA donor is delivered on a second plasmid. In addition, NGS was used to both confirm and quantify integration efficiency, which showed that about 1.5% of sequencing reads had evidence of target-specific integration. We believe the ability to target payloads to a single copy, safe-harbor locus now allows for further therapeutic-driven optimization and development.

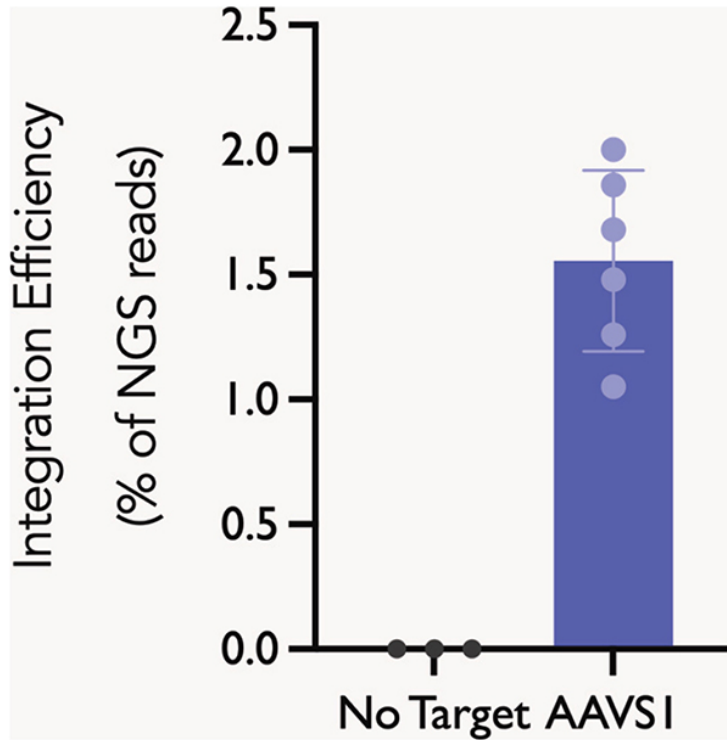
Figure 22. Our CASTs Demonstrated Targeted Integration of a DNA Template at a Safe-harbor Locus in the Genome of Human Cells.

Figure 22a. Targeted integration confirmed by PCR.



- * PCR of junction between template and target confirms integration at target loci in HEK293T cells.
- * Successful transposition is indicated by a band of the correct size in the gel in treated samples, but not in the null target (control) sample.
- * Sequencing of PCR products from the junction between the template and target confirmed integration.

Figure 22b. Integration efficiency measured by NGS.



- * On-target integration efficiency measured by NGS sequencing.
- * Quantified integration efficiencies are shown as the mean (bar) of six AAVS1 or three "No Target" biological replicates (dots) with one standard deviation (whisker). "No Target" represents the non-targeting spacer (negative control), AAVS1 is the targeted safe-harbor locus.

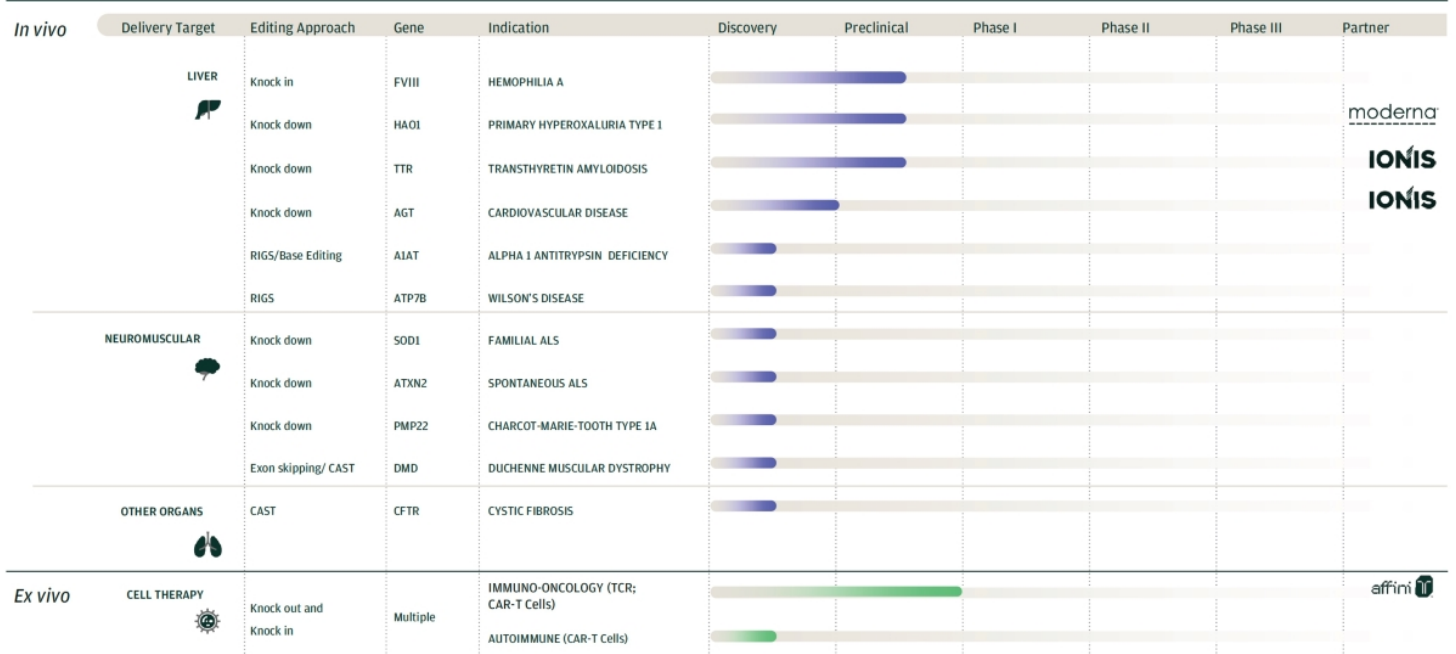
Future Novel Editing System Discoveries

Our scientific underpinnings based in metagenomics provides a continuous engine for discovering and developing potentially next generation genome editing systems. As we continue to build upon our metagenomic library, we expect to make additional discoveries of novel technology, and expand our toolbox to further unlock the field of genome editing.

Our Pipeline

We are taking a stepwise approach deploying our genome editing toolbox to develop potentially curative therapies for patients. Our lead programs are selected to both address important diseases and to establish new standards in targetability, precision, efficiency, and scope of editing capabilities. Figure 23 summarizes the portfolio of programs that we and our partners are advancing, as we aim to match the optimal genome editing tools for each indication. Each of these indications were chosen based on our conviction in the underlying biology, existence of validating preclinical and clinical data, availability of pharmacodynamic and translational tools to assess early proof-of-concept, relevant value-supporting outcome measures, and ongoing clinical unmet need. Our lead programs capture an ever-growing set of translational learnings and insights that will inform and accelerate future programs.

Figure 23. Therapeutic Translation.



Hemophilia A—novel, durable, knock-in approach for expression of Factor VIII

The Disease

Hemophilia A is the most common X-linked inherited bleeding disorder and is caused by mutations in the FVIII gene leading to loss of functional FVIII protein that impacts the body's ability to form normal clots in response to injury. FVIII is normally produced in the liver within sinusoidal endothelial cells and is then secreted into the bloodstream where it acts as a cofactor for the catalytic activation of Factor X in the clotting pathway. The lack of functional FVIII disrupts the normal clotting cascade and predisposes patients to increased risk of bleeding, either spontaneously or in response to injury or surgery. Repeated bleeding episodes in joints or soft tissues can lead to progressive joint damage, inflammation, pain, and mobility impairment. Intracranial bleeding is of greatest concern as this can be rapidly fatal or lead to major morbidity.

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The severity of hemophilia A is directly correlated to the amount of residual FVIII activity. Severe hemophilia is defined as less than 1% of normal FVIII activity, moderate hemophilia defined as 1-5% of normal FVIII activity and mild hemophilia defined as 5 to 40% of normal FVIII activity. There are estimated to be nearly 30,000 patients with hemophilia A in the United States and more than 500,000 patients with hemophilia A globally. Of these, approximately 60% have severe disease and are at the greatest risk of spontaneous life-threatening bleeding events. In these patients, diagnosis typically occurs in infancy due to exaggerated bleeding in response to minor injury or routine medical procedures. As the inheritance of hemophilia A is X-linked, the vast majority of patients are male.

Limitations of Current Approaches

The standard of care for patients with severe hemophilia A involves life-long repeated IV infusions of recombinant FVIII preparations prophylactically and in response to bleeding events. The major limitation of this approach is fluctuating FVIII activity levels, with trough values that can still result in breakthrough microscopic and macroscopic bleeding events, particularly within sensitive and previously damaged joints. Additionally, frequent FVIII infusions are inconvenient, which can be associated with suboptimal compliance, and in some patients result in inhibitor formation (antibodies against FVIII) that compromise efficacy. More recently, emicizumab, a bispecific antibody, has been approved for hemophilia A in the United States that acts as functional FVIII mimetic in binding Factors IXa and X to support catalytic activation. This antibody approach has the benefit of a longer half-life than typical recombinant FVIII protein infusions that allows for less frequent administration but has the drawback of not being a true FVIII protein replacement therapy and breakthrough bleeding has been reported. Both the bispecific antibody and FVIII protein replacement approaches have a high economic burden (estimated lifetime cost of \$15 to 18 million per patient).

Valoctocogene roxaparvec, the first hemophilia A gene therapy, was conditionally approved for use in Europe in August 2022 and was approved in the United States in June 2023. This genetic medicine delivers a FVIII gene construct to the liver using an AAV vector. Once transduction of liver cells occurs, the FVIII gene resides in an episomal state (meaning not integrated in the genome) where it is transcribed from an artificial engineered exogenous promoter to produce FVIII mRNA which is translated into FVIII protein. This gene therapy approach has the potential benefit of constant production of FVIII protein by the liver; however, longitudinal clinical data has demonstrated that FVIII levels drop over time. To date, repeat dosing of a gene therapy has not been possible due to the production of high titers of neutralizing antibodies to the AAV vector. Importantly, AAV gene therapy is also not a feasible treatment approach for infants or children due to the high degree of liver growth during pre-adulthood that would dilute out the episomal FVIII gene during progressive rounds of liver cell division. Thus, there continues to be a significant unmet need in hemophilia A for a curative therapy that can provide life-long protection from bleeding events and joint damage in adults and children.

Our Approach and Results

Experience with early hemophilia A gene therapy approaches suggest that morbidity and mortality from the disease can be markedly reduced by achieving only moderate amounts of stable FVIII expression. For instance, achieving stable FVIII activity above 5-10% of normal activity level has the potential to convert a patient with severe hemophilia at risk of catastrophic bleeding into a patient only at risk for bleeding in the setting of major trauma or surgery. Achieving stable levels of FVIII above 15% activity level could provide complete joint protection and may allow patients to have a functional cure from their disease.

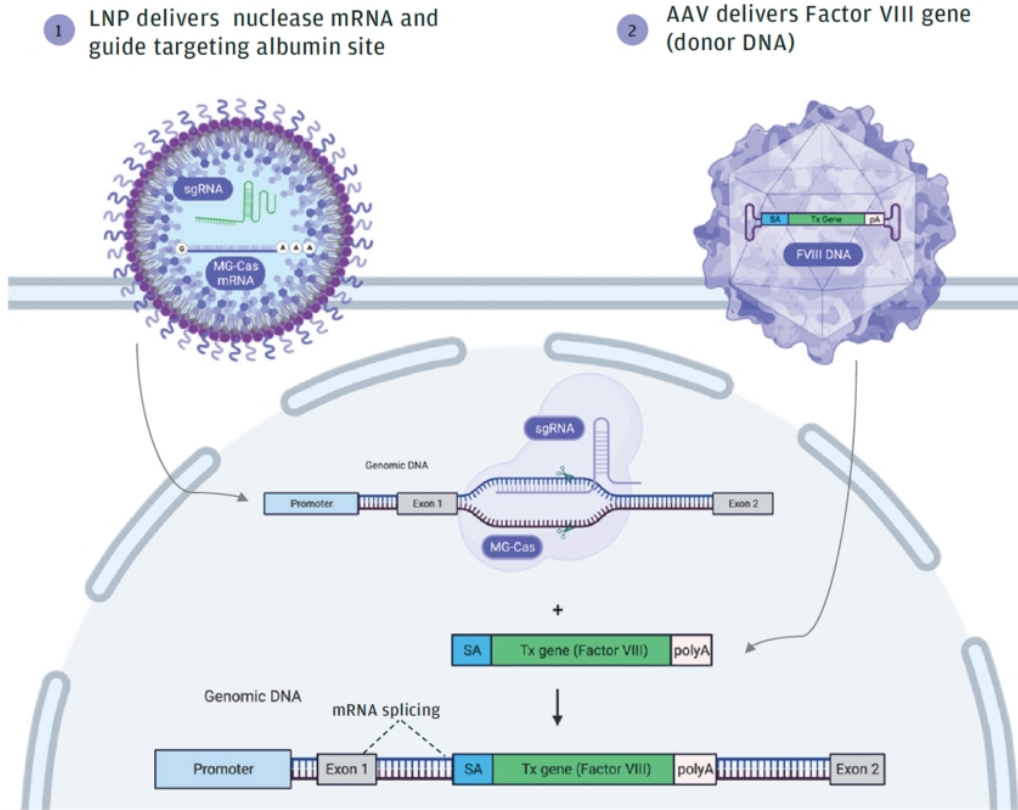
Rather than provide the FVIII gene in an episomal location, which risks dilution from cell division or cell death as well as episomal transcriptional silencing, our approach is to insert a FVIII DNA cassette into a "safe harbor location," within an intron of the albumin gene that is not expected to have deleterious effects. FVIII expression is then driven by the strong native albumin promoter. This approach has previously been demonstrated in

preclinical studies to lead to therapeutically relevant expression of a different clotting factor (Factor IX) with negligible impact to systemic circulating albumin levels. Our FVIII knock-in approach is designed to provide stable expression and clinically relevant circulating levels of FVIII, even at low integration rates because of the strength of the albumin promoter.

Our approach is fundamentally different from the AAV gene therapy approaches. AAV gene therapy approaches use a viral vector to deliver a replacement FVIII gene driven off a non-natural promoter that exists in an episomal state (not integrated in the genome). This AAV FVIII gene therapy approach has been associated with the loss of FVIII expression over time in patients, a phenomenon hypothesized to be due to a combination of loss of the DNA encoding the FVIII gene (due to liver cell replication) and silencing of the episomal FVIII expression. Because our approach is designed to permanently integrate the FVIII gene into the genome of the patient, the FVIII gene should not be lost from the liver when the liver cells divide (because it is integrated in the genome and therefore transferred to the daughter cells during cell division), which may allow for a therapeutic option for children with hemophilia. Silencing of expression may be less likely to occur with our approach because we are using an endogenous albumin promoter rather than a synthetically designed promoter in a non-natural episomal state.

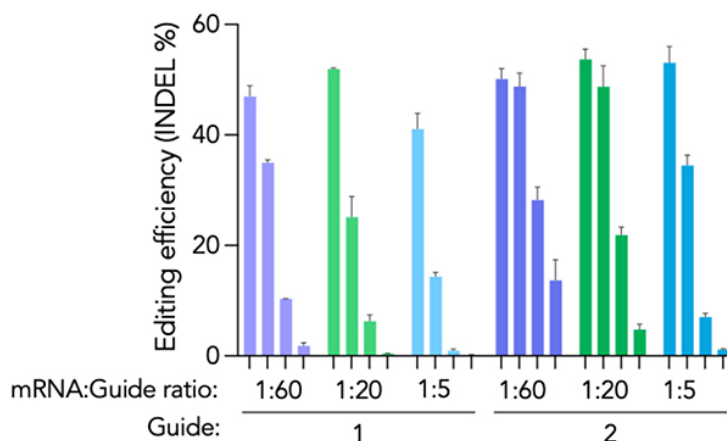
As shown in Figure 24, our hemophilia A genome editing program has two components: a LNP component that is designed to deliver mRNA along with a gRNA to the liver to produce a highly efficient and specific nuclease to create a precise cut at the albumin safe harbor gene locus; and an AAV vector that is designed to deliver the donor template FVIII DNA that becomes inserted into the nuclease cut site by the naturally occurring DNA repair process called non-homologous end joining. The DNA template encodes a FVIII protein, and the sequence has been optimized to improve expression. In both preclinical mouse and NHP models we have demonstrated that this FVIII knock-in approach leads to stable integration and clinically relevant circulating levels of FVIII.

Figure 24. Therapeutic Approach to Hemophilia A Genome Editing.



We have performed gRNA screening in human and mouse cells to identify both candidate clinical guides and mouse surrogate guides. In the case of the human guide screen, a total of 77 guides for three of our nucleases were screened against albumin intron 1 in liver cell lines, and two guides (called guide 1 and guide 2) were selected as leads. Primary human hepatocytes ("PHH") isolated from the livers of deceased individuals are the most appropriate preclinical model to evaluate human liver genome editing. Guide 1 and guide 2 displayed dose dependent editing in PHH with guide 2 exhibiting the highest potency (Figure 25).

Figure 25. Editing at the Human Albumin Locus by Lead Nuclease and Guides in Primary Human Hepatocytes. Each Set of Four Bars is a Dose Response (from High Dose to Low Dose Going from Left to Right) Performed at Three Different Molar Ratios of mRNA to gRNA.



* Each set of four bars is a dose response (from high dose to low dose going from left to right) performed at three different molar ratios of mRNA to gRNA.

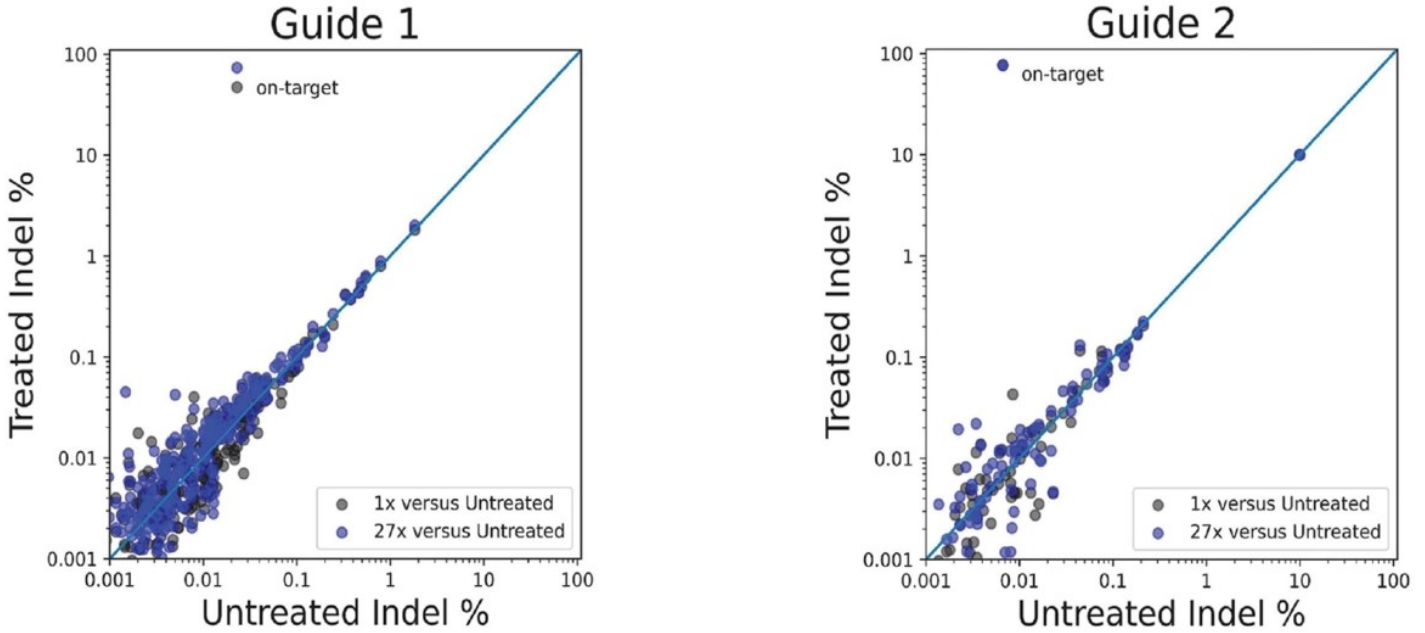
Genome editing nucleases can edit at sites other than the intended target site, an activity that is dependent on the specific nuclease and guide. Editing at non-target sites (called off-target editing) is undesirable due to the potential to cause damage to the host cell DNA (sometimes called "genotoxicity"). In accordance with recent FDA guidelines and insights from the FDA workshop we have applied a combination of 3 methods; in-cell oligo integration in PHH, a biochemical assay, and in silico prediction (using an algorithm called CRISPRitz) to identify potential off-target sites for our two lead guides. These combined methods nominated a total of 372 potential off-target sites for guide 1 and 113 potential off-target sites for guide 2. Editing at these potential off-target sites was then evaluated in PHH by amplicon sequencing in which a pair of PCR primers flanking each predicted off-target site is used to PCR amplify that site followed by next generation sequencing. To efficiently analyze all of the potential off-target sites, sets of barcoded PCR primers to multiple sites are carefully designed and combined in a single PCR amplification (a methodology called rhAMP-Seq). Any sites that failed to be detected from the rhAMP-Seq panels were re-tested as single amplicons. The sequence data was analyzed using the CRISPResso software to quantify InDels in each of the amplicons representing the potential off-target sites. The sensitivity of this method is high because of the depth of sequencing reads that can be readily achieved, typically enabling detection of InDels at frequencies as low as 0.1% (i.e. 1 InDel in 1,000 sequencing reads). Because double strand breaks can occur naturally in cells and because of sequence specific background signals arising from PCR primer slippage we compared the InDel rates in PHH edited at a dose that results in saturating editing (1x dose) and at a 27-fold higher dose (27x dose) to the InDel rate in un-edited PHH. We used LNP to deliver the MG29-1 mRNA and gRNA to mimic in vivo delivery and because it provided high editing efficiency and low toxicity. We believe the cells edited with the dose 27-fold higher than that which results in saturating

editing provides an additional safety margin for the detection of off-target editing that may occur at undetectable frequencies at saturating doses but is detectable at a higher dose. The InDel frequencies of the potential off-target sites were plotted as a scatter plot (Figure 26). InDel frequencies that are the same in the edited and unedited cells lie on the diagonal axis of Figure 26. Sites that have a higher InDel frequency in the edited cells than in the un-edited cells and thus represent a true off-target edit will appear as a point significantly above the diagonal axis of Figure 26. In addition, real off-target sites will have InDel frequencies higher than the lower limit of detection of the assay of 0.1%. Only the on-target site lies above the diagonal axis of the scatter plot in Figure 26 having a InDel rate in both 1x and 27x treated cells of 60% to 90% and an InDel rate in untreated cells of 0.01 to 0.05%. No editing significantly above the signal in the control cells was detected at any of the off-target sites for either guide 1 or guide 2. The InDel frequency for the majority of potential off-target sites was below 0.05% which is below the limit of detection of 0.1%. The small number of potential off-target sites with InDel frequencies above 0.1% had near identical InDel rates in both treated and un-treated cells indicating that they are not a result of the gene editing but are likely due to either natural hot spots of DNA damage or primer slippage during PCR amplification.

In summary, no editing was detectable at any of the potential off-target sites for the lead albumin targeting guides in the most relevant human cell, primary human hepatocytes, including at a super saturating dose that is 27-fold higher than that required for saturating editing.

We are expanding the number of potential off-target sites to be evaluated by amplicon sequencing by including sites from in silico prediction with a wider cutoff (more mismatches) as well as from a variant aware version of in silico prediction called CRISPRme that evaluates the impact of naturally occurring sequence variation within the human population on predicted off-target sites.

Figure 26: Measurement of editing at potential off-target sites for the two lead guides for Hemophilia A in PHH using amplicon sequencing.



* 372 and 113 sites were nominated and evaluated for guide 1 and guide 2, respectively at both a 1x and a 27x saturating dose. For each potential off-target site as well as the on-target site, the InDel frequency was plotted for 1x compared to untreated (black points) and for 27x compared to untreated (blue points). For Guide 2 the on-target site for 1x vs untreated (black dot) and 27x vs untreated (blue dot) overlap and so appear as only a blue dot.

We have demonstrated the feasibility of the human FVIII gene knock-in approach in mice with a mouse specific guide and 11 different FVIII DNA donor cassettes as shown in Figure 27, which shows the human FVIII protein levels achieved in the blood at day 10 post LNP dosing. A FVIII level of 1 IU/ml is equivalent to 100% of the normal level of FVIII in humans. FVIII levels ranged from 0.02 IU/ml (2% of normal) to 0.75 IU/ml (75% of normal). Seven of the 11 FVIII donor designs achieved human FVIII levels at or above 15% of normal, a level that would be sufficient to prevent the majority of bleeding events in hemophilia patients. We quantified integration of the FVIII gene in the liver in the correct (forward) orientation at the target site in the albumin locus in selected groups of mice at the end of the study (day 14 post LNP). The mean forward integration frequency in these groups was between approximately 0.5% and 2.5% (meaning approximately 0.5 to 2.5 copies per 100 mouse genomes, Figure 28). The finding that different human FVIII donor designs resulted in a range of FVIII levels in the blood of mice despite similar levels of integration implicate the donor DNA design as a critical component to maximize FVIII protein expression and these learnings are being incorporated into FVIII donor designs that will be evaluated in NHP studies to enable final development candidate selection.

Figure 27. Expression of FVIII in Mice after Genome Editing.

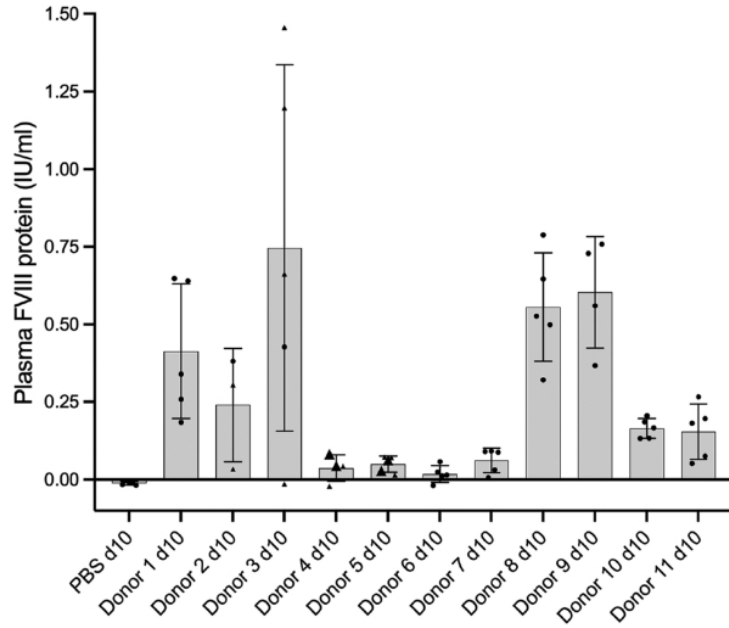
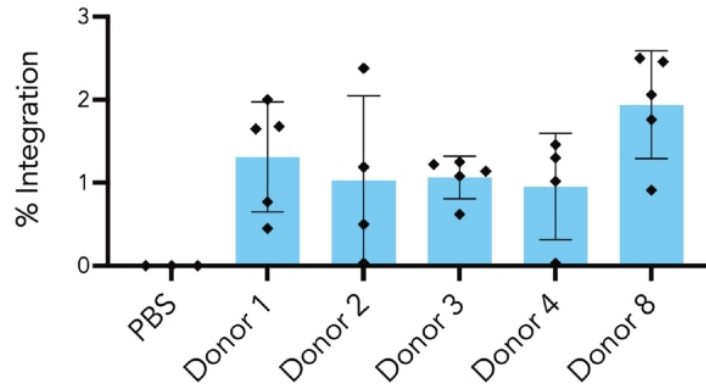


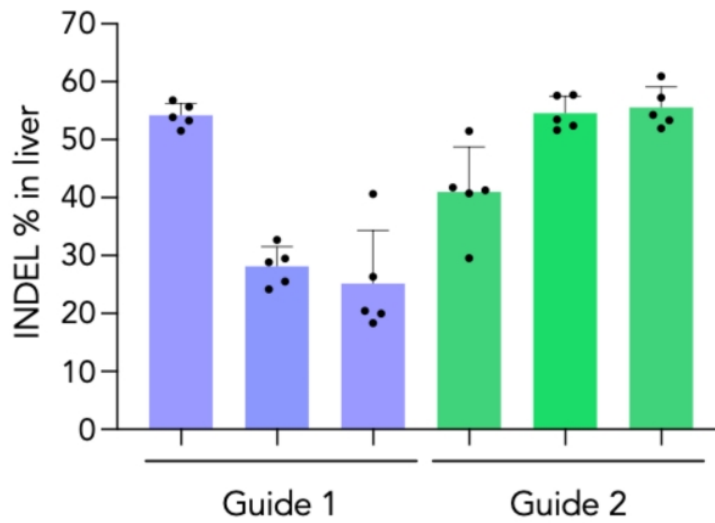
Figure 28. Integration of FVIII in Mice after genome editing.



* Results are from a subset of the groups of Mice in Figure 27 (Integration was only measured for selected donors for technical reasons).

The editing efficiency of the two lead gRNA sequences (guide 1 and guide 2) were evaluated in non-human primates ("NHPs"). Guide 1 is a perfect match to the target sequence in the NHP genome while guide 2 required a single nucleotide change in the spacer to match perfectly to the target sequence in NHPs. The same nuclease mRNA sequence was used with both guides and the guide and mRNA were co-delivered with the same LNP formulation by IV infusion of three cynomolgus macaques per group at a dose of 1.25 mg RNA per kg body weight. The editing efficiency in five different regions of the liver (representing the different liver lobes) were measured by determining the InDels at the target site using next generation sequencing in each of the three animals per treatment group as shown in Figure 29. Editing levels were similar across the five liver regions (represented by the five dots in each bar) demonstrating that editing was homogenous across the entire liver. Guide 2 resulted in a mean editing efficiency of 50% amongst the three animals. This represents editing in approximately 80% of hepatocytes because hepatocytes make up about 60% of the cells in the liver of NHPs and the LNP delivers primarily to hepatocytes.

Figure 29. Efficient Editing in NHPs at the Safe Harbor Locus for the Hemophilia A Program.



* Each bar is an animal and each datapoint represents a different lobe of the liver.

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To evaluate our FVIII gene integration approach in a more relevant preclinical species we performed combined AAV-FVIII and LNP dosing in three NHP (cynomolgus macaques). The monkeys were pre-screened for neutralizing antibodies ("NaB") against AAV and only animals with a titre of less than 1:5 (meaning that no Nab were detected at a 1:5 fold dilution of the monkey plasma) were selected for the study. The target site in albumin intron 1 was sequenced from each animal to confirm the absence of sequence differences that might otherwise impact recognition by the gRNA. Plasma was collected prior to dosing to provide a baseline for the FVIII activity assay. A small amount of liver tissue was collected by biopsy two weeks prior to dosing to provide a baseline for the measurement of FVIII mRNA in the liver. The three animals were given a single dose of the anti-inflammatory drug dexamethasone (2 mg/kg) prior to AAV dosing and again prior to LNP dosing. It is well known that human FVIII is immunogenic in monkeys resulting in generation of anti-human-FVIII antibodies (typically within weeks to months of exposure) which prevents the detection of the human FVIII protein. A cellular immune response against human FVIII is also likely to occur in monkeys which may result in the destruction of liver cells expressing the human FVIII. We therefore used the cynomolgus FVIII gene in the AAV construct to ensure that the monkeys would not have an immune response against the FVIII protein expressed from the integrated FVIII gene and thereby enable a long term evaluation of the durability of FVIII expression. The AAV construct was designed with a codon optimized B-domain deleted cynomolgus FVIII (cFVIII) coding sequence with a single amino acid change that had no observed impact on the function of the cFVIII protein but enables the specific detection of the AAV encoded cFVIII protein in the background of the endogenous cFVIII protein. All three monkeys received a single dose of the AAV-cFVIII virus followed five weeks later by a liver trophic LNP encapsulating the mRNA encoding MG29-1 and guide 2 at a dose of 1 mg/kg body weight. Plasma was collected either weekly or bi-weekly starting at 14 days post LNP dosing and assayed for the vector derived cFVIII using a commercial activity assay (chromogenic assay). As of the November 11, 2023 data cutoff date, we have collected and assayed cFVIII activity up to day 126 post LNP (18 weeks, 4.5 months) and results are shown in Table 1. The plasma for each post-LNP time point was assayed multiple times (between 5 and 7 times) and the mean value and standard deviation were calculated. Plasma collected prior to dosing (day -14, n=3 replicates) had no detectable cFVIII using this assay, demonstrating that the assay method does not detect endogenous cFVIII. The mean FVIII activity derived from the administered c-FVIII gene over the time period from day 14 to 126 was 0.75 IU/ml, 0.13 IU/ml and 0.29 IU/ml in the 3 animals which corresponds to 75%, 13%, and 29% of normal FVIII activity in humans. These average levels of FVIII are within the desirable therapeutic range (approximately 10% to 150% of normal).

Samples of liver tissue were collected on day 7 and day 70 post LNP dosing by biopsy of all three NHP. The day 7 liver biopsy was analyzed for editing at the target site in albumin intron by NGS which revealed that the cleavage by MG29-1 was efficient and consistent, with InDel frequencies of 45%, 50%, and 55% in the 3 animals, similar to what was observed in our earlier editing only study in NHP with the same guide 2 (Figure 29). Integration of the cFVIII gene encoded in the AAV at the target site in albumin intron 1 was quantified by a digital droplet PCR assay that specifically detects the junction between the albumin intron 1 sequence at the target site and the 5' end of the AAV encoded cFVIII gene. Integration was detected in all 3 animals and the integration frequency ranged from 0.7 to 2.9 copies per 100 genomes, similar to the frequency observed in mice.

The specific albumin-cFVIII hybrid mRNA that is generated by the precise splicing between albumin exon 1 and the 5' end of the integrated cFVIII gene derived from the AAV was quantified in liver tissue from the day 7 and day 70 biopsies as well as the pre-dose biopsy using a digital droplet PCR assay. No signal was detected in the liver tissue from the pre-dose biopsy as expected, demonstrating that this assay does not detect endogenous cFVIII mRNA. The specific albumin-cFVIII hybrid mRNA was clearly detected in all three animals at both the day 7 and day 70 timepoints with no significant change in the mRNA level between day 7 and day 70. The mean of the albumin-cFVIII hybrid mRNA levels at day 7 and day 70 post LNP dose were 177, 79, and 131 in the 3

animals (the units are percentage of an endogenous control mRNA that was quantified in the same samples). The integration frequency and the hybrid albumin-cFVIII mRNA levels correlated with the plasma FVIII activity. The data in Table 1 provides important proof of concept for our gene editing approach in a relevant NHP model. We intend to continue this study up to 12 months with continued measurement of FVIII activity to evaluate the durability of FVIII expression from the integrated cFVIII gene.

Table 1. cFVIII donor integration frequency, FVIII mRNA level and Mean FVIII activity level in NHPs.

Animal ID	Editing in the liver (InDel %) ¹	FVIII gene integration frequency (copies per 100 genomes) ²	FVIII mRNA (% of endogenous control mRNA) ³	Mean FVIII activity (% of normal (d14 to d126)) ⁴
1001	45%	2.9	177	75 +/- 9
1002	50%	0.7	79	13 +/- 4
1003	55%	1.4	131	29 +/- 5

Table footnotes: (1) InDelS at the on-target site in albumin intron 1 were measured by NGS in a liver biopsy taken at day 7 post LNP dosing. (2) The FVIII donor gene integration frequency in the forward orientation was quantified by droplet digital PCR analysis of the liver biopsy at day 7 post LNP and is normalized to an endogenous single copy gene. (3) FVIII mRNA was quantified with a digital droplet PCR assay specific for the hybrid mRNA created by correct splicing between albumin exon 1 and the 5' end of the FVIII gene and is the average of the levels in the liver biopsy at day 7 and day 70 post LNP dosing and is normalized to the levels of an endogenous mRNA. (4) The mean of the FVIII activity in IU/ml measured at each time point between day 14 and day 126 was calculated and converted to the percentage of normal by multiplying by 100 (1 IU/ml is approximately 100% FVIII activity in a healthy human being).

No safety signals of concern were observed during this NHP study as of the November 11, 2023 cut-off date. A comprehensive set of safety markers were measured in the blood of the monkeys after both AAV and LNP dosing. These included assays for coagulation, serum chemistry and hematology as well as liver enzymes (transaminases and bilirubin levels) and a panel of 10 cytokines. We observed mild and transient elevations of alanine aminotransferases ("ALT") and aspartate aminotransferase ("AST") and no significant change in total bilirubin post AAV and post LNP (Figure 30). Importantly we observed no changes in serum albumin levels over the course of the study demonstrating that the high level of editing in albumin intron 1 (mean 48% InDels which converts to approximately 78% of hepatocytes) did not alter expression of the albumin protein. Three cytokines (IL-6, MCP-1 and IL-12/IL-23) exhibited mild and transient increases in the blood post AAV and post LNP. The data for IL-6 is shown in Figure 31. As of the data cut-off date, all three animals in the study remained healthy, without notable clinical observations, and continued to gain weight as expected.

Figure 30a: ALT, AST, and total bilirubin levels in the blood of NHP up to day 8 after AAV dosing in the integration study.

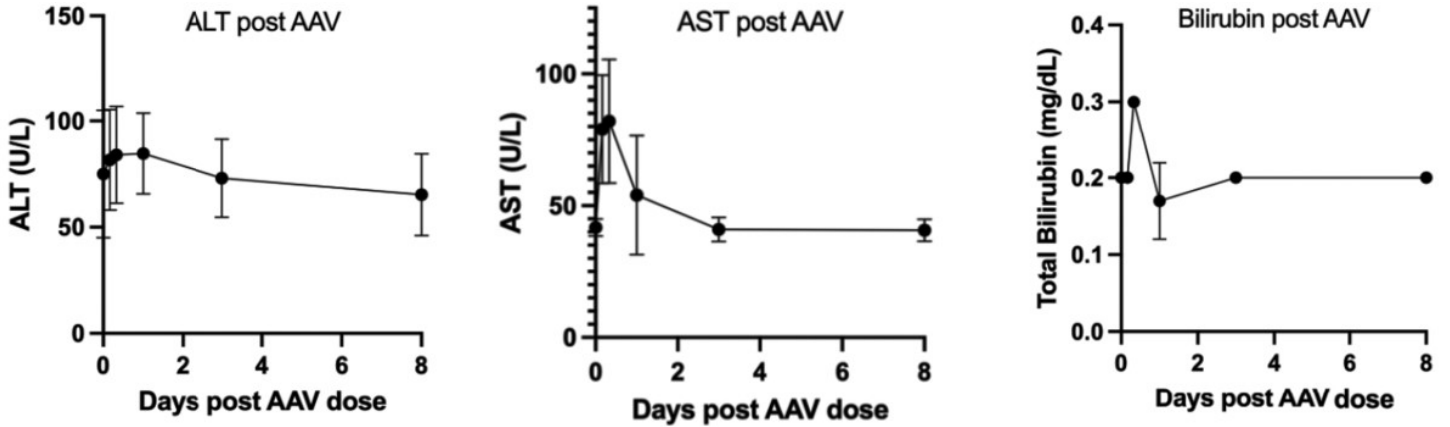


Figure 30b: ALT and AST levels in the blood of NHP up to day 10 after LNP dosing in the integration study.

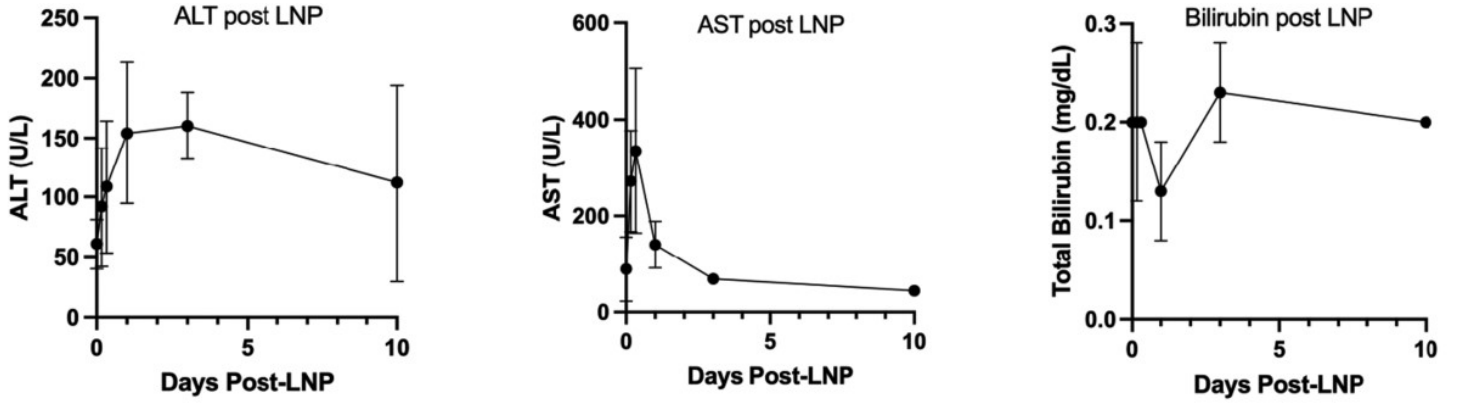


Figure 30c: ALT, AST and total bilirubin levels in the blood of NHP throughout the study to the data cut-off date.

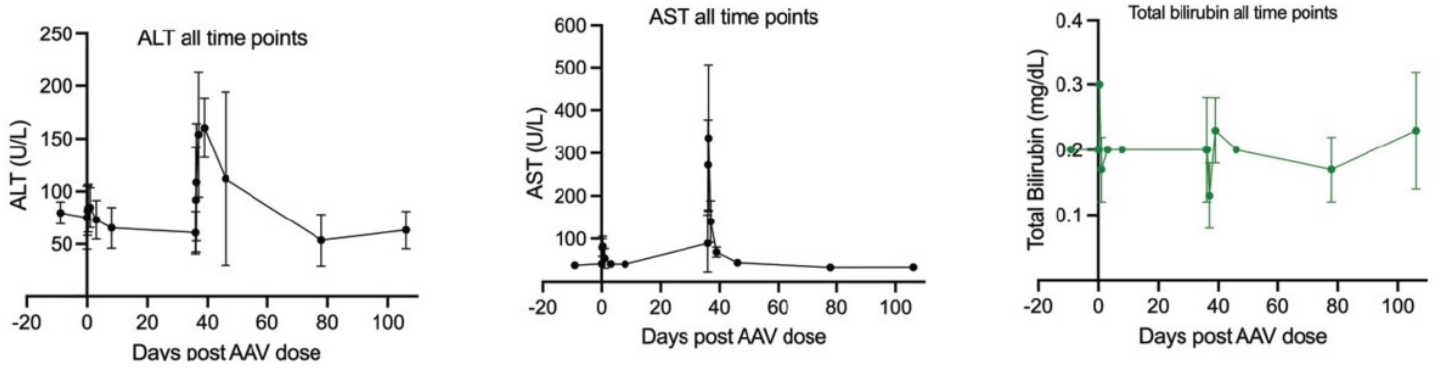


Figure 30: Albumin levels in the blood of the 3 NHP after AAV and LNP dosing in the integration study.

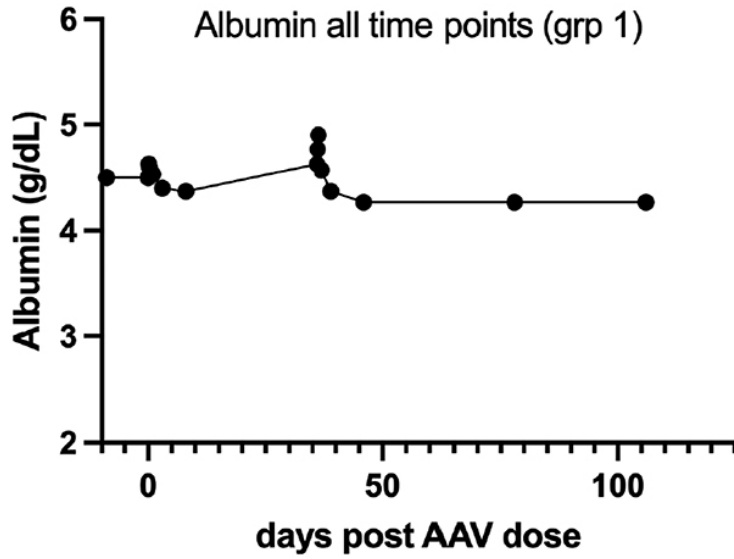


Figure 31: Levels of the cytokine IL-6 in the blood of the 3 NHP in the integration study post AAV dosing and post LNP dosing.

Figure 31a: Levels of the cytokine IL-6 in the blood of the 3 NHP in the integration study post AAV dosing.

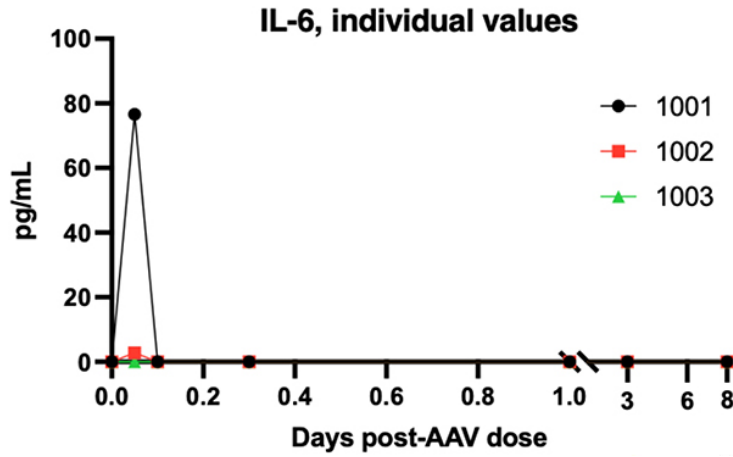
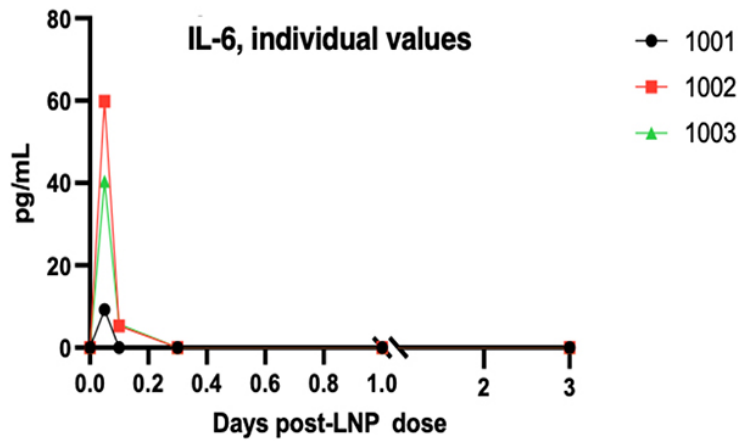


Figure 31b: Levels of the cytokine IL-6 in the blood of the 3 NHP in the integration study post LNP dosing.



Next Steps

We have selected two human FVIII donor DNA cassette designs, and are in the process of producing the AAV, mRNA and gRNA to perform a second NHP integration study to select a single donor and guide and expect to nominate a development candidate by Q2 2024. In parallel, we are initiating GxP manufacturing of mRNA, gRNA, AAV and LNP to support future IND-enabling studies. The progress we have made on this program not only validates the efficiency and specificity of our novel nucleases in rodent and NHP models, but also supports our ongoing efforts with other large gene integration approaches.

Primary Hyperoxaluria, Type 1—a durable knockdown of HAO1 for substrate reduction therapy

The Disease

PH1 is a rare autosomal recessive metabolic disease arising from loss of function mutations in the AGXT gene that encodes alanine glyoxylate aminotransferase. This enzyme is found in peroxisomes of the liver where it catalyzes the conversion of glyoxylate to glycine and pyruvate. Lack of functional AGXT leads to an accumulation of glyoxylate substrate, which is then converted to oxalate and excreted in the kidney. The excess urinary oxalate forms an insoluble complex with urinary calcium that leads to the production of calcium oxalate crystal precipitates. This pathologic process results in the formation of repeated calcium oxalate urolithiasis and nephrolithiasis, which in turn leads to obstructive uropathy, inflammation, fibrosis, tubular toxicity, and progressive loss of kidney function.

PH1 is a serious disease that causes kidney failure. More than 70% of individuals with PH1 mutations will develop end-stage renal disease, with a median age in young adulthood. Patients with PH1 continue to experience morbidity and mortality even after the development of end-stage renal disease due to progressive

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systemic calcium oxalate precipitation in various organs (systemic oxalosis). Despite renal replacement therapy or kidney transplantation, patients with PH1 have an overall shorter lifespan than patients with other causes of renal failure, highlighting the progressive and severe nature of this metabolic disease.

PH1 is the most common of the primary hyperoxalurias but is a rare disease with an estimated prevalence of approximately one to three in 1,000,000 individuals. While epidemiologic data on PH1 is limited, these estimates suggest there are approximately 1,000 to 3,000 patients in both the United States and Europe, and possibly up to 20,000 patients globally.

Limitations of Current Approaches

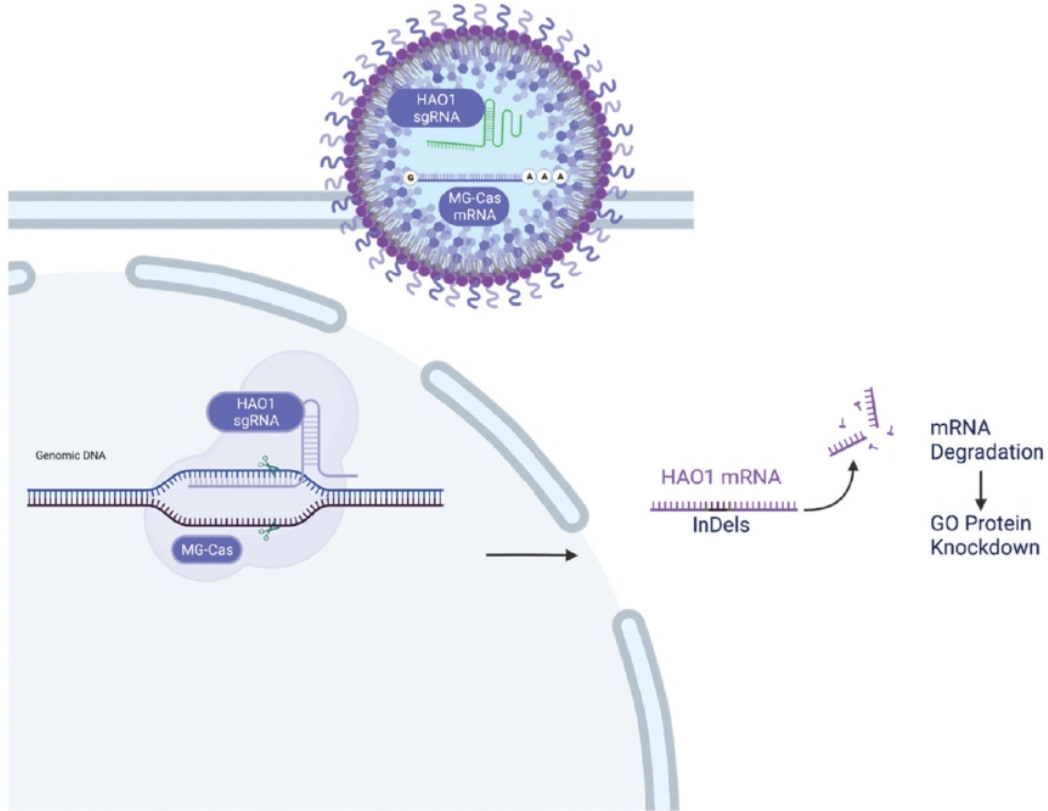
Until recently, the standard of care for treating PH1 was primarily supportive in nature, with hydration and diuretics used to reduce urinary oxalate concentration, pyridoxine (vitamin B6) to enhance residual function of alanine glyoxylate aminotransferase catalytic activity, and hemodialysis once renal function progressed to end stage. Liver transplantation has also been explored as a means of providing patients with a normal copy of AGXT and has been used alone in early-stage patients or as a combined liver-kidney transplant in more advanced patients. Transplantation approaches have limitations due to donor availability, morbidity associated with the surgical procedure, and lifelong immunosuppression required to inhibit graft rejection.

More recently, the standard of care has been updated to include treatment with lumasiran, a siRNA therapeutic approved in adults and children with PH1 that acts to reduce the levels of urinary oxalate. Using a therapeutic approach known as substrate reduction therapy, lumasiran targets mRNA from a separate gene, HAO1, that encodes GO. By inhibiting GO, levels of glyoxylate are reduced, which results in reduced downstream levels of oxalate. As a result, lower urinary oxalate results in decreased urinary calcium oxalate stone formation. It is anticipated that inhibition of renal oxalate accumulation and stone formation can slow or prevent continued loss of renal function. Lumasiran has been generally well tolerated in clinical studies of adults and children with PH1 but it requires repeat subcutaneous administration indefinitely in order to maintain its effect. In addition, injection site reactions are common among patients taking lumasiran and the degree of urinary oxalate reduction has been observed to not reach normal levels in many patients. An additional RNAi drug, Nedosiran, which targets LDH, a different enzyme in the same pathway as HAO1, was also granted marketing approval by the FDA for adults and children with PH1 in October 2023. Thus, there is a potential to improve clinical outcomes for PH1 patients with a one-time administration of a therapy that inhibits urinary oxalate accumulation, prevents calcium oxalate stone formation, and protects renal function.

Our Approach and Results

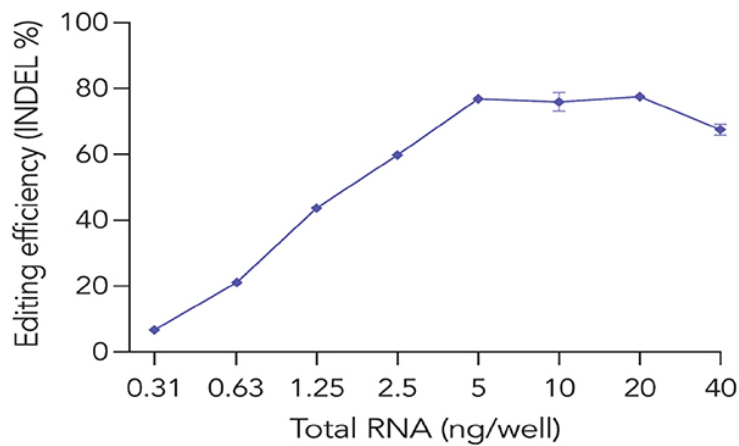
The goal of our genome editing approach is to durably knock down HAO1 resulting in stable and permanent reduction of oxalate levels to effect a lifelong benefit. We plan to deliver mRNA for one of our lead nucleases and a guide encapsulated within a single LNP as shown in Figure 32 below. We expect the mRNA and HAO1 gRNA will be released in hepatocytes (the cell type in the liver that expresses the HAO1 gene) where the mRNA will be expressed into the nuclease that forms a complex with the guide and create a double stranded break in the HAO1 gene and inhibits gene expression.

Figure 32. Genome Editing Strategy for Targeting HAO1.



The safety of this durable knockdown of HAO1 is supported by human genetic observations of an individual lacking a functional copy of the HAO1 gene with no evidence of a pathologic phenotype. The safety of this approach is also supported by up to three years of clinical data using a siRNA approach to silence this gene.

We have performed nuclease and guide screening to select an optimal nuclease and gRNA combination. The double strand break created by the selected nuclease has been observed to be efficiently and rapidly repaired by the cell via a process that introduces small InDels to the sequence at the target site. When these InDels alter the reading frame of the gene (so called "out of frame" InDels) this results in degradation of the HAO1 mRNA. Because different nucleases and guides generate distinct InDel profiles, we included analysis of the InDel profile as a selection criterion during our nuclease /gRNA screen. In addition to the InDel profile, we also screened for the efficiency of HAO1 mRNA reduction and impact on the HAO1 mRNA sequences using whole transcriptome RNA sequencing ("RNAseq"). This screening process resulted in selection of a lead guide that targets an identical sequence in humans and mice which enables the evaluation of the lead human guide in mouse models. The potency of this lead nuclease and guide was tested in PHH *in vitro* as shown in Figure 29, demonstrating dose-dependent editing when delivered by a LNP with tropism to the liver.

Figure 33. Editing Dose Response in Primary Human Hepatocytes with the Lead Nuclease mRNA and Guide Targeting HAO1 Delivered in a LNP.

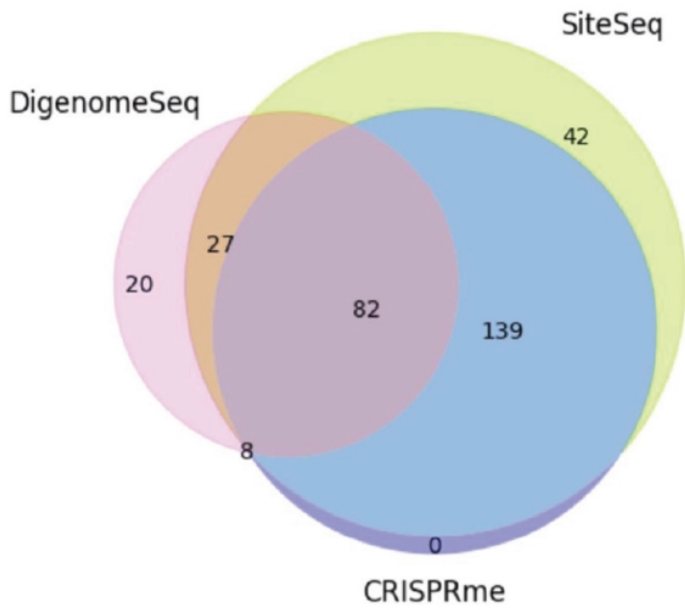
The off-target profile of the lead human guide targeting HAO1 is being evaluated in accordance with FDA guidelines published in March 2022. Potential off-target sites were identified using a combination of *in silico* prediction, biochemical discovery assays, and a cell-based discovery assay. To predict potential off-target sites *in silico* we used the variant aware CRISPRme software using a permissive PAM for MG29-1 (TYYN) and permitting up to 4 changes from the HAO1 reference protospacer to identify potential off-target sites referencing both the GRCh38 human genome reference and a variant call file (vcf) for more than 2,000 alternative genomes from the 1000 genomes consortium.

We applied two biochemical off-target discovery methods, Digenome-seq and SITE-Seq both of which digest purified human genomic DNA with the editing nuclease/guide complex *in vitro*.

To identify potential off-target sites with a cell-based discovery method we transfected primary human hepatocytes with MG29-1 and the lead guide together with a short double stranded oligonucleotide that integrates into the genome of cells at double strand breaks. Using a PCR based method we selectively amplified the DNA junction between the integrated oligonucleotide and the human genome and evaluated the profile of potential off-target sites by NGS.

A total of 318 potential sites were identified by the combination of the three methods; the overlap of potential off-target sites identified from each of these methods is shown in Figure 34.

Figure 34: Venn diagram demonstrating the overlap in potential off-target sites nominated for the lead HAO1 targeting guide.



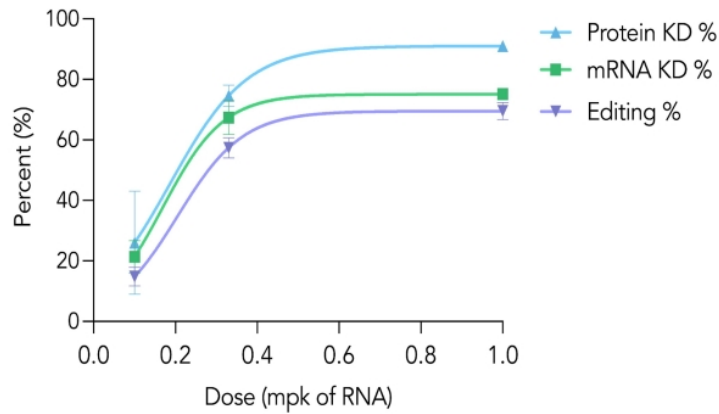
These 318 potential off-target sites were tested in primary human hepatocytes that had been edited by MG29-1 and the lead *HAO1* targeting gRNA using LNP delivery.

Off-target editing at all 318 potential off-target sites was measured in the genomic DNA from primary human hepatocytes edited by MG29-1 and the lead *HAO1* targeting gRNA. No editing was detectable at any of the 318 potential off-target sites for the lead *HAO1* targeting guide in the most relevant human cell, primary human hepatocytes, indicating that MG29-1 in combination with the lead *HAO1* targeting gRNA is highly specific.

In normal mice we have demonstrated dose dependent saturating levels of hepatocyte genome editing of *HAO1* and up to 90% reduction of target GO protein, providing strong preclinical proof-of-concept as shown in Figure 35.

Figure 35. Dose Dependent Editing, mRNA Knockdown and Protein Knockdown of *HAO1* in Normal Mice after a Single Administration of the Lead Nuclease mRNA and Lead Guide Encapsulated in a LNP with Tropism to the Liver.

HAO1 PROTEIN KNOCKDOWN



~70% editing in whole liver = ~100% editing in hepatocytes

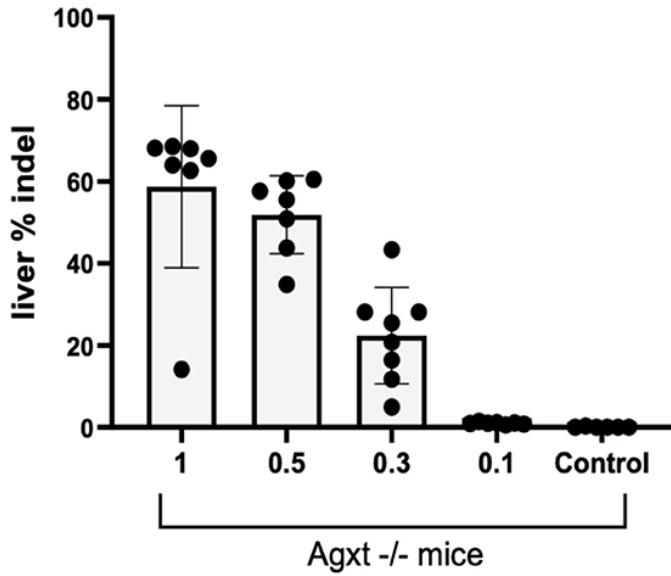
Additionally, along with our partner Moderna, we have achieved preclinical proof-of-concept in an AGXT knock-out mouse which is an accepted disease model of PH1 (Figure 36). AGXT knock-out mice have elevated oxalate in

the urine (measured with a mass spec assay) of about 500 mg per gram of creatinine compared to about 190 mg per gram of creatinine in mice of the same strain (BL/6) with a wild type AGXT genotype. Cohorts of male and female mice were given a single administration of the lead nuclease mRNA and gRNA encapsulated in a LNP with tropism to the liver. Dose dependent editing at the target site in HAO1 in the liver was measured at the end of this study (when the mice were sacrificed). The editing of HAO1 had the expected effect of dose dependently reducing urinary oxalate, with the highest dose achieving oxalate levels comparable to that of wild type mice.

Figure 36. Preclinical Proof of Concept in PH1 Disease Model (AGXT ^{-/-} mice).

Figure 36a. Dose dependent editing of the HAO1 gene in AGXT ^{-/-} mice.

Dose dependent editing of HAO-1 gene

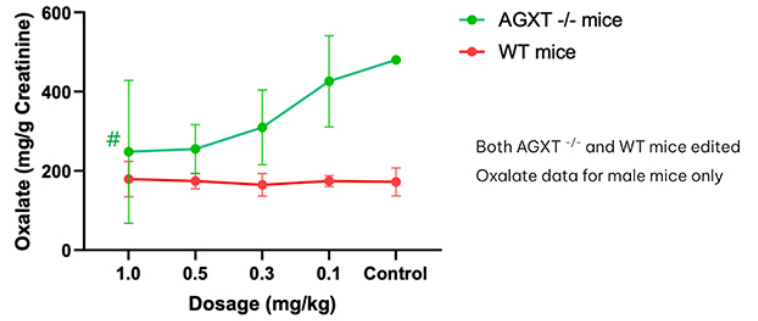


Source: Moderna

The durability of this approach was demonstrated by continued knockdown of GO protein even after partial hepatectomy (removal of about two thirds of the liver) and rapid liver re-growth (Figure 37). In this study wild type mice were given a single injection of either buffer or a liver tropic LNP encapsulating the MG nuclease mRNA and the lead gRNA targeting HAO1. As a control a Cas9 mRNA and a potent Cas9 guide targeting HAO1 from a published source were also packaged in the LNP with tropism to the liver and tested at a single dose. Eight days after dosing a liver hepatectomy was performed in which about two thirds of the liver was removed. This stimulates the majority of the remaining liver cells to enter cell division and results in rapid re-growth of the liver that restores the normal liver size within 7 to 10 days. Eight days after partial hepatectomy the levels of GO protein (the product of the HAO1 gene) in the liver were reduced by more than 90%, the same as the level of knockdown in edited mice that did not undergo hepatectomy. This result demonstrates that the knockdown of HAO1 expression was not compromised by extensive liver growth and that the fitness of edited hepatocytes was not impacted by editing.

Figure 36b. Dose-dependent reduction in urinary oxalate reaching normalization at highest dose.

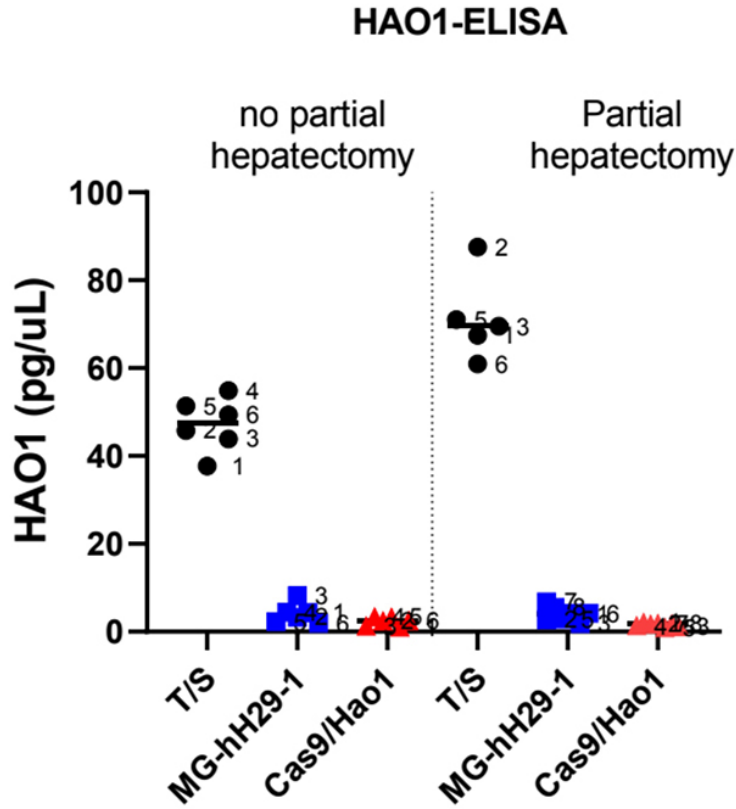
Dose dependent reduction of urinary oxalate



#: 1 mouse with low editing in 1 mg/kg dose group (likely failed iv injection) had high oxalate levels (450 mg/g) resulting in larger error bar. When excluded the oxalate levels in this group are same as WT mice

Source: Moderna

Figure 37. Knockdown of the Protein Encoded by HAO1 after HAO1 Gene Editing was Maintained Following Partial Hepatectomy. Control Mice were Injected with Buffer as a Control.



Source: Moderna

Next Steps

We are in the final stages of confirming the candidate to take into NHP studies and expect to have NHP data in 2024 to support final development candidate selection.

This program is partnered with Moderna for both development and commercialization. The partnership enables us to leverage Moderna’s expertise in mRNA and LNP technology to ensure efficient delivery of our nuclease to hepatocytes. In turn, we provide the novel programmable nuclease and guide chemistry to support precise targeting of the HAO1 gene. In addition to further validating our therapeutic platform, to the best of our knowledge this program represents the first time a type V nuclease is being developed for a therapeutic *in vivo* genome editing approach.

Transthyretin Amyloidosis—a single treatment to knockdown TTR gene expression

The Disease

Transthyretin amyloidosis is a disease of misfolded and aggregated TTR protein that can deposit in tissues causing organ dysfunction, primarily in the heart and/or peripheral nerves. The TTR protein is normally produced in the liver and circulates in a homotetramer (four copies of the same TTR protein bound together) where it serves as a carrier protein for vitamin A and thyroxine. Certain mutations have been identified that can cause TTR homotetramers to fall apart, misfold, and aggregate into insoluble fibrils that deposit in cardiac tissue and peripheral nerves. However, more commonly, the normal aging process is associated with an increased propensity for TTR misfolding and aggregation in the heart without any known genetic sequence variation. These distinctions lead to TTR amyloidosis being characterized as either ATTRv caused by mutations in TTR, or ATTRwt. It is estimated that globally there are approximately 50,000 patients with ATTRv and between 300,000 and 500,000 patients with ATTRwt. Among the larger ATTRwt patient population, the most common presentation is a rapidly progressive, restrictive, and hypertrophic cardiomyopathy due to progressive deposition of insoluble TTR fibrils, which result in thickening of the myocardium and stiffening of the ventricles.

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These pathologic processes lead to impaired diastolic function and progressive cardiomyopathy that typically leads to progressive heart failure and often death within three to five years from disease onset. Although cardiac manifestations are more common and severe, patients with neurologic manifestations also experience significant morbidity, loss of functionality, and impaired quality of life.

Limitations of Current Approaches

To date, treatment options for patients with TTR amyloidosis, including those with either cardiomyopathy or polyneuropathy manifestations, consist of efforts to stabilize the TTR tetramer with a small molecule (tafamadis) or knock down TTR levels through antisense oligonucleotides (i.e., inotersen and eplontersen which is currently under regulatory review in the U.S.) or siRNA strategies (i.e., patisiran and vutrisiran).

Tafamadis was studied in a randomized trial of patients with either ATTRv and ATTRwt cardiomyopathy and demonstrated reductions in all-cause mortality and cardiovascular-related hospitalizations and reduced the decline in quality of life and functional capacity over 30 months compared to placebo. Tafamadis is currently approved to treat patients with ATTR cardiomyopathy in the U.S. and patients with ATTRv and ATTR cardiomyopathy in the EU and in other parts of the world. Inotersen has demonstrated benefit in patients with ATTRv and polyneuropathy and is approved in the U.S., EU, and in other parts of the world. Eplontersen has demonstrated benefit in patients with ATTRv and polyneuropathy and is currently under regulatory review in the U.S. Eplontersen is also being studied in a Phase 3 trial for patients with ATTR cardiomyopathy. Patisiran is approved for the treatment of polyneuropathy of ATTRv in adults in the U.S., EU, and other parts of the world. Patisiran is currently under regulatory review for the treatment of patients with ATTR cardiomyopathy based on a randomized study demonstrating improvement in the 6-Minute Walk Test and quality of life over 12 months compared to placebo. Vutrisiran has demonstrated benefit in patients with ATTRv and polyneuropathy and is approved for use in ATTRv in the U.S., EU, and other parts of the world. Although these approaches have improved clinical outcomes for patients with TTR amyloidosis, the disease is still associated with significant morbidity and mortality and requires lifelong therapy to maintain therapeutic benefit.

Our Approach/Next Steps

More recently, early-stage third-party studies have demonstrated the feasibility of knocking down TTR (wild type or mutated versions) using a CRISPR based genome editing approach in a small number of patients. Clinical validation of this TTR knockdown approach is provided by antisense and siRNA clinical experience and further suggests the potential longer-term safety and tolerability of this approach.

Using our novel nucleases, we aim to provide efficient TTR knockdown and halt further deposition of amyloid fibrils. Previous experience suggests a clinical correlation between the degree of TTR knockdown and potential for benefit in familial forms of the disease, which are expected to translate similarly to wild type forms. The high degree of *in vivo* editing efficiency and specificity of our nuclease platform suggest the potential for a single treatment to knockdown TTR gene expression and remove the requirement for life-long therapy.

Along with our partner Ionis, we are currently in advanced stages of nuclease and guide selection and expect to move into NHP studies in 2024. We believe one of the strengths of our technology platform is applying our multiple nucleases that have distinct non-overlapping PAMs to create a larger number of guides for a given target. Starting with a larger number of guides should increase the chance of finding highly active and specific guides/nuclease combinations. Leveraging multiple nucleases with a diversity of PAMs enabled a high targeting density for the TTR gene as illustrated in Figure 38a. By comparison significantly fewer (3.8-fold fewer) guides are available when using SpCas9 (Figure 38b). We have screened more than 500 guides against the human TTR gene using six of our nucleases. With one additional nuclease in progress we will ultimately have screened 535 guides. Our high throughput screening platform has enabled us to screen approximately 500 guides in a four-month time span.

Figure 38a. High density of gRNA targeting the coding and regulatory regions of the TTR gene enabled by our platform of nucleases with diverse PAMs.

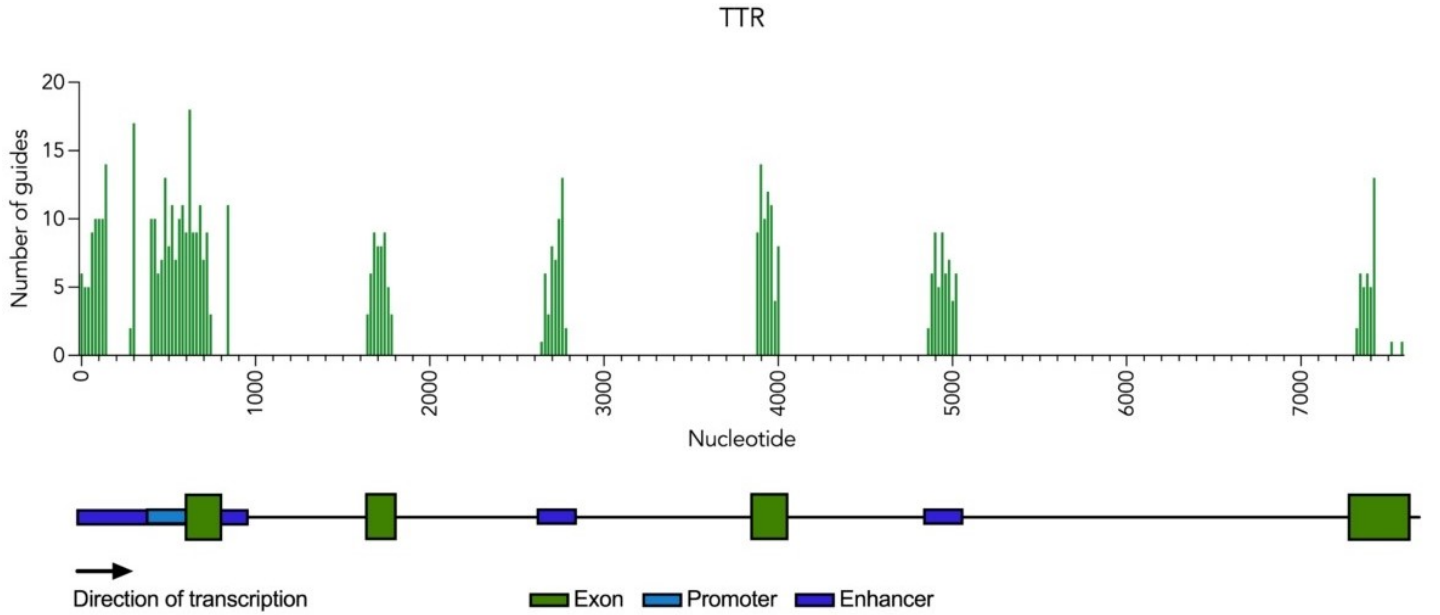
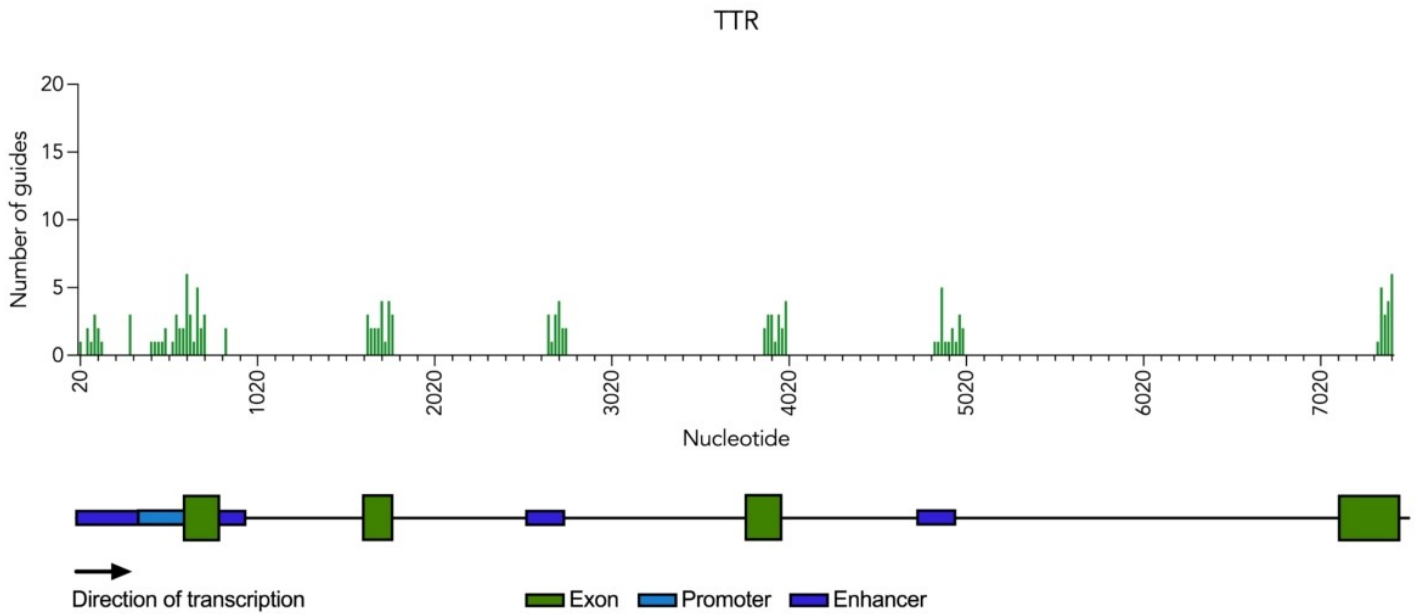


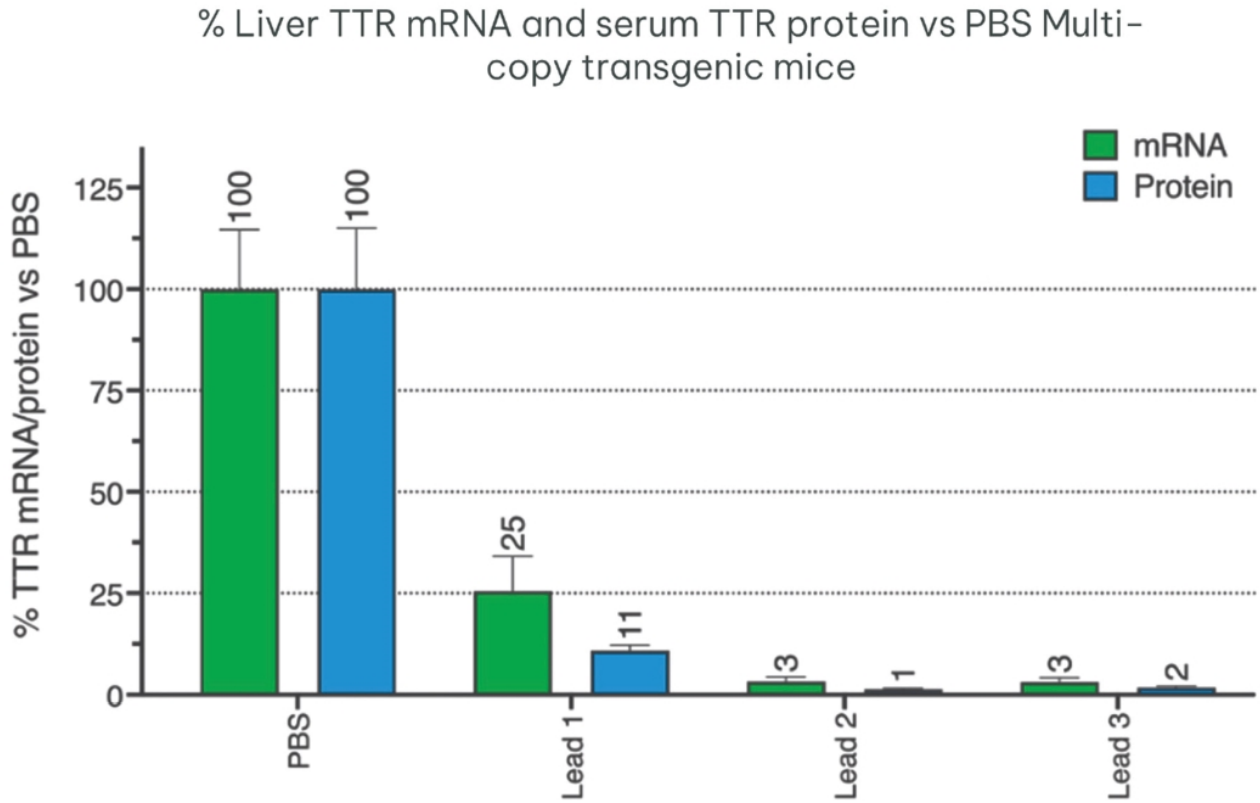
Figure 38b. Density of SpCas9 gRNA targeting the coding and regulatory regions of the TTR gene.



We are in the process of selecting lead guides and nucleases for evaluation in mouse models that carry the human TTR gene. Promising early leads have shown potent TTR mRNA knockdown in primary human hepatocytes. We plan to deliver our programmable nuclease and its associated gRNA to the liver using LNP technology, which has been shown to be highly selective for hepatocytes. This program not only provides a novel nuclease approach to knocking down TTR levels, but also leverages our partner's long-standing clinical development expertise in the TTR amyloidosis field to accelerate our efforts.

A preliminary evaluation of the *in vivo* potency of lead human guides was performed in a humanized mouse model in which multiple copies of the human TTR gene were integrated at random sites in the mouse genome. These mice express human TTR protein which can be measured in the blood using an assay specific for the human TTR protein. In this study, Lead 1 reduced the human TTR mRNA and protein by 75% and 88%, respectively. Leads 2 and 3 both reduced the human TTR mRNA and protein by 97% and 98%, respectively. Leads 2 and 3 are particularly attractive because these guides and mRNA have undergone only minimal sequence and chemistry optimization to date. Additional leads are currently being evaluated in this mouse model.

Figure 39. Proof of concept for knockdown of human TTR protein by lead nucleases/guides in human TTR transgenic Mice.



Cardiovascular Disease – a gene editing solution to eliminate angiotensinogen gene expression

The Disease

Cardiovascular disease is the leading cause of death worldwide and implicated in the deaths of approximately 17.9 million individuals each year. Although cardiovascular diseases are not genetically defined diseases, there are well validated gene targets and signaling pathways that address potent sources of vasoconstriction allowing for the creation of an important genetic medicine for these common diseases. Among the most important of these signaling pathways that have demonstrated marked clinical benefit in both hypertension and heart failure is the renin-angiotensin-aldosterone system (RAS) pathway, that has been successfully targeted by a number of important medications including renin inhibitors, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and aldosterone antagonists. Beyond its effect on blood pressure control, inhibitors of the RAS pathway have been shown to provide meaningful clinical benefit in ischemic heart disease and chronic heart failure as well as in diabetic nephropathy, and other forms of chronic renal insufficiency. However, continuous 24-hour inhibition of the RAS pathway with oral agents is not always successful, especially if compliance is suboptimal. Importantly, despite use of RAS inhibitors, diurnal variability in blood pressure and nocturnal blood pressure elevations can still occur. Recent early stage clinical studies using antisense and siRNA approaches to durably suppress the RAS pathway by targeting liver derived angiotensinogen provides important clinical validation of this approach as a means of safely reducing blood pressure without incurring hypotension, hypokalemia, or acute renal injury.

Limitations of Current Therapy

Although there are numerous approved classes of drugs that have demonstrated clinical benefit in patients with cardiovascular disease and refractory hypertension patients, many patients do not reach their blood pressure

goals or continue to have cardiovascular disease progression. In addition to contributions from underlying stiffened arteries and/or increased sympathetic tone, patients may have suboptimal adherence in taking a large number of daily oral pills. Importantly, current treatments often do not fully provide reliable and consistent 24-hour control of blood pressure which can leave patients exposed to diurnal variation and early morning blood pressure surges associated with cardiovascular events. Adverse effects of polypharmacy approaches and complicated food effects or drug-drug interactions can further negatively affect compliance and lead to poor outcomes. Therefore, despite the availability of oral medications, there remains a significant unmet need for a well-tolerated, durable approach to blood pressure control and cardiovascular protection with a clinically validated target.

Our Approach/Next Steps

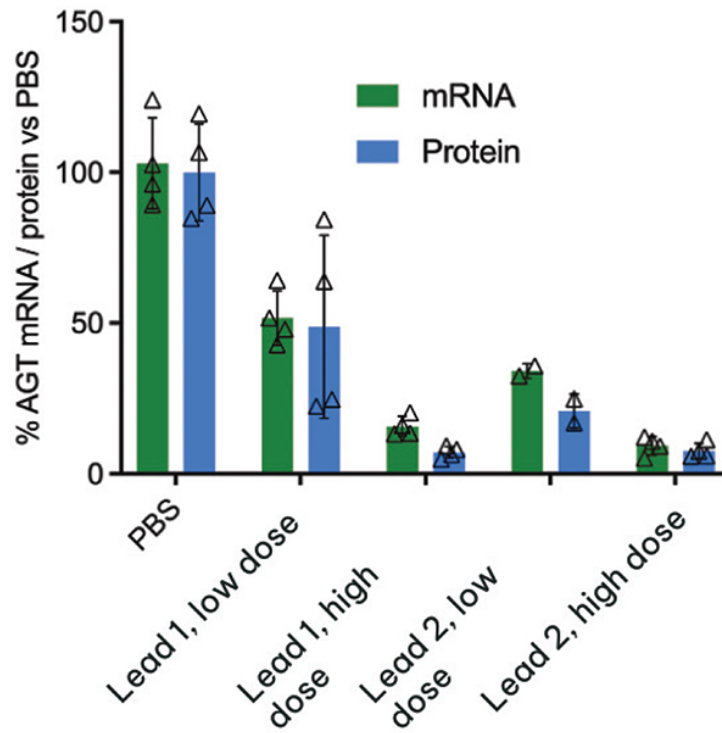
Our goal is to knockdown the expression of angiotensinogen in the liver using one of our programmable nucleases to generate a durable reduction in blood pressure from a single treatment. Angiotensinogen, encoded by the gene AGT, is at the top of the RAS pathway and the precursor to highly vasoconstrictive peptides angiotensin I and II and is thus an attractive and novel target for reduction of blood pressure. Inhibiting angiotensinogen protein production from the liver has the advantage of minimizing inhibition of the RAS pathway in the kidney which will provide a better safety profile by keeping the small amount of kidney production of AGT intact and thus avoiding renal dysfunction that is common with current medications and ensuring adequate vasoactive homeostasis in stress situations. A second potential advantage of targeting AGT is that it may limit escape mechanisms that restore angiotensin II levels or angiotensin II signaling. Clinical proof of concept for reduction of AGT protein levels comes from ongoing clinical trials of antisense (IONIS-AGT-L_{Rx}) and siRNA (ALN-AGT) drug candidates that have shown reduced mRNA levels of AGT in the liver and consequently reduced levels of AGT protein in the blood. We plan to deliver a programmable nuclease and its associated gRNA to the liver using LNP technology.

Along with our partner Ionis Pharmaceuticals we are currently in advanced stages of nuclease and guide screening and expect to move into NHP studies in late 2024 or early 2025. We believe one of the strengths of our technology platform is being able to access a larger proportion of the human genome by applying our multiple nucleases that have distinct non-overlapping PAMs. We have the potential to screen up to 1,490 guides using six MG nucleases against the AGT gene. To date we have screened 441 guides and are planning to screen an additional 420 guides. Leveraging the multiple MG nucleases with a diversity of PAMs enables a high targeting density as illustrated for the seven MG nucleases that are being screened against AGT. By comparison significantly fewer guides (2.5-fold fewer) are available when using spCas9. Multiple guides with potent editing of the AGT gene in human cells were identified in our initial guide screen against the coding sequence. We are in the process of completing the guide screen and selecting lead guides/nucleases for evaluation in mouse models that carry the human AGT gene.

We believe that this program is expected to be one of the first co-development efforts to develop a gene editing therapy for more common, non-genetically defined cardiovascular indications.

A preliminary evaluation of the in vivo potency of lead human guides was performed in a humanized mouse model in which multiple copies of the human AGT gene were integrated at random sites in the mouse genome. These mice express human AGT protein which can be measured in the blood using an assay specific for the human AGT protein. In this study, human AGT protein in the blood and the human AGT mRNA in the livers were measured 7 days post LNP dosing at both 1 and 0.3 mg/kg (Figure 40). At a dose of 1 mg/kg, lead 1 reduced the human AGT mRNA and protein by 85% and 93%, respectively. Lead 2 reduced the human AGT mRNA and protein by 91% and 92%, respectively. Additional leads are currently being evaluated in this mouse model.

Figure 40. Proof of concept for knockdown of human AGT protein by lead nucleases/guides in transgenic human AGT mice.



A1AT Deficiency

The Disease

A1AT deficiency is an autosomal recessive disease arising from loss of the normal A1AT protein encoded by the gene SERPINA1. Clinical manifestations of A1AT deficiency are primarily in the lung due to the toxic loss of normal function of A1AT, and occasionally in the liver due to the toxic effects of accumulation of abnormal A1AT.

A1AT is a highly abundant plasma protein that acts as an inhibitor of the potent proteolytic enzyme neutrophil elastase. Neutrophil elastase is involved in the host response to infection, but when unchecked can degrade connective tissue. In the lung, clinical manifestations of A1AT deficiency include emphysema and bronchiectasis from destruction of normal alveolar connective tissue. In patients with liver disease, the primary pathophysiology is liver inflammation and cirrhosis due to buildup of abnormal A1AT protein. Liver disease is more often found in children with A1AT deficiency, and lung disease is more often found in adults with A1AT.

A1AT deficiency is a clinically underrecognized disease, especially those with pulmonary manifestations as it is often mistaken for other forms of chronic obstructive pulmonary disease. Recent estimates from genetic screening suggest that 80,000 to 100,000 individuals in the United States have severe deficiencies of A1AT and approximately 40,000 to 60,000 have clinically manifest emphysema caused by A1AT deficiency. As not all individuals with A1AT deficiency present similarly, it is believed that environmental factors such as exposure to smoke, allergens, chemicals, and other environmental factors likely impact the severity and clinical manifestations.

Limitations of Current Therapy

Patients with A1AT deficiency are often treated with protein augmentation therapy. The goal of augmentation therapy is to increase circulating levels of A1AT sufficiently to balance the adverse effects of unchecked

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neutrophil elastase and slow the progression of emphysema. Augmentation therapy consists of an IV infusion of purified pooled donor plasma enriched for A1AT protein levels given weekly. While studies have demonstrated the ability to achieve higher circulating levels of A1AT with augmentation therapy, longer term impacts on protecting lung function are limited. This approach is also costly and not available for many patients. Infusions have also been associated with adverse events including flu-like reactions, fever, and rarely anaphylaxis. In severe cases of lung or liver disease, organ transplantation may be required to preserve life but are associated with post-transplant risks and long-term immunosuppression requirements.

Our Approach/Next Steps

The most frequent mutation responsible for A1AT deficiency is the PiZ mutation that changes the normal amino acid at position 342, which is glutamic acid, to lysine (E342K). Patients that are homozygous for the PiZ allele (called ZZ allele) make up more than 90% of the patients globally. We propose to correct this mutation back to normal using either an adenine base editor or Little RIGS. Because individuals that are heterozygous for the PiZ mutation (so called ZM allele) have minimal pathology, it is expected that editing of 50% of the alleles would be therapeutic. The most common DNA sequence change that creates the E342K mutation is a G to A change at the first position of the codon; GAG (normal) to ΔAG (PiZ). Converting the PiZ sequence (ΔAG) to the normal sequence (GAG) requires changing the underlined A to G which can be achieved using an adenine base editor. For this approach to be successful, a potent gRNA needs to be identified that targets the editing window to the ABE at the precise location of the codon for amino acid 342. There are five additional A bases within 5 bp on either side of the target A base in the 342 codon which could be subject to bystander edits (defined as edits at non-target bases within the site targeted by the guide), several of which would change additional aa with unpredictable impacts on the structure and function of the protein. Given the complexity of this edit, we will evaluate multiple genome editing systems, including base editors and RIGS, in order to advance the most effective genome editing approach.

Wilson's Disease

The Disease

Wilson's disease is an autosomal recessive disease of copper metabolism resulting from impaired function of the intracellular copper transporter encoded by the gene ATP7B. Mutations in ATP7B lead to impaired biliary excretion of copper, leading to copper accumulation in multiple organs including liver, brain, and eye. Given the large size of the gene and allelic heterogeneity, the disease has been difficult to target with any genetic medicine to date. While impaired copper excretion begins at birth, the effect is typically not observed clinically until later in childhood or early adulthood and the majority of patients are diagnosed between ages five and 35. The most common manifestation is chronic active hepatitis that can progress to liver cirrhosis; however, a variety of neurologic and psychiatric manifestations may also be present and undiagnosed. Such symptoms may include dysarthria, gait impairment, dystonia, depression, irritability, and personality changes. Diagnosis is typically suggested by abnormalities in blood ceruloplasmin and/or 24-hour urine copper as well as the presence of Kayser-Fleisher rings on ocular examination. Additional diagnostic certainty can come from liver biopsy and ATP7B sequencing.

Wilson's disease has an estimated global prevalence of one patient per 10,000 to 30,000 individuals although recent genotyping studies suggest that the actual genetic prevalence may be substantially higher. This estimate suggests that there are more than 30,000 patients with Wilson's disease in the United States alone.

Limitations of Current Therapy

Wilson's disease is a serious disease that is fatal if left untreated, typically from cirrhosis and liver failure. Once diagnosed, the standard of care for Wilson's disease involves chronic treatments to try and remove copper from

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the body using copper chelators and efforts to minimize copper absorption from the gastrointestinal tract. Treatment must be lifelong to prevent copper reaccumulation and side effects from chelator therapy (e.g. hypersensitivity reactions, fever, changes to blood counts) are common and can lead to treatment discontinuation. If treatment is discontinued, patients are at risk for hepatic decompensation or the development of new neurologic symptoms. In patients with delayed diagnosis or rapidly progressive disease, liver transplant may be required with associated post-transplant risks and need for immunosuppression.

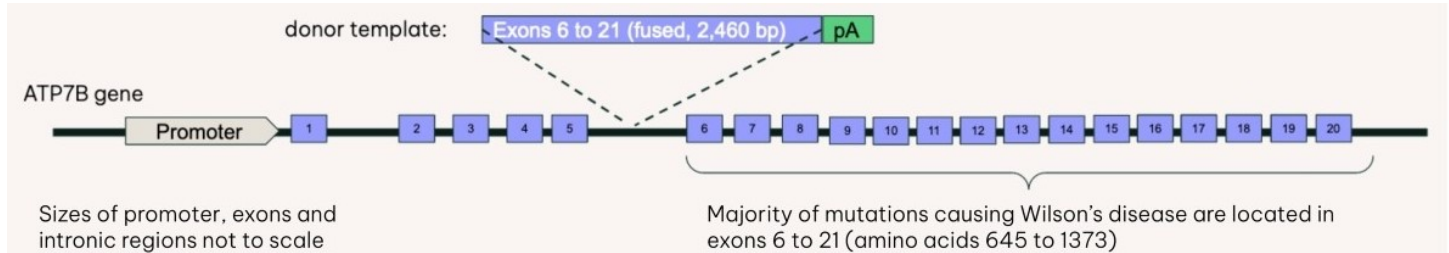
There are no genetic medicines approved for Wilson's disease. A genetic medicine has the potential to eliminate the need for life-long therapy and copper monitoring as well as reduce the risk for adverse events.

Our Approach/Next Steps

Wilson's disease is inherited in a recessive manner meaning that heterozygotes (people having one mutant allele and one wild type allele) are not affected. This means that correction of only one of the two mutant alleles should be sufficient to confer a normal phenotype on the hepatocyte, the cell type in the liver in which the ATP7B gene performs its function. Patients with Wilson's disease have a diverse spectrum of different mutation types (point mutations, deletions, splice site mutations) that are located throughout the ATP7B gene although different ethnic groups bear different predominant mutations. Common mutations in specific population groups include H1069Q (30-70% of Wilson's disease patients in Germany, 30-70% in US Caucasians), M645R (approximately 30% of Wilson's disease patients in Spain), R778L (40% of Wilson's disease patients in Korea, approximately 30% in China).

We are working to treat Wilson's disease using a Big RIGS insertion, potentially the first known instance of a targeted large gene insertion with this approach. We believe this represents the ideal approach for genome editing for Wilson's disease because we expect that it could enable the majority of patients to be treated with the same therapy irrespective of their specific mutation(s) in ATP7B. The ATP7B gene spans 76,000 bp of DNA in the human genome, and the protein coding sequence of ATP7B is 4,398 bp in length which encodes a protein of 1,465 aa. The majority of the pathogenic mutations identified in ATP7B are located in the C-terminal half of the protein between amino acid positions 645 and 1373 which are encoded in exons 6 to 21 (Figure 41). This region includes the three most frequent mutations (H1069Q, R778L, M645R, I1148T) as well as many other less common mutations. We are evaluating a genome editing approach in which a donor template that encodes exons 6 to 21 of the ATP7B gene (2460 bp) is inserted in to the ATP7B locus at intron 6 (downstream of exon 5) such that exons 1 through 5 of the endogenous gene are functionally fused to the inserted wild type exons 6 to 21. We believe this will generate a wild type ATP7B protein driven from the endogenous ATP7B promoter thereby preserving the normal levels of ATP7B and normal regulation of expression. This approach should be applicable to all Wilson's disease patients except for those with mutations in exons 1 to 5 which represent only a small fraction of the patient population. This approach leverages an all RNA based editing system such that the editing components could theoretically be delivered in a single LNP that is taken up by the hepatocytes of the liver.

Figure 41. Genome Editing Strategy for Wilson's Disease.



Familial Amyotrophic Lateral Sclerosis ("ALS")

The Disease

ALS is a rapidly progressive neurodegenerative disorder of upper and lower motor neurons leading to weakness, disability, and death. The prevalence of ALS is approximately four to six patients per 100,000 individuals and it is estimated that over 5,000 patients are diagnosed each year in the United States. While the majority of ALS cases have no known family history, it is estimated that approximately 10% of cases are due to inherited causes. Of these, among the more prominent causes is from a mutation in the gene superoxide dismutase 1 ("SOD1"). SOD1 ALS (occasionally referred to as ALS1), is an autosomal dominant condition associated with toxic gain of function of SOD1 leading to protein misfolding and intraneuronal cytotoxicity. While the mechanism of action of SOD1 pathophysiology is poorly understood, it is unique in that histopathologically it does not contain typical cytoplasmic inclusions of the nuclear binding protein TDP-43 seen in other spontaneous and familial forms of ALS. The median age of diagnosis of SOD1 ALS is mid-to-late 40s, and similar to other forms of ALS, progressive weakness and loss of voluntary function is rapid with a median survival after diagnosis of approximately three years.

Limitations of Current Therapy

Despite significant investment in research over recent decades, the standard of care for treating all forms of ALS is suboptimal and there remains no cure. There are currently three drugs approved in the United States to treat all forms of ALS (riluzole, sodium phenylbutyrate and taurursodiol, edaravone), and one recent accelerated drug approval for SOD1 ALS (tofersen). To date, only modest benefit in slowing disease progression or improving survival has been observed, and all of these medications require repeat administration or dosing and are associated with adverse effects. In a Phase 3 clinical trial, tofersen, which is an antisense oligonucleotide targeting SOD1 delivered directly to the cerebrospinal fluid and that requires repeated lumbar puncture monthly, did not result in a statistically significant change on clinical measures after 28 weeks of treatment, but did show a nominally statistically significant benefit on a biomarker, neurofilament light chain, and longer term administration was associated with slowing of disease. Clinically significant adverse reactions with tofersen include myositis and/or radiculitis, papilledema and elevated intracranial pressure, and aseptic meningitis, and additionally adverse reactions can occur from repeated lumbar puncture procedures. Thus, despite this precision medicine approach, there remains significant unmet need for effective therapies that can halt disease progression and improve overall survival from SOD1 ALS.

Our Approach/Next Steps

Our approach is to build upon the data generated by tofersen and use one of our programmable nucleases to durably knock down SOD1 levels with a single administration, thus capturing durable benefit with a clinically validated disease target without requiring the patient burden of repeat intrathecal administrations of an oligonucleotide. We plan to deliver the nuclease and associated guide using an AAV vector with sufficient tropism for lower motor neurons. We have performed guide screening with 8 of our small MG nucleases that can fit in a single AAV. A total of 99 lead guides were identified for SOD1 and 60 leads for ATXN2 which are being evaluated in neuronal cells in culture. We are in the process of optimizing AAV vector designs to package and efficiently express our small nucleases and gRNA from a single virus to enable evaluation of lead SOD1 and ATXN2 guides in mouse models.

[Spontaneous ALS](#)

The Disease and Limitations of Current Therapy

As noted above, ALS is a relentless and ultimately fatal disease of motor neurons with no known cure. Approximately 90% of ALS does not have a known family history or clear genetic cause. While the underlying cause of ALS in most cases is unknown, a common histopathologic finding involves misfolded cytoplasmic protein aggregates that include TDP-43. As TDP-43 is a highly conserved nuclear RNA and DNA binding protein involved in RNA processing, the clinical manifestations of ALS may arise both from the toxic cytoplasmic TDP-43 aggregates as well as RNA processing abnormalities from the loss of normal nuclear functions of TDP-43. The initial symptom of ALS is a gradual onset of muscle weakness that is typically painless. These symptoms are often followed by muscle twitching, loss of coordination, falls, and fatigue that impair functionality. As the disease progresses, loss of ambulation, spasticity, and diaphragmatic weakness progresses with the most common cause of death being respiratory failure. Despite the approval of several classes of oral compounds for spontaneous ALS, effects on preserving clinical functionality and survival are modest. There remains significant unmet need for safe and effective therapies that can halt disease progression and improve overall survival from spontaneous ALS.

Our Approach/Next Steps

TDP-43 intracytoplasmic inclusions and proteinopathy are hallmarks of the vast majority of ALS histopathology; however, targeting TDP-43 directly has not been feasible due to its critical role in RNA processing and other cellular functions. We intend to develop an ALS therapy that targets the ATXN2 gene, which we believe is an attractive target based on strong third-party preclinical data targeting the gene ATXN2, which encodes the protein Ataxin 2, and has been shown to be a powerful genetic modifier of TDP-43 in yeast and flies, and importantly, knockdown of Ataxin 2, either by antisense oligonucleotides or by genetic manipulation has improved survival and motor function in a mouse model of ALS. A Phase 1/2 clinical trial of an investigational antisense oligonucleotide targeting Ataxin 2 in adults with ALS that is administered intrathecally is in progress, which will provide further information about the safety and efficacy of this approach.

Our plan is to deliver a nuclease and associated guide using an AAV vector with sufficient tropism for lower motor neurons. We are currently initiating guide screening efforts to potently and selectively knock down Ataxin 2 levels and determining the appropriate nuclease/guide system for AAV packaging.

[Charcot-Marie-Tooth Type 1a \("CMT1a"\)](#)

The Disease

CMT1a is part of a larger classification of hereditary peripheral motor and sensory neuropathies caused by pathogenic mutations in proteins associated with myelin formation and axonal signal propagation. CMT1a is an autosomal dominant disease arising from a gene duplication of PMP22 (peripheral myelin protein-22) and overexpression of PMP22 protein. PMP22 is tightly regulated and expressed in Schwann cells that control the production of myelin sheaths around axons. Patients with CMT1a have altered myelination that impairs nerve conduction and neuromuscular function. Patients typically present in the first or second decade of life with lower extremity weakness, atrophy, falls, and sensory deficits. The disease is slowly progressive and impairs mobility, and can also involve changes to distal upper extremities and limb deformities. Although life expectancy is typically preserved, CMT1a leads to significant disability and impaired quality of life.

Although exact prevalence estimates vary, CMT is believed to affect one patient per 2,500 individuals, with approximately 126,000 patients in the United States alone. Of those approximately half are believed to have CMT1a, the most common form of the disease.

Limitations of Current Therapy

The treatment of CMT1a and other forms of CMT are largely supportive and there are no approved treatments. Existing standard of care involves physical therapy, stretching, orthotics, and occasional foot surgery to improve deformities that impair ambulation. Patients should be screened for conditions that can exacerbate neuropathies such as vitamin deficiencies or diabetes in an attempt to mitigate against more rapid progression. There are investigational efforts for RNA targeted therapeutics to reduce PMP22 overexpression with strong preclinical data to support the approach, but clinical studies are very early and therapies would need to be given lifelong.

Our Approach/Next Steps

Our approach to CMT1A is a permanent reduction of PMP22 protein levels to the normal range by knockdown of PMP22 expression using our nuclease platform. There is preclinical proof-of-concept for this approach in a mouse model of CMT1A using AAV9 to express a siRNA against PMP22. We intend to use our novel nucleases to introduce InDels in the promoter region of PMP22 that lead to a reproducible reduction of PMP22 expression to the normal range. We anticipate that this editing approach will be delivered via an AAV with the goal of achieving uniformly high levels of genome editing while minimizing the risk of toxicity resulting from reducing PMP22 levels to below normal at a cellular level.

We believe the diversity of our nuclease platforms including type V systems such as MG29-1 that create larger deletions and are more likely to inactivate promoters by eliminating transcription factor binding sites, lends itself to identification of nuclease guide combinations that are efficient and result in partial reduction in the expression of the PMP22 gene. We plan to perform a guide screen targeting the promoter region first in HEK293 cells (a cell line that expresses PMP22 mRNA) and active guides with promising InDel profiles and editing potency will be further evaluated for PMP22 mRNA knockdown. Lead systems will be vectorized into AAV9 viruses and evaluated in the CMT1a mouse model. Once reduction of PMP22 expression is confirmed, the therapeutic benefit can be evaluated via various endpoints including tissue morphology, nerve conduction velocity, circulating biomarkers and behavioral tests to support candidate selection.

Duchenne Muscular Dystrophy ("DMD")

The Disease

DMD is an X-linked recessive myopathic disease involving loss of function mutations of dystrophin, a large protein critical for the stabilization and protection of muscle fibers encoded by the DMD gene. In the setting of absent or abnormal dystrophin, muscle fibers are prone to injury, degeneration, fibrosis, and ultimately fatty infiltration and replacement. DMD typically presents in early childhood with initial symptoms of muscle weakness and progresses rapidly to loss of ambulation as well as respiratory muscle fatigue and cardiomyopathy. In general, large proximal muscles are affected earlier than smaller distal muscles, and lower extremity muscles are affected earlier than upper extremity muscles. Patients are often wheelchair bound before teen years and often die in their late teens and early twenties from cardiopulmonary complications. Prior to clinically overt findings, patients typically have marked elevations in the muscle enzyme creatine kinase that can serve as the earliest indicator of muscle inflammation and degeneration. DMD is estimated to occur in one of every 3,500 live births, and as an x linked recessive disease is observed almost entirely in males.

DMD is the largest gene identified in humans to date spanning approximately 2.3 Mbp, and the severity of clinical manifestations of the muscular dystrophy is in part related to the location and type of dystrophin mutation and resulting residual amount of dystrophin present. Accordingly, in-frame mutations with residual dystrophin of 5-50% are associated with a less severe clinical course than early truncating mutations with

residual dystrophin levels of 0-5%. These findings have led to drug development efforts to restore out of frame mutations into in-frame mutations that result in an abnormal but partially effective dystrophin protein. Additionally, it has been observed that in-frame deletions of large portions of the central part of the dystrophin protein coding region are well tolerated, which has provided the basis for gene transfer approaches of a "microdystrophin" protein.

Limitations of Current Approaches

Despite significant efforts to develop precision medicines for DMD, results to date have not led to meaningful improvements in the standard of care for patients. The mainstay of treatment for DMD is glucocorticoids to address muscle inflammation and improve proximal muscle strength and respiratory function. However, the benefits of glucocorticoids have to be weighed against their long-term risks that include excessive weight gain, impact on growth, cataract formation, bone loss/fracture risk, and behavioral changes. More recently several genetic therapies that induce exon skipping have been approved in the United States to address specific mutations (e.g., exon 45 (casimersen), exon 51 (etipilsen), exon 53 (golodirsen)) or induce readthrough of stop mutations (ataluren). These therapies have shown modest improvement in muscle dystrophin levels but their overall impact on clinical outcomes has not been established.

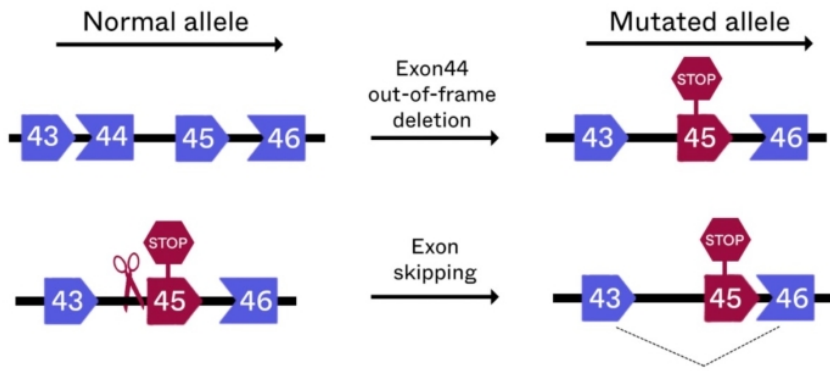
Our Approach/Next Steps

DMD patients often have deletions of entire exons (frequently in the hotspot region of exons 45-55) which results in the flanking exons being spliced out of frame at the mRNA level. Approved therapies have aimed to correct these mutations by restoring the open reading frame through "exon skipping", thus avoiding degradation of the mRNA and/or premature protein termination.

Our proposed genome editing approach is to more effectively facilitate exon skipping by making permanent changes at the DNA level using genome editing that inactivate the splice acceptor (5' exon splice junction sequence) of the exon that follows the deleted exon such that after transcription the RNA splicing machinery "skips" over that exon, splices to the following exon, and restores the proper reading frame. The resulting proteins will lack the domains encoded by the mutated and skipped exons but these are known to function nearly as well as normal dystrophin.

For example, one common mutation is deletion of exon 44, which results in exon 43 being aberrantly spliced to exon 45 and an out of frame mRNA (designated as "STOP" in Figure 42) which is then degraded or translated into a truncated protein. As shown in the Figure 42 below, skipping of exon 45 results in splicing from exon 43 to 46 and restores protein expression.

Figure 42. Example of Exon Skipping Approach for Dystrophin Exon 45 that Results in Splicing of Exon 43 to 46 Thereby Restoring the Correct Translational Reading Frame and Thus Dystrophin Function.



We believe a similar strategy can be employed for deletions of exons 50, 51, and 53, creating a franchise of development programs for DMD. We are in the process of initiating a guide screen using our toolbox of DSB nucleases and base editors that are small enough to package in a single AAV vector to inactivate the splice acceptors of the various exons within this hotspot region. The splice acceptor sequence is short (composed of a poly-pyrimidine tract of about 10 to 15 bases followed a short distance away by the three base consensus sequence C/T-A-G) which limits the number of guides that can be designed to inactivate the splice acceptor when using a single nuclease. We are leveraging our collection of small nucleases that have a variety of different PAMs to enable more guides to be designed against each splice acceptor. Hits from this guide screen will be assayed in cardiac and/or skeletal muscle cells *in vitro*. The nuclease/guide combinations that show potent activity in muscle cells will then be evaluated in human cells in which the DMD gene contains the relevant pathogenic mutations to evaluate exon skipping activity. *In vivo* evaluation of leads will be performed in mouse models of DMD.

Because DMD affects skeletal and cardiac muscles throughout the body of DMD patients, effective therapy will require delivery to a large proportion of these muscles with the diaphragm and heart muscle being of particular importance. To date the only delivery system that is able to deliver to these tissues is AAV, with AAV serotype 9 showing the most promising delivery profile. Because a maximum of up to 5 kb of DNA can be packaged inside the AAV virus it is not possible to deliver SpCas9 and a guide or current SpCas9 derived base editors and a guide in a single AAV. While these larger systems can be split between two AAVs, this reduces potency due to the dose limiting toxicity of AAV and the need to administer two viruses (effectively doubling the dose). A dual AAV approach also increases manufacturing complexity and costs. We are leveraging our collection of smaller editing systems that can be packaged in a single AAV (currently three nucleases).

The potential therapeutic benefit of editing the DMD gene in mouse models will be assayed at the mRNA and protein level, and by functional endpoints such as maximum force output.

Cystic fibrosis

Cystic fibrosis is an autosomal recessive lung disease caused by mutations in the CFTR gene. Mutations impact electrolyte transport in cells that produce mucus, sweat, and digestive fluids causing these secretions to be thicker and more viscous than normal. As a result, these secretions become sticky and can clog passageways and ducts, particularly in the lung and pancreas. Over time, these thick mucus secretions in the lung cause

chronic lung infections, inflammation, fibrosis and ultimately destructive bronchoalveolar lung disease resulting in progressive pulmonary failure. The pancreas is similarly affected and blockage of ducts in the pancreas lead to loss of exocrine function and pancreatic insufficiency.

The overall incidence of cystic fibrosis is estimated at one patient in 3,000 to 6,000 live births in the US and Europe, but rates depend strongly on geographic location and ethnicity with higher rates in Caucasians of northern European descent and much lower rates in Asians. It is estimated that there are approximately 30,000 individuals living with cystic fibrosis in the US and 70,000 individuals worldwide. Over the past few decades, improvements in antibiotic treatments, supportive measures, multidisciplinary care centers, and newer targeted medications have increased the overall life expectancy from late childhood to the fourth decade.

Limitations in Current Approaches

One of the challenges in developing precision medicines for cystic fibrosis is the large nature of the gene and the varied mutations along the gene that result in loss of protein expression, loss of function, misfolding and mislocalization within the cell. Accordingly, therapeutic efforts have required individualized approaches tailored to certain mutations to improve CFTR function. Although such medications have improved rates of lung function decline, not all patients have mutations amenable to CFTR targeted therapies. Further, none of these therapies offer a true cure to the underlying gene mutation, and patients continue to experience morbidity and mortality from cystic fibrosis disease progression.

Our Approach/Next Steps

Our goal for a genome editing based treatment for cystic fibrosis is two-fold: (1) a permanent curative therapy from a single treatment, and (2) a therapy that is applicable to the majority of cystic fibrosis patients. We believe this could be achieved by integrating a functional version of the CFTR gene into the genome of the lung basal stem cells (alternatively called bronchioalveolar stem cells). The basal stem cells are believed to give rise to the lung epithelial cells that are the site of CFTR expression that is defective in cystic fibrosis patients. Stem cells are a specialized population of cells that are maintained for a person's lifetime and are the source for renewal of differentiated cells. Editing the stem cells should ensure that the introduced functional CFTR gene is not lost over time due to the shedding of differentiated epithelial cells. By integrating a functional CFTR gene rather than correcting individual cystic fibrosis causing mutations, a single therapy could treat the majority of cystic fibrosis patients.

We intend to explore two of our genome editing modalities in cystic fibrosis. The Big RIGS technology and CAST systems both have the potential to integrate large pieces of DNA (in this case encoding a CFTR gene) into a specific site in the genome. For the Big RIGS approach, the CFTR gene would be delivered as an RNA that is reverse transcribed into DNA to provide the DNA template for integration. In the case of CAST, the CFTR gene would be delivered as double stranded DNA that is recognized by the CAST system and integrated at the desired site by the transposase. Delivery to the basal stem cells of the lungs can theoretically be achieved by IV dosing. We may also evaluate a non-viral delivery system for lung delivery.

We believe the Big RIGS system has the advantage that it can be delivered using only RNA for which non-viral RNA delivery technologies such as LNP are well established. In contrast, delivery of DNA (that would be required for CAST) by non-viral delivery vectors is not well established with the main barrier being transit of the DNA into the nucleus. However, in a preliminary study we have recently demonstrated delivery of a 4.6 kb double stranded DNA to the nuclei of cells in the liver of mice by IV administered LNP.

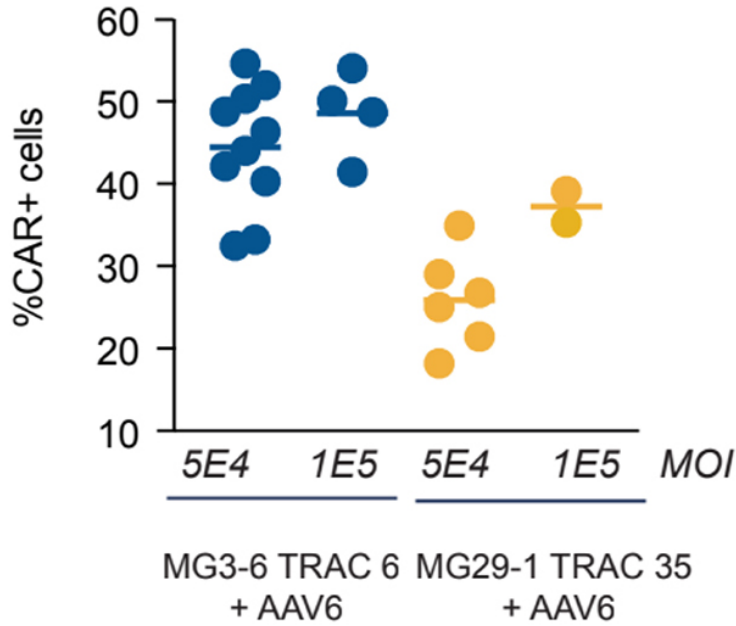
Cell Therapy Applications Using Our Platform

Identifying and optimizing novel nucleases from our metagenomics platform has involved a series of stringent efficiency, activity, and specificity testing in a variety of immune cell types which yields a comprehensive dataset that demonstrates our genome editing capabilities for cell therapy applications. Many cell therapies require multiple simultaneous genome edits to enhance efficacy, safety, and/or durability of these products. In the allogeneic cell therapy setting, additional gene edits are required to decrease the immunogenicity of the cell therapies to prevent rejection by the host immune system. Our toolbox provides an important advantage compared to the current cell therapy landscape as we are able to use either single or multiple genome editing enzymes to implement multiple gene edits ("multiplex editing") with high efficiency and specificity. These gene edits could be either knock outs or knock ins.

We are currently working on various discovery stage projects in-house and with collaborators to evaluate the efficacy and specificity of our enzymes for the engineering CAR-T and TCR-T cell product candidates. Our initial lead nucleases can be used to efficiently engineer primary human T cells, demonstrating utility for cell therapy applications.

Our programmable nucleases have achieved key requirements for T cell engineering, including genome editing dsDNA-break induced knock-in of a chimeric antigen receptor (CAR, Figure 43).

Figure 43. Example of Two Lead Nucleases, Type II MG3-6 and Type V MG29-1, Capable of Engineering Primary Human T Cells.



* Nucleases were delivered as RNP and CAR donor template by AAV.

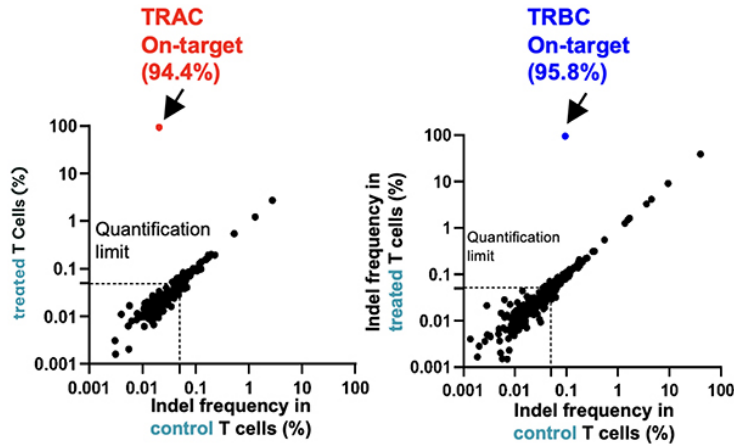
* Nucleases were programmed to target the TRAC locus.

* CAR integration into T cells from 10 T cell donors with MG3-6 and MG29-1 and either 5E4 or 1E5 MOI.

Data generated by Metagenomi.

Our MG29-1 nuclease is a highly active and specific nuclease being used for ex vivo T cell engineering in collaboration with Affini-T Therapeutics. Affini-T Therapeutics is developing a cell therapy based on engineering the TCR of T cells to recognize mutant KRAS for the treatment of patients with solid tumors. Affini-T scientists showed that the knock-out of the endogenous TCR improved expression of a transgenic TCR, and that MG29-1 can be used to engineer functional TCR T cells by knock-in of a transgene into the TRAC locus.

Figure 44a. MG29-1 tested in primary human CD4/CD8 T cells showed specificity in two loci.

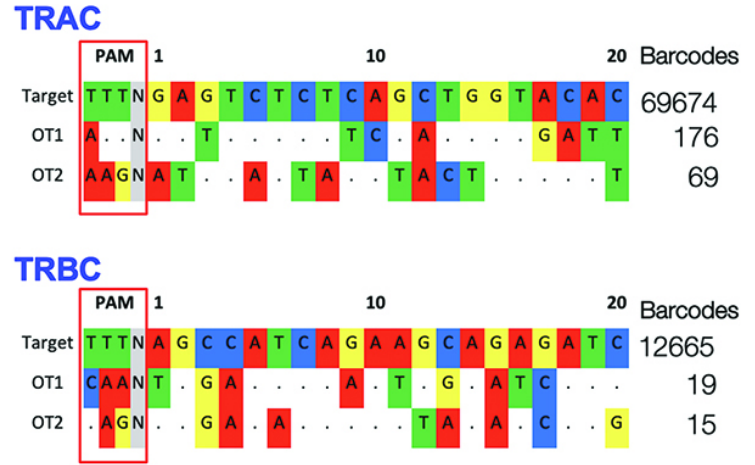


* InDel formation was evaluated for 590 computationally predicted off-targets across TRAC and TRBC, allowing for up to six mismatches.

Data generated by Affini-T Therapeutics.

We plan to use our gene editing enzymes to engineer different T cell subsets with either chimeric antigen receptors (CARs) or engineered TCRs targeting antigens expressed in various tumor indications, including hematological and solid tumor malignancies. We are currently investigating different tumor targets and tumor indications to select future T cell therapy product candidates. In addition, we plan to use CAR-T cells in auto-immune diseases driven by the production of autoantibodies, including conditions such as systemic lupus erythematosus, rheumatoid arthritis, myasthenia gravis, autoimmune hemolytic anemia, immune-mediated thrombotic thrombocytopenic purpura, and possibly others. We will use T cells engineered with chimeric antigen receptors against B cell markers to deplete the B cell compartment and eliminate the production of autoantibodies.

Figure 44b. Oligonucleotide capture in primary T cells identified putative MG29-1 off-targets. More sensitive methods did not verify such results.



- * Off-targets had 100-fold fewer barcodes compared with target sites.
- * Off-target sites could not be validated with amplicon-based NGS sequencing.
- * The presence of >9 mismatches in the off-target sites may indicate that they are not likely to be true positives.

Our License and Collaboration Agreements

Moderna Strategic Collaboration and License Agreement

On October 29, 2021, the effective date, we entered into a Strategic Collaboration and License Agreement (the "Moderna Agreement") with Moderna. We will collaborate with Moderna on the research and development of *in vivo* genome editing therapies directed at certain targets and the commercialization of such genome editing therapies. The collaboration provides Moderna with exclusive access to our technology platform during the research period in (1) the field of *in vivo* gene editing technology for a therapeutic, ameliorative or prophylactic application by way of knock-out through InDel formation or base editing or insertion of an exogenous DNA template (such field, "DT Field") and (2) the field of *in vivo* gene editing technology for a therapeutic, ameliorative or prophylactic application outside the use of (a) DNA donor templates and (b) no exogenous template at all but including (c) correction by base editing (such field, "RT Field"). We formed a joint steering committee, a joint research subcommittee and a joint patent subcommittee to oversee the collaboration activities. Each of us and Moderna must use commercially reasonable efforts to perform and complete our respective activities under research plans and commercialization plans approved by the joint steering committee.

Under the terms of the Moderna Agreement, we and Moderna will collaborate on one or more programs in the RT Field (the "Moderna RT program") and two programs in the DT Field (the "Moderna DT program" and the "DT Co-Co program"). We and Moderna have each granted the other party a non-exclusive license in such party's (i) background technology, including intellectual property rights controlled by each party related to each respective program, and (ii) the know-how and patents that come into control of each party relating to the program and during the respective program term, in each case to carry out activities in the applicable research programs. We shall own certain intellectual property that relates to our technology platform ("Metagenomi Program Technology"). Moderna shall own certain intellectual property that relates to Moderna's technology platform ("Moderna Program Technology"). Any intellectual property discovered, invented, conceived or created during an applicable research term that is not Metagenomi Program Technology or Moderna Program Technology shall be jointly owned by us and Moderna. Further, we granted Moderna a perpetual, irrevocable, royalty-free, nonexclusive license under Metagenomi Program Technology to the extent pertaining to the exploitation of donor templates or guides to which Moderna has any inventive contribution.

With respect to the Moderna RT and Moderna DT programs, we will collaborate on the research and development of product candidates under the approved research plans. The initial research term of the Moderna RT program is four years, which may be extended by Moderna for an additional three years upon written notice and a payment of extension fees. The initial research term of the Moderna DT program is four years. We granted to Moderna an option to obtain an exclusive license to develop, manufacture and commercialize up to ten Moderna RT program candidates and up to two Moderna DT program candidates at any time during the research term and prior to filing of an investigational new drug ("IND") application with the Food and Drug Administration ("FDA") or any similar application filed with a regulatory authority in a country other than the United States ("U.S."), subject to Moderna's payment of an option exercise fee of \$10.0 million per target. If we or any of our affiliates wish to grant any third party rights in certain targets in the DT Program prior to the earlier of the (a) second anniversary of the agreement or (b) 90 days after achievement of certain readiness standards, we shall provide Moderna with written notice thereof and Moderna shall have a right of first negotiation to negotiate an agreement on the terms of a collaboration and license agreement for such targets.

With respect to the DT Co-Co program, we will work together with Moderna on the co-development and commercialization of products and share costs and profits equally. We granted Moderna a co-exclusive (with us and our affiliates) license under our patents and know-how related to PH1, the DT Co-Co target, to exploit all applications

of such target in the DT Co-Co program. We maintain commercialization rights in the U.S. (subject to Moderna's right to appoint up to 50% of the U.S. sales force for the DT Co-Co program), while Moderna maintains these rights in countries other than the U.S. The initial research term for the DT Co-Co program is four years, and each party has a right to opt-out of the DT Co-Co program at any time, at which point the other party has the right to solely continue the development and commercialization activities, provided that the party which has opted-out shall have a right of first offer in the event that the other party wishes to grant a license or sublicense to a third party with respect to the DT Co-Co program. If there is no development candidate nomination by the end of the initial research term, the DT Co-Co program will expire, unless we have mutually agreed to continue the program.

During the year ended December 31, 2021, we received a non-refundable upfront payment of \$40.0 million and a \$5.0 million payment for the first year of research costs. Concurrent with the Moderna Collaboration Agreement, Moderna also provided \$30.0 million in cash in the form of a convertible promissory note (see Note 9 in our audited consolidated financial statements included elsewhere in this prospectus) pursuant to a convertible promissory note agreement dated October 29, 2021 (the "Moderna Convertible Promissory Note Agreement"). The convertible promissory note was converted into shares of Series B redeemable convertible preferred units in January 2022. Moderna will reimburse us up to \$5.0 million in annual research and development costs related to the Moderna DT and Moderna RT programs, or up to the agreed amount of expenses per the budget. As of September 30, 2023, we have received a total of \$49.6 million under the Moderna Collaboration Agreement, not including cost-sharing payments under the DT Co-Co program.

For the Moderna RT and Moderna DT programs, we are eligible to receive (i) technology milestone fees related to the achievement of certain preclinical research objectives of up to \$75.0 million, (ii) development and regulatory milestones of up to \$100.0 million per target, (iii) sales milestones of up to \$200.0 million per target, and (iv) royalties ranging from a mid-single digit to a low-teens percentage of annual net sales of a licensed product. Any profits and losses from the co-development and commercialization of the DT Co-Co program are shared equally between us and Moderna. With respect to the DT Co-Co program for which the opt-out party has exercised its opt-out right, the continuing party will pay to the opt-out party, certain development, regulatory and sales milestone payments that will not exceed an aggregate \$239.0 million per DT Co-Co target, and opt-out royalties ranging from a high-single digit to a low-teens percentage of annual net sales of a licensed product.

The term of the Moderna Agreement will continue on a licensed product-by-licensed product and country-by-country basis, until the expiration of the applicable royalty term. The royalty term commences on the first commercial sale of a licensed product and terminates on the latest of: (a) the expiration or abandonment of the last valid claim of a patent within the licensed Moderna DT or RT technology; (b) 10 years after the first commercial sale of a licensed product; and (c) expiration of the regulatory exclusivity. Upon the expiration of the term of a licensed product in the Moderna DT or Moderna RT program, the licenses granted to Moderna will survive and become perpetual, fully paid and royalty-free. Each party may terminate the Moderna Agreement on a program-by-program basis upon written notice to the other party for an uncured material breach or insolvency. In lieu of termination for our material breach, Moderna may, upon written notice, continue the agreement with respect to the relevant collaboration target at Moderna's amounts payable reduced by 50%, or in the case of a DT Co-Co-Target, Moderna may propose, subject to arbitration, to adjust the profit and loss share for DT Co-Co Products to provide Moderna with an additional share of the net profits (not to exceed 75% of the total net profits). We may terminate the Moderna Agreement upon written notice to Moderna for a patent challenge. Additionally, Moderna may terminate the agreement at its convenience with respect to Moderna DT or Moderna RT programs for any reason upon at least: (a) 60 days' prior written notice if a first commercial sale has not occurred for the products in such program, or (b) 180 days' prior written notice if a first commercial sale of a product in such program has occurred. Upon termination, all licenses granted under the agreement with respect to the applicable products under the agreement shall terminate, subject to an orderly wind-down period, provided that any permitted sublicense granted to a third party shall survive (provided such third party did not cause the termination through uncured material breach).

Affini-T Development, Option and License Agreement

On June 14, 2022, the effective date, we entered into a Development, Option and License Agreement (the "Affini-T Agreement") with Affini-T. Pursuant to the Affini-T Agreement, we and Affini-T have agreed to identify, develop or optimize certain reagents using our proprietary technology for Affini-T to use such reagents to develop and commercialize gene edited TCR-based therapeutic products exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with any engineered primary TCR alpha/beta T cells and non-exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with certain other engineered immune cells worldwide. A joint steering committee was established by both parties to assign alliance managers and project leaders to oversee the collaboration activities. We must use commercially reasonable efforts to perform and complete our obligations under research plans approved by the joint steering committee.

Pursuant to the Affini-T Agreement, we granted Affini-T options to receive, on a pre-specified target-by-pre-specified target basis, for up to six pre-specified targets, either (i) an exclusive, royalty-bearing, sublicensable worldwide license under all of our applicable intellectual property to research, develop, manufacture, use, commercialize and otherwise exploit any TCR-based therapy, preventative treatment, or diagnostic for humans that is directed to such pre-specified target, contains or comprises Primary TCR alpha/beta T Cells and is derived from *ex vivo* application of our reagent (the "Exclusive Option") or (ii) a non-exclusive, royalty-bearing, sublicensable worldwide license under all our applicable intellectual property to research, develop, manufacture, use commercialize and otherwise exploit any TCR-based therapy, preventative treatment, or diagnostic for humans that is directed to such pre-specified target, contains or comprises TCR natural killer ("NK") cells derived from iPSC immune cells or TCR T cells derived from donor-derived or iPSC immune cells. Affini-T can exercise its options for either an exclusive license or a non-exclusive license, or both, for each pre-specified target by providing written notice prior to the earlier of (x) the end of the Affini-T Agreement term or (y) 90 days following the filing of an IND for a licensed product directed to a pre-specified target, subject to the payment of certain fees per each option exercised. After the option exercise, Affini-T has agreed to use commercially reasonable efforts to conduct all development and commercialization activities for a licensed product, and development and commercialization of all licensed products will be at Affini-T's sole cost and expense.

On a target-by-target basis, (1) until the earlier of Affini-T's (a) exercise of an Exclusive Option, (b) written notice not to exercise an Exclusive Option or (c) expiration of an applicable Exclusive Option or (2) upon exercise of an Exclusive Option, we and our affiliates shall not exploit, or work with any third party to exploit, any *ex vivo* gene edited products directed to the applicable target covered by such Exclusive Option.

In connection with the Affini-T Agreement, we received upfront equity consideration of 719,920 shares of Affini-T's common stock with an estimated fair value of \$1.3 million in June 2022. The fair value of Affini-T's shares of common stock was estimated by our management, considering the most recent third-party valuation. Affini-T has also agreed to reimburse us for expenses incurred while performing research activities under the research plans. As of September 30, 2023, we received a total of \$3.2 million from Affini-T related to reimbursable expenses. Additionally, we are eligible to receive (i) 933,650 shares of Affini-T's common stock upon the achievement of a regulatory milestone, which is the earlier of a submission of a drug master file to the FDA or an acceptance of an IND filing for a licensed product by the FDA, (ii) up to \$18.8 million in future developmental milestone payments depending on the completion of or the number of patients dosed in, the relevant human clinical trial, or the initiation of a pivotal trial, and \$40.6 million in future regulatory approval milestone payments, which include regulatory approvals in the U.S. and other markets for licensed products directed to a pre-specified target if options for both exclusive and non-exclusive licenses are exercised with respect to such target, (iii) up to \$250.0 million in sales-based milestones for aggregate sales of all licensed products directed to a given pre-specified target and (iv) royalties ranging from a low-single digit to high-single digit percentage of worldwide annual net sales of licensed products.

The initial term of the Affini-T Agreement is five years from the effective date. If Affini-T exercises an Exclusive Option with respect to any pre-specified target during the initial term, the initial term will be extended by an additional five years. Following the expiration of the extended term, if any, the agreement will continue on a

target-by-target basis and expire with respect to such target upon the expiration of the royalty term for all licensed products directed to such target. The Affini-T Agreement may be terminated during the term by either party for an uncured material breach by, or bankruptcy of, the other party. Additionally, Affini-T may terminate the Affini-T Agreement for convenience, in its entirety, on a research plan-by-research plan basis, on a target-by-target basis or on a licensed product-by-licensed product basis, by providing prior written notice. Upon a material breach and with written notice to us, in lieu of termination, Affini-T shall have the right to continue the agreement at payments payable at a certain percentage reduction.

Ionis Collaboration and License Agreement

On November 10, 2022, the effective date, we entered into a Collaboration and License Agreement (the "Ionis Agreement") with Ionis to collaborate on drug discovery and exploratory research activities to advance new medicines using gene editing strategies, with the goal of discovering novel medicines. Pursuant to the terms of the Ionis Agreement, we granted Ionis and its affiliates a worldwide exclusive, royalty-bearing license, with the right to grant sublicenses, to use all licensed systems and licensed products in the field of *in vivo* gene editing for all therapeutic, prophylactic, palliative, and analgesic uses in humans. In connection with the Ionis Agreement, we also have the right to exercise an exclusive option to co-develop and co-commercialize certain products under a drug discovery program. A joint steering committee was established by both parties to coordinate, oversee, and monitor the research and drug discovery activities under the Ionis Agreement. Each party must use commercially reasonable efforts to perform and complete its respective activities under the applicable program plans approved by the joint steering committee.

We will collaborate to discover therapeutic products under a drug discovery program and develop a drug discovery plan for each target, selected by Ionis. The target selection is divided into two waves: up to four targets in Wave 1 and up to four targets in Wave 2. For each drug discovery program, once the parties identify a development candidate that is suitable for further development, Ionis will be responsible for the development and commercialization of products resulting from such program. Per the terms of the Ionis Agreement, at any time prior to the designation of a development candidate for a drug discovery program and for any reason, Ionis may replace the collaboration target, provided such target has not previously been substituted out. Ionis may substitute (i) up to two Wave 1 targets and (ii) up to two Wave 2 targets.

The drug discovery activities for a program commence on the selection of a target and expire upon the earlier of (a) completion of all drug discovery activities for such program, (b) the fifth anniversary of the effective date and (c) selection of a development candidate for such drug discovery program. If one or more Wave 2 targets become collaboration targets as a result of the parties achieving enabled delivery and less than two years are remaining in the drug discovery term, then the term will be extended to the earlier of (i) the time that we complete all of our activities under the applicable drug discovery plan and (ii) the seventh anniversary of the effective date, subject to our consent.

We will also conduct an exploratory research program, and will jointly optimize gRNA and select delivery technologies and other activities. The exploratory research activities commence on the effective date and expire upon the earlier of (a) completion of all exploratory research activities established in the exploratory research plan, and (b) the fifth anniversary of the effective date.

We have the exclusive option to co-develop and co-commercialize the licensed products under a drug discovery program (the "Co-Co Option") with Ionis. The Co-Co Option may be exercised for (a) the initial Wave 1 target ("Target 1"), (b) no more than one of the other three discovery programs for the Wave 1 targets, and (c) no more than two drug discovery programs for the Wave 2 targets that become collaboration targets. If we exercise the Co-Co Option for a particular drug discovery program, that drug discovery program will automatically be deemed a "Co-Co Program", all corresponding licensed products be deemed "Co-Co Products," we will be obligated to pay Ionis an option exercise fee, and we and Ionis will enter into a separate co-development and co-commercialization agreement. The Co-Co Option exercise fee will equal 50% of Ionis'

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internal costs and out-of-pocket costs incurred in the conduct of the drug discovery activities prior to the exercise of the Co-Co Option and be reduced by 50% of our corresponding costs incurred. Future development and commercialization costs will be shared equally. We may elect to reduce our cost-share percentage anywhere between 50% and 25% on a go-forward basis, provided we will continue to bear 50% of the costs of any clinical trials ongoing at the time of the election through the completion of the clinical trials.

We will manufacture all licensed systems and certain components of the applicable licensed products that are needed by Ionis for use in its development activities and all of our manufactured components needed by Ionis for use in its commercialization activities. We will provide the manufactured components at a price that represents the cost of goods plus 15%.

Pursuant to the terms of the Ionis Agreement, we have also been granted an option to obtain a non-exclusive, royalty-bearing license, with the right to grant sublicenses, for certain Ionis' background technology to use in up to eight therapeutic products discovered by us in the field of *in vivo* gene editing and directed to a Collaboration Target (each such product, a "Metagenomi Product" and each such option an "Ionis IP Option"), but subject to encumbrance checks with respect to particular targets. A Collaboration Target is a target that is selected by Ionis, and, with respect to us, is not the subject of discussions with a third party, is not the subject of a contractual grant of rights to a third party nor the subject of an internal research and development program. If we exercise our Ionis IP Option, we will pay to Ionis up to several million dollars per Metagenomi Product upon achievement of certain clinical and regulatory milestones. We are also obligated to pay Ionis royalties in an amount equal to a low single-digit royalty on the net sales of the applicable Metagenomi Product on product-by-product and country-by-country basis.

In November 2022, we received an \$80.0 million upfront payment from Ionis for the Wave 1 drug discovery research collaboration and selected Target 1. Ionis selected its second target ("Target 2") in Wave 1 in December 2022 and its third target ("Target 3") in Wave 1 in November 2023. In November 2023, we agreed to extend the period during which we expect Ionis will select its fourth target ("Target 4") in Wave 1 by an additional three months from the 12-month anniversary of the effective date, as permitted under the arrangement. Ionis has an option to select up to four Wave 2 targets at any time during the drug discovery term, if (a) an IND for any licensed product directed to a Wave 1 target is filed with the applicable regulatory authority or (b) the parties achieve enabled delivery for a non-liver target under the exploratory research activities, by providing written notice and by paying a Wave 2 target selection fee of \$15.0 million or \$30.0 million, depending on and per the selected target.

Ionis is obligated to reimburse us for all internal costs and out-of-pocket costs incurred in the performance of the exploratory research activities, up to an aggregate of \$10.0 million, which is payable in quarterly installments of \$0.5 million during the exploratory research term. As of September 30, 2023, we received a total of \$1.5 million related to the reimbursable expenses. We are also eligible to receive (a) up to \$29.0 million in future development milestone payments for each licensed product; (b) up to \$60.0 million in future regulatory milestone payments for each licensed product; (c) up to \$250.0 million in sales-based milestones for each licensed product; and (d) royalties on annual net sales of licensed products from a mid-single-digit to low-teens percentage, subject to customary reductions.

The term of the Ionis Agreement will continue (i) with respect to the drug discovery programs, until the expiration of all applicable royalty terms for a licensed product, (ii) with respect to the Co-Co Programs, until the parties cease all exploitation for the Co-Co Products that are the subject to such Co-Co Program, and (iii) with respect to the Metagenomi Products, until the expiration of the royalty term for a Metagenomi Product. The royalty term ends on the latest of the following two dates: (i) the expiration of (A) the last claim of any issued and unexpired patent, or (B) a claim within a patent application that has not been pending for more than seven years from the earliest date to which the claim or applicable patent application is entitled to claim priority and which claim has not been revoked, cancelled, withdrawn, held invalid, or abandoned, or (ii) 12 years following the first commercial sale of a licensed product.

The Ionis Agreement may be terminated during the term by either party for an uncured material breach or bankruptcy by the other party. Additionally, Ionis may terminate the Ionis Agreement for convenience and without penalty, in its entirety or on a licensed product-by-licensed product basis, by providing 90 days' written notice. Upon termination, Ionis will transfer to us ownership of all regulatory approvals, and all licenses granted under the agreement with respect to the applicable products under the agreement shall terminate, subject to an orderly wind-down period and a right for Ionis to sell or otherwise dispose of applicable products on hand at the time of such termination. Upon our written request within 30 days following termination, Ionis will grant us an exclusive, royalty-bearing (as agreed by the parties at such time), right and license, with the right to grant sublicenses through multiple tiers, to patent rights and know-how controlled by Ionis and used in the development, commercialization, or exploitation of terminated products, solely for the exploitation of such terminated products in the terminated countries.

Competition

The pharmaceutical and biotechnology industries, including the gene therapy and genome editing fields, are characterized by rapidly advancing technologies, intense competition, and a reliance on strong intellectual property. We believe our metagenomics powered discovery platform along with our expertise in genome editing, drug discovery, clinical development, manufacturing and our ever-increasing IP portfolio, provide us with several key competitive advantages over our peers. Despite our competitive advantages, we face competition from several companies. There are numerous publicly traded companies utilizing CRISPR/Cas nuclease technology, including Caribou Biosciences, Inc., Editas Medicine, Inc., CRISPR Therapeutics AG, Intellia Therapeutics, Inc., and Graphite Bio, Inc., among others. Beam Therapeutics Inc. and Verve Therapeutics, Inc. utilize base editing technology and Prime Medicine utilizes prime editing technology. Several other companies such as Sangamo Therapeutics, Inc., Precision BioSciences, Inc., Collectis S.A., and bluebird bio, Inc. utilize first-generation nuclease-based genome editing technologies, including ZFNs, engineered meganucleases and TALENs. We also face competition from companies utilizing gene therapy, oligonucleotides, and CAR-T therapeutic approaches.

There are several other private companies such as Arbor Biotech, Chroma Medicine, Inc., Mammoth Biosciences, Scribe Therapeutics, Tessera Therapeutics, Tome Biosciences, and Tune Therapeutics, Inc. that have announced they are working on genome- and epigenome-editing therapies.

Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for our product candidates. This may include other genome editing companies using antiquated or next generation genome editing approaches or other types of therapies, such as small molecule, antibody, and/or protein therapies.

In addition, many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials and approved products than we do today. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. We also compete with these companies in recruiting, hiring, and retaining qualified scientific and management talent, establishing clinical trial sites and patient registration for clinical trials, obtaining manufacturing slots at contract manufacturing organizations. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, particularly if they represent cures, have fewer or less severe side effects, are more convenient, or are less expensive than

any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience, and availability of reimbursement.

Manufacturing

Our genome editing technology is composed of multiple genome editing components including the nuclease, mRNA, gRNA, and in some instances may include a donor DNA or RNA template for insertions. We have extensively characterized each of these components and have made significant investment in scalable manufacturing and process automation to meet stringent current good manufacturing practices ("cGMP"). Our in-house cGMP facility is capable of manufacturing clinical grade nucleases and mRNA to supply both wholly-owned and collaboration programs. We partner with contract manufacturing organizations ("CMOs") for gRNA and DNA template development and supply and continue to invest in both viral and non-viral delivery technologies internally and with partners. We believe our ability to develop, characterize, and manufacture complex human genome editing components is essential to maintaining a competitive edge while pursuing a successful regulatory pathway for genetic medicine.

Intellectual Property

Our success depends in large part upon our ability to obtain and maintain our technology and intellectual property. To protect our intellectual property rights, we primarily rely on patents and trade secret laws, confidentiality procedures, and employee disclosure and invention assignment agreements. Our intellectual property is critical to our business and we strive to protect it through a variety of approaches, including by obtaining and maintaining patent protection in various countries for our genome editing technology and other inventions that are important to our business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. The time required for development, testing, and regulatory review of our genome editing systems limits the commercially useful lifespan of our patents.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of patentable claims in the field of genome editing has emerged, for example, in the United States and in Europe. Changes in the patent laws and rules, either by legislation, judicial decisions, or regulatory interpretation may diminish our ability to protect our inventions and enforce our intellectual property rights. These changes could affect the scope and value of our intellectual property.

Filing, prosecuting, enforcing, and defending patents protecting our genome editing systems in all countries throughout the world would be prohibitively expensive. We cannot seek patent protection for our genome editing systems throughout the world. Furthermore, the intellectual property rights we obtain in some countries outside the United States can be less extensive than those obtained in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products.

Our ability to stop third parties from infringing any of our patented inventions, either directly or indirectly, will depend in part on our success in obtaining, defending, and enforcing patent claims that cover our genome editing systems. We cannot be sure that any patents will be granted with respect to any of our pending patent

applications or with respect to any patent applications filed by us in the future. We cannot be sure that any of our existing patents or any patents that may be granted to us in the future will be found by a court to be enforceable. Protecting our competitive position around our genome editing systems may involve lawsuits to enforce our patents or other intellectual property, which is expensive and time consuming, and may ultimately be unsuccessful. Furthermore, our issued patents and those that may issue in the future may be challenged, narrowed, circumvented, or invalidated, which could limit our ability to stop competitors from marketing related genome editing systems or limit the length of the term of patent protection that we may have for our genome editing systems and future gene therapies. We cannot be sure that any of our existing patents or any patents that may be granted to us in the future will be useful in protecting our commercialized genome editing systems. The rights granted under any issued patents may not provide us with complete protection or competitive advantages against competitors with similar but not identical technology or technologies that achieve similar outcomes but with different approaches. For these reasons, we may have competition for our genome editing systems.

Our issued patents and those that may issue in the future do not guarantee us the right to practice our genome editing systems. Third parties may have issued patents or be granted patents in the future that could block our ability to commercialize our genome editing systems.

We and third parties rely on trade secrets to protect certain aspects of our genome editing systems. If we are unable to protect the confidentiality of our trade secrets, our competitive position could be harmed. Furthermore, reliance on trade secrets does not prevent third parties from independently inventing those aspects of our genome editing systems. While we take commercially reasonable steps to ensure that our employees do not use the trade secrets of third parties, third parties may file claims asserting that we or our employees have misappropriated their trade secret.

For this and other risks related to our technology, inventions, improvements, platforms, and genome editing technology, please see the section entitled "Risk Factors—Risks Related to Our Intellectual Property."

Patent Portfolio

As of September 30, 2023, we own three issued U.S. patents, 15 pending U.S. non-provisional patent applications, 36 pending U.S. provisional patent applications, six issued foreign patents in Great Britain, Hong Kong, Mexico and Australia, 94 pending foreign patent applications, including in Australia, Canada, China, Europe, Great Britain, Hong Kong, India, Japan, Korea, Mexico and Brazil, and 20 Patent Cooperation Treaty ("PCT") patent applications.

The patent portfolios for our genome editing systems as of September 30, 2023 are summarized below.

Our type II CRISPR systems are protected by two issued U.S. patents with composition of matter claims covering genome editing systems using Type II nucleases, four pending U.S. non-provisional patent applications with composition of matter claims covering genome editing systems using Type II nucleases and methods of using them, and one pending U.S. provisional patent application with composition of matter claims covering genome editing systems using Type II nucleases and methods of using them. Our type II CRISPR systems are also protected by three issued foreign patents with composition of matter claims covering genome editing systems using Type II nucleases, including in Great Britain, Australia and Mexico, 25 pending foreign patent applications with composition of matter claims covering genome editing systems using Type II nucleases and methods of using them, including in Australia, Canada, China, Europe, Great Britain, Hong Kong, India, Japan, Korea, Mexico, and Brazil, and two PCT patent applications with composition of matter claims covering genome editing systems using Type II nucleases and methods of using them. The aforementioned issued US patents will expire on February 14, 2040, and the issued foreign patents will expire on February 14, 2040. If issued, the aforementioned patent applications are expected to expire between February 14, 2040 and May 6, 2041.

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Our type V CRISPR systems are protected by one issued U.S. patent and two pending U.S. non-provisional patent applications with composition of matter claims covering genome editing systems using Type V nucleases and one pending U.S. provisional patent application with composition of matter claims covering genome editing systems using Type V nucleases and methods of using them. Our type V CRISPR systems are also protected by two issued foreign patents with composition of matter claims covering genome editing systems using Type V nucleases, including in Great Britain and Hong Kong, 11 pending foreign patent applications with composition of matter claims covering genome editing systems using Type V nucleases and methods of using them, including in Australia, Brazil, Canada, China, Europe, Great Britain, Hong Kong, India, Japan, South Korea, and Mexico, and two PCT patent applications with composition of matter claims covering genome editing systems using Type V nucleases and methods of using them. If issued, the aforementioned patent applications are expected to expire between March 6, 2041 and July 29, 2043. The aforementioned issued foreign patents will expire on March 6, 2041.

Our base editor systems are protected by four pending U.S. non-provisional patent applications with composition of matter claims covering genome editing systems using nucleases and base editors and methods of using them, and two pending U.S. provisional patent applications with composition of matter claims covering genome editing systems using nucleases and base editors and methods of using them. Our base editor systems are also protected by 12 pending foreign patent applications with composition of matter claims covering genome editing systems using nucleases and base editors and methods of using them, including in Australia, Canada, China, Europe, Great Britain, Hong Kong, India, Japan, Korea, Mexico, and Brazil, and one PCT patent applications with composition of matter claims covering genome editing systems using nucleases and base editors and methods of using them. If issued, the aforementioned patent applications are expected to expire on September 10, 2041.

Our CAST systems are protected by two pending U.S. non-provisional patent applications with composition of matter claims covering genome editing systems using nucleases in combination with either recombinases or transposases and methods of using them, and one pending U.S. provisional patent application with composition of matter claims covering genome editing systems using nucleases in combination with either recombinases or transposases and methods of using them. Our CAST systems are also protected by 20 pending foreign patent applications with composition of matter claims covering genome editing systems using nucleases in combination with either recombinases or transposases and methods of using them, including in Australia, Brazil, Canada, China, Europe, Great Britain, Hong Kong, India, Japan, South Korea, and Mexico, and two PCT patent applications with composition of matter claims covering genome editing systems using nucleases in combination with either recombinases or transposases and methods of using them. If issued, the aforementioned patent applications are expected to expire between August 23, 2041 and March 23, 2043.

Our Cas chimera systems are protected by one pending U.S. non-provisional patent application with composition of matter claims covering genome editing systems using chimeric nucleases and methods of using them. Our Cas chimera systems are also protected by one issued foreign patent in Great Britain and ten pending foreign patent applications, including in Australia, Brazil, Canada, China, Europe, India, Japan, South Korea, Mexico and Hong Kong with composition of matter claims covering genome editing systems using chimeric nucleases, one PCT patent application with composition of matter claims covering genome editing systems using chimeric nucleases and two PCT patent applications with composition of matter claims covering genome editing systems using chimeric nucleases and methods of using them. If issued, the aforementioned patent applications are expected to expire on January 21, 2042.

Our SMART nuclease systems are protected by two pending U.S. non-provisional patent applications with composition of matter claims covering genome editing systems using small nucleases, and one pending U.S. provisional patent application with composition of matter covering genome editing systems using small nucleases and methods of using them. Our SMART nuclease systems are also protected by 10 pending foreign

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patent applications with composition of matter covering genome editing systems using small nucleases and methods of using them, including in Australia, Canada, China, Europe, Great Britain, Hong Kong, India, Japan, Korea, and Mexico, and two PCT patent applications with composition of matter claims covering genome editing systems using small nucleases and methods of using them. If issued, the aforementioned patent applications are expected to expire on March 31, 2040.

We cannot predict whether the patent applications we pursue or may license in the future will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide any protection from competitors. Even if our pending patent applications are granted as issued patents, those patents, as well as any patents we may license in the future from third parties now or in the future, may be challenged, circumvented or invalidated by third parties. Consequently, we may not obtain or maintain adequate patent protection for any of our programs and genome editing systems.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. In the United States, the patent term of a patent may be extended by patent term adjustment, which compensates the patent owner for patent office delays. Additionally, in the United States, patents that cover an FDA-approved drug or biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug or biologic is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug or biologic may be extended and only those claims covering the approved drug or biologic, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in European Member States and other foreign jurisdictions to extend the term of a patent that covers an approved drug or biologic. In the future, if our investigational gene therapies receive FDA approval, we expect to apply for patent term extensions where applicable on patents covering those products. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the U.S. Patent and Trademark Office ("USPTO") in the United States, will agree with our assessment of whether these extensions should be granted, and if granted, the length of these extensions.

Our intellectual property is critical to our business and we strive to protect it through a variety of approaches, including by obtaining and maintaining patent protection in various countries for our genome editing technology and other inventions that are important to our business.

Trademarks

As of September 30, 2023, we own the trademark registrations for Metagenomi in the United States.

Trade Secrets and Proprietary Information

In addition to our reliance on patent protection for our inventions, investigational gene therapies and research programs, we also rely on trade secrets, know-how, confidentiality agreements and continuing technological innovation to develop and maintain our competitive position. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees, advisors and consultants, these agreements may be breached and we may not have adequate remedies for any breach. In addition, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. As a result, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside

scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived of by the individual during the course of employment, and which relate to or are reasonably capable of being used in our current or planned business or research and development are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our technology by third parties. However, such agreements and policies may be breached and we may not have adequate remedies for such breaches. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

Government Regulation

In the United States, biological products, including gene therapy products, are subject to regulation under the Federal Food, Drug, and Cosmetic Act ("FD&C Act"), and the Public Health Service Act ("PHS Act"), and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the research, development, clinical trial, testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising, and other promotional practices involving biological products. Each clinical trial protocol for a gene therapy product must be reviewed by the FDA. FDA approval must be obtained before the marketing of biological products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

U.S. Biological Product Development Process

The process required by the FDA before a biological product candidate may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices ("GLPs"), unless justified and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an application for an IND, which must become effective before human clinical trials may begin;
- approval of the protocol and related documentation by an independent institutional review board ("IRB"), or ethics committee at each clinical trial site before each study may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practices ("GCPs"), and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;
- submission to the FDA of a biologics license application ("BLA"), for regulatory approval that includes sufficient evidence of establishing the safety, purity and potency of the proposed biological product for its intended indication, including from results of nonclinical testing and clinical trials;

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- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practices ("CGTPs"), for the use of human cellular and tissue products;
- potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA in accordance with any applicable expedited programs or designations;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- payment of user fees for FDA review of the BLA (unless a fee waiver applies); and
- FDA review and approval, or licensure, of the BLA.

Before testing any biological product candidate, including a gene therapy product, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product biological characteristics, chemistry, toxicity, and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

An IND is an exemption from the FD&C Act that allows an investigational product candidate to be shipped in interstate commerce for use in a clinical trial and a request for FDA authorization to administer such investigational product candidate to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved BLA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Information about certain clinical trials, including clinical trial results, must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for regulatory approval or licensing. In particular, such studies must be conducted in accordance with GCP, including review and approval by an independent ethics committee ("IEC"), and informed consent from subjects. The FDA must be able to validate the data through an onsite inspection, if deemed necessary by the FDA.

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An IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients. Some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee ("DSMB"). This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, certain human clinical trials involving recombinant or synthetic nucleic acid molecules may be subject to oversight of institutional biosafety committees ("IBCs"), as set forth in the National Institutes of Health ("NIH"), Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules ("NIH Guidelines"). Under the NIH Guidelines, recombinant and synthetic nucleic acids are defined as: (i) molecules that are constructed by joining nucleic acid molecules that can replicate in a living cell (i.e., recombinant nucleic acids); (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (i.e., synthetic nucleic acids); or (iii) molecules that result from the replication of those described in (i) or (ii). Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding for recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials typically are conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some biological product candidates for severe or life-threatening diseases, especially when the product candidate may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2. The biological product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product candidate and provide an adequate basis for approval and product labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial regulatory approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA generally recommends that sponsors of human gene therapy product candidates and genome editing product candidates observe subjects for potential gene therapy-related delayed adverse events for up to a 15-year period, including five years of annual examinations followed by ten years of annual queries, either by telephone or by questionnaire, of study subjects.

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During all phases of clinical development, the FDA requires extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected suspected adverse events, any findings from other studies, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. The FDA or the sponsor, acting on its own or based on a recommendation from the sponsor's data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product candidate has been associated with unexpected serious harm to patients.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the physical characteristics of the biological product candidate as well as finalize a process for manufacturing the product candidate in commercial quantities in accordance with cGMP. To help reduce the risk of the introduction of adventitious agents with use of biological product candidates, the PHS Act emphasizes the importance of manufacturing control for product candidates whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency, and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

After the completion of clinical trials of a biological product candidate, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Within 60 days following submission of the application, the FDA reviews a BLA to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. In most cases, the submission of a BLA is subject to a substantial application user fee, although the fee may be waived under certain circumstances. Under the performance goals and policies implemented by the FDA under the Prescription Drug User Fee Act ("PDUFA"), for original BLAs, the FDA targets ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification. This review typically takes 12 months from the date the BLA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

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Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, pure, and potent for its intended use, and whether the product is being manufactured in accordance with cGMP to ensure the continued safety, purity, and potency of such product. The FDA may refer applications for novel biological products or biological products that present difficult or novel questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy ("REMS"), is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA typically will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. For a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with the CGTPs. These are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue-based products ("HCT/PS"), which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the CGTP requirements is to ensure that cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/PS with the FDA and, when applicable, to evaluate donors through appropriate screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP, CGTP and GCP compliance, an applicant must incur significant expenditure of time, money, and effort in the areas of training, record keeping, production and quality control.

Under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA for a novel product (e.g., new active ingredient, new indication, etc.) must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the biological product will be manufactured, the FDA may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter will usually describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification, which may include the potential requirement for additional preclinical studies or clinical trials or additional manufacturing activities. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application or request an opportunity for a hearing. The

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FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, including to subpopulations of patients, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings precautions or interactions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post-marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product candidate intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product candidate available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product candidate that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full BLA, to market the same product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or if the holder of the orphan drug exclusivity cannot assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the product was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application fee. A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan drug designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Development and Review Programs

The FDA has various programs, including fast track designation, breakthrough therapy designation, priority review and accelerated approval, that are intended to expedite or simplify the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life-threatening diseases or conditions. These programs do not change the standards for approval but may help expedite the development or approval process. To be eligible for fast track designation, new drugs and biological products must be intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the product and the

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specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast track product at any time during the clinical development of the product. One benefit of fast track designation, for example, is that the FDA may consider for review sections of the marketing application for a product that has received fast track designation on a rolling basis before the complete application is submitted.

Under the FDA's breakthrough therapy program, products intended to treat a serious or life-threatening disease or condition may be eligible for the benefits of the fast track program when preliminary clinical evidence demonstrates that such product may have substantial improvement on one or more clinically significant endpoints over existing therapies. Additionally, the FDA will seek to ensure the sponsor of a breakthrough therapy product receives timely advice and interactive communications to help the sponsor design and conduct a development program as efficiently as possible.

Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Under priority review, the FDA's goal is to review an application in six months once it is filed, compared to ten months for a standard review.

Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on an intermediate clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials with due diligence, and, under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a product or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the agency, that all advertising and promotional materials intended for dissemination or publication be submitted to the agency for review, which could adversely affect the timing of the commercial launch of the product.

RMAT Designation

As part of the 21st Century Cures Act, Congress amended the FD&C Act to facilitate an efficient development program for and expedite review of regenerative medicine advanced therapies ("RMAT"), which include cell and gene therapies, therapeutic tissue engineering products, human cell and tissue products and combination products using any such therapies or products. RMAT do not include those HCT/Ps regulated solely under section 361 of the PHS Act and 21 CFR Part 1271. This program is intended to facilitate efficient development and expedite review of regenerative medicine therapies, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and qualify for RMAT designation. A drug sponsor may request that FDA designate a drug as a RMAT concurrently with or at any time after submission of an IND. FDA has 60 calendar days to determine whether the drug meets the criteria, including whether there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for a serious or life-threatening disease

or condition. A BLA for a regenerative medicine therapy that has received RMAT designation may be eligible for priority review or accelerated approval through use of surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. Benefits of RMAT designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine therapy with RMAT designation that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence from clinical trials, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. Like some of the FDA's other expedited development programs, RMAT designation does not change the standards for approval but may help expedite the development or approval process.

Rare Pediatric Disease Designation and Priority Review Vouchers

Under the FD&C Act, as amended, the FDA incentivizes the development of product candidates that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects 200,000 or more in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug or biologic for such disease or condition will be received from sales in the United States of such drug or biologic. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent marketing application after the date of approval of the rare pediatric disease drug product. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its BLA. A rare pediatric disease designation does not guarantee that a sponsor will receive a priority review voucher ("PRV") upon approval of its BLA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times. Congress has extended the PRV program until September 30, 2024, with the potential for PRVs to be granted until September 30, 2026.

Post-Approval Requirements

Maintaining substantial compliance with applicable federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. If there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement, which may require the development of additional data or preclinical studies and clinical trials. Such regulatory reviews can result in denial or modification of the planned changes, or requirements to conduct additional tests or evaluations that can substantially delay or increase the cost of the planned changes. The FDA may also impose a number of post-approval requirements as a condition of approval of a BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

Manufacturers of biological products are required to comply with applicable requirements in the cGMP, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products include reporting of cGMP deviations that may affect

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the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors or other stakeholders, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products, and those supplying products, ingredients, and components of them, are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some U.S. patents that may issue from our pending patent applications may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to

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the expiration of the patent. In addition, only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended, and a patent can only be extended once and only for a single product. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of the patents that may issue from our pending patent applications, if and as applicable, to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA. However, there can be no assurance that our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustments to the terms of any patents we may own or in-license in the future.

A biological product can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHS Act attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

A reference biological product is granted four- and 12-year exclusivity periods from the time of first licensure of the product. FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product, and FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until twelve years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

Regulation Outside of the United States

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing clinical studies, commercial sales, and distribution of our products. Most countries outside of the United States require that clinical trial applications be submitted to and approved by the local regulatory authority for each clinical study. In the European Union, for example, an application must be submitted to the

national competent authority and an independent ethics committee in each country in which we intend to conduct clinical trials, much like the FDA and IRB, respectively. Under the new Clinical Trials Regulation (EU) No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022, a single application is now made through the Clinical Trials Information System ("CTIS") for clinical trial authorization in up to 30 EU/EEA countries at the same time and with a single set of documentation.

The assessment of applications for clinical trials is divided into two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all European Union Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State concerned. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Member State concerned, however overall related timelines are defined by the Clinical Trials Regulation. The new Clinical Trials Regulation also provides for simplified reporting procedures for clinical trial sponsors.

In addition, whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of countries outside the United States before we can commence marketing of the product in those countries. The approval process and requirements vary from country to country, so the number and type of nonclinical, clinical, and manufacturing studies needed may differ, and the time may be longer or shorter than that required for FDA approval.

To obtain regulatory approval of our medicinal products under the European Union regulatory system, we are required to submit a marketing authorization application ("MAA"), to be assessed in the centralized procedure. The centralized procedure allows applicants to obtain a marketing authorization ("MA") that is valid throughout the European Union, and the additional Member States of the European Economic Area (Iceland, Liechtenstein and Norway) ("EEA"). It is compulsory for medicinal products manufactured using biotechnological processes, orphan medicinal products, advanced therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines) and human products containing a new active substance which is not authorized in the European Union and which is intended for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, auto-immune and other immune dysfunctions, viral diseases or diabetes. The centralized procedure is optional for any other products containing new active substances not authorized in the European Union or for products which constitute a significant therapeutic, scientific, or technical innovation or for which a centralized authorization is in the interests of patients at European Union level. When a company wishes to place on the market a medicinal product that is eligible for the centralized procedure, it sends an application directly to the European Medicines Agency ("EMA"), to be assessed by the Committee for Medicinal Products for Human Use ("CHMP"). The CHMP is responsible for conducting the assessment of whether a medicine meets the required quality, safety, and efficacy requirements, and whether the product has a positive risk/benefit profile. The procedure results in a European Commission decision, which is valid in all European Union Member States. The centralized procedure is as follows: full copies of the MAA are sent to a rapporteur and a co-rapporteur designated by the competent EMA scientific committee. They coordinate the EMA's scientific assessment of the medicinal product and prepare draft reports. Once the draft reports are prepared (other experts might be called upon for this purpose), they are sent to the CHMP, whose comments or objections are communicated to the applicant. The rapporteur is therefore the privileged interlocutor of the applicant and continues to play this role, even after the MA has been granted.

The rapporteur and co-rapporteur then assess the applicant's replies, submit them for discussion to the CHMP, and taking into account the conclusions of this debate, prepare a final assessment report. Once the evaluation is completed, the CHMP gives a favorable or unfavorable opinion as to whether to grant the authorization. When the opinion is favorable, it shall include the draft summary of product characteristics ("SmPC"), the

package leaflet, and the texts proposed for the various packaging materials. The time limit for the evaluation procedure is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). The EMA then has fifteen days to forward its opinion to the European Commission, which will make a binding decision on the grant of an MA within 67 days of the receipt of the CHMP opinion.

There are two other procedures in the European Union for the grant of an MA in multiple European Union Member States. The decentralized procedure provides for approval by one or more other, or Concerned Member States, of an assessment of an application performed by one Member State, known as the Reference Member State. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft SmPC, and draft labeling and package leaflet, to the Reference Member State and Concerned Member States. The Reference Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the Reference Member State's assessment report, each Concerned Member State must decide whether to approve the assessment report and related materials. If a Member State cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all Member States. Where a product has already been authorized for marketing in a European Union Member State, this national MA can be recognized in other Member States through the mutual recognition procedure.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as an orphan medicinal product if it is intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition that affects no more than five in 10,000 persons in the European Union when the application is made. In addition, orphan designation can be granted if the product is intended for a life threatening, seriously debilitating, or serious and chronic condition in the European Union and, without incentives, it is unlikely that sales of the product in the European Union would be sufficient to justify the necessary investment in its development. Orphan designation is only available if there is no other satisfactory method approved in the European Union of diagnosing, preventing, or treating the applicable orphan condition, or if such a method exists, the proposed orphan medicinal product will be of significant benefit to patients affected by such condition, as defined in Regulation (EC) 847/2000.

Orphan designation provides opportunities for fee reductions, protocol assistance, and access to the centralized procedure. Fee reductions are limited to the first year after an MA, except for small and medium enterprises. In addition, if a product which has an orphan designation subsequently receives a centralized MA for the indication for which it has such designation, the product is entitled to orphan market exclusivity, which means the EMA may not approve any other application to market a similar medicinal product for the same indication for a period of ten years. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The exclusivity period may be reduced to six years if, at the end of the fifth year, it is shown that the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, an MA may be granted to a similar medicinal product for the same indication at any time if:

- the second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior;
- the MA holder of the authorized product consents to a second orphan medicinal product application; or
- the MA holder of the authorized product cannot supply enough orphan medicinal product.

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A pediatric investigation plan ("PIP"), in the European Union is aimed at ensuring that the necessary data are obtained to support the authorization of a medicine for children, through studies in children. All applications for MAs for new medicines have to include the results of studies as described in an agreed PIP, unless the medicine is exempt because of a deferral or waiver. This requirement also applies when an MA holder wants to add a new indication, pharmaceutical form, or route of administration for a medicine that is already authorized and covered by intellectual property rights. Several rewards and incentives for the development of pediatric medicines for children are available in the European Union. Medicines authorized across the European Union with the results of studies from a PIP included in the product information are eligible for an extension of their supplementary protection certificate ("SPC") by six months (provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires). This is the case even when the studies' results are negative. For orphan medicinal products, the incentive is an additional two years of market exclusivity. Scientific advice and protocol assistance at the EMA are free of charge for questions relating to the development of pediatric medicines. Medicines developed specifically for children that are already authorized but are not protected by a patent or supplementary protection certificate are eligible for a pediatric-use MA ("PUMA"). If a PUMA is granted, the product will benefit from ten years of market protection as an incentive.

In March 2016, the EMA launched an initiative, the PRiority Medicines ("PRIME") scheme, to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIME scheme is intended to encourage development of products in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies on the basis of compelling non-clinical data and tolerability data from initial clinical trials. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated MAA assessment once a dossier has been submitted. Importantly, once a candidate medicine has been selected for the PRIME scheme, a dedicated contact and rapporteur from the CHMP or from the Committee for Advanced Therapies ("CAT") are appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting with the CHMP/CAT rapporteur initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies. PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

The aforementioned European Union rules are generally applicable in the EEA.

The United Kingdom left the European Union on January 31, 2020, and the United Kingdom and the European Union have concluded a trade and cooperation agreement ("TCA") which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021.

The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not provide for wholesale mutual recognition of United Kingdom and European Union pharmaceutical regulations. At present, Great Britain has implemented European Union legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended). Except in respect of the new European Union Clinical Trials Regulation, the regulatory regime in Great Britain therefore largely aligns with current European Union medicines regulations, however it is possible that these regimes will diverge more significantly in future now that Great Britain's regulatory system is independent from the European Union and the TCA does not provide for mutual recognition of United Kingdom and European Union pharmaceutical

legislation. However, notwithstanding that there is no wholesale recognition of European Union pharmaceutical legislation under the TCA, under a new framework mentioned below which will be put in place by the Medicines and Healthcare products Regulatory Agency ("MHRA"), the United Kingdom's medicines regulator, from January 1, 2024, the MHRA has stated that it will take into account decisions on the approval of Mas from the EMA (and certain other regulators) when considering an application for a Great Britain MA.

On February 27, 2023, the United Kingdom government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the United Kingdom. In particular, the MHRA will be responsible for approving all medicinal products destined for the United Kingdom market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single United Kingdom-wide MA will be granted by the MHRA for all medicinal products to be sold in the United Kingdom, enabling products to be sold in a single pack and under a single authorization throughout the United Kingdom. The Windsor Framework was approved by the European Union-United Kingdom Joint Committee on March 24, 2023, so the United Kingdom government and the European Union will enact legislative measures to bring it into law.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure and new routes of evaluation for novel products and biotechnological products. All existing European Union Mas for centrally authorized products were automatically converted (grandfathered) into United Kingdom Mas free of charge on January 1, 2021. For a period of three years from January 1, 2021, the MHRA may rely on a decision taken by the European Commission on the approval of a new MA in the centralized procedure, in order to more quickly grant a new Great Britain MA. A separate application will, however, still be required. On January 24, 2023, the MHRA announced that a new international recognition framework will be put in place from January 1, 2024, which will have regard to decisions on the approval of Mas made by the EMA and certain other regulators when determining an application for a new Great Britain MA. There is now no pre-MA orphan designation in Great Britain. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding MAA. The criteria are essentially the same, but have been tailored for the Great Britain market, i.e., the prevalence of the condition in Great Britain (rather than the European Union) must not be more than five in 10,000. Should an orphan designation be granted, the period of market exclusivity will be set from the date of first approval of the product in Great Britain.

Other Healthcare Laws and Compliance Requirements

Other Healthcare Laws

Biotechnology companies are subject to additional healthcare laws in the jurisdictions in which they conduct their business that may constrain the financial arrangements and relationships through which we research, as well as, in the future sell, market and distribute any products for which we obtain regulatory approval. Such laws include, without limitation, state and federal patient data privacy and security laws, federal and state anti-kickback laws, physician-self referral laws, false claims and transparency laws and regulations with respect to drug pricing and payments and other transfers of value made to physicians and other health care providers, and similar healthcare laws and regulations in the EU and other jurisdictions. Violations of any of such laws or any other governmental regulations that apply may result in significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations to resolve allegations of noncompliance, and exclusion from participation in federal and state healthcare programs and imprisonment.

Coverage and Reimbursement

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. These third-party payors are increasingly reducing coverage and reimbursement for medical products, drugs and services. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

The U.S. government, state legislatures and foreign governments have also continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic (or biosimilar) products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Healthcare Reform

In the United States, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, each as amended, collectively known as the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year.

Additionally, President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. There has also been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation. The Inflation Reduction Act of 2022 ("IRA"), includes several provisions that impact the pharmaceutical industry, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries to \$2,000 starting in 2025; impose new manufacturer financial liability on certain drugs under Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for drug prices that increase faster than inflation; and delay until January 1, 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The effects of the IRA on our business and the healthcare industry in general is not yet known.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could impact the amounts that federal and state governments and other third-party payors will pay for healthcare products and services.

Data Privacy & Security

Numerous state, federal and foreign laws govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. As our operations and business grow, we may become subject to or affected by U.S. federal and state laws and regulations, including the Health Information Portability and Accountability Act of 1996, and its implementing regulations, as amended ("HIPAA"), that govern the collection, use, disclosure, and protection of health-related and other personal information. In California the California Consumer Protection Act ("CCPA"), which went into effect on January 1, 2020 and was amended effective January 1, 2023, establishes a new privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. While clinical trial data and information governed by HIPAA are currently exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope. Other states, including Virginia (effective January 1, 2023), Colorado (effective July 1, 2023), Connecticut (effective July 1, 2023), and Utah (effective December 31, 2023) have passed privacy legislation and more states may do so in the future, including Iowa, where the Iowa state legislature passed a comprehensive privacy legislation on March 15, 2023. State and non-U.S. laws, including for example the EU General Data Protection Regulation, also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Employees and Human Capital Resources

As of September 30, 2023, we had 223 full-time employees, of which 74 have M.D. or Ph.D. degrees. Within our workforce, 187 employees are engaged in research and development and 36 are engaged in business development, finance, legal, and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase shareholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Facilities

Our corporate headquarters is located in Emeryville, California, where we lease and occupy approximately 23,851 square feet of laboratory and office space at 1545 Park Avenue, Emeryville, California 94608. The current term of our lease expires in February 2031. The company also leases approximately 23,155 square feet of office space at 1485 Park Avenue, Emeryville, California 94608 and subleases approximately 75,662 square feet of combined office, research and laboratory space at 5959 Horton Street, Emeryville, California 94608.

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We believe that our facilities are adequate for our current needs and for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space. We believe that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

Legal proceedings

From time to time, we may become involved in legal proceedings arising from the ordinary course of business. We record a liability for such matters when it is probable that future losses will be incurred and that such losses can be reasonably estimated. Significant judgment by us is required to determine both probability and the estimated amount. Our management is currently not aware of any legal matters that could have a material adverse effect on our financial position, results of operations or cash flows.

MANAGEMENT

The following table sets forth information about our executive officers and directors as of the date of this prospectus.

Name	Age	Position(s)
<i>Executive Officers</i>		
Brian C. Thomas, Ph.D.	55	Chief Executive Officer
Jian Irish, Ph.D., MBA	60	President and Chief Operating Officer
Pamela Wapnick	58	Chief Financial Officer
Sarah Noonberg, M.D., Ph.D.	56	Chief Medical Officer
Simon Harnest, M.Sc	37	Chief Investment Officer and Senior Vice President of Strategy
Luis G. Borges, Ph.D.	61	Chief Scientific Officer
Simren Delaney, Ph.D., LL.M	38	Vice President of Legal
<i>Non-Employee Directors</i>		
Juergen Eckhardt, M.D., MBA	57	Director
Sebastián Bernales, Ph.D.	48	Director
Risa Stack, Ph.D. ⁽¹⁾	55	Director
Willard Dere, M.D.	69	Director
Santhosh Palani, Ph.D. ⁽²⁾	41	Director
<i>Other Key Personnel</i>		
Christopher T. Brown, Ph.D.	35	Vice President of Discovery
Michael Conway, MBA, CPA	48	Vice President of Finance
Alan Brooks, Ph.D.	58	Senior Vice President of Preclinical

⁽¹⁾ Dr. Stack has notified us that she will resign from our board of directors effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

⁽²⁾ Dr. Palani has notified us that he will resign from our board of directors effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

The following is a biographical summary of the experience of our executive officers and directors. There are no family relationships among any of our executive officers or directors.

Executive Officers

Brian C. Thomas, Ph.D., is our founder and has served as our Chief Executive Officer since September 2016. Since December 2022, Dr. Thomas has served as Chairman of the Board of Directors of Haya Therapeutics, Inc. Previously, from 2001 to 2017, Dr. Thomas served as a program manager at University of California, Berkeley. From 1999 to 2001, Dr. Thomas served as a lead bioinformatics scientist at EOS Biotechnology (now PDL, Inc.). Dr. Thomas received his B.Sc. in cellular biology and his Ph.D. in biochemistry from University of Kansas and completed his post-doctoral research in computational biology at University of California, Berkeley.

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Our board of directors believes that Dr. Thomas is qualified to serve as a director because of his considerable academic and research expertise, as well as his expansive knowledge about our Company as our founder and Chief Executive Officer.

Jian Irish, Ph.D., MBA, has served as our President since November 2021 and our Chief Operating Officer since January 2021. Prior to joining us, Dr. Irish held positions as Senior Vice President, Global Head of Manufacturing and Senior Vice President of Supply Chain at Kite Pharma (now a subsidiary of Gilead) from September 2016 to December 2020. Dr. Irish served as Interim Chief Operating Officer of Affini-T Therapeutics from January 2021 to January 2022. Dr. Irish also served as Interim Chief Technology Officer and a board member for Fosun Kite, a joint venture between Kite Pharma and Fosun Pharma, from October 2018 to April 2020. From December 2014 to August 2016, Dr. Irish held positions as Vice President of Biologics Supply, Outsourcing, Partnerships, and External Manufacturing and Vice President of Product Development at Sanofi. From January 2000 to September 2014, Dr. Irish held various leadership positions at Amgen in operations, including Executive Director of JAPAC Supply, Executive Director of Contract Manufacturing, Officer for Kirin-Amgen JV, and Global Operations Team Leader. Dr. Irish currently serves as an advisor to Ori Biotech, ORCA Biosystems, and ViTToria Biotherapeutics. Dr. Irish received a B.S. in chemical engineering from East China University of Science and Technology, an M.S. and Ph.D. in pharmaceutical sciences from Chiba University, and an MBA from University of California, Los Angeles, Anderson School of Management.

Pamela Wapnick, has served as our Chief Financial Officer since September 2023. Prior to joining us, Ms. Wapnick served as Chief Financial Officer of Diality Inc. from June 2022 to September 2023, as Chief Financial Officer of Capsida Biotherapeutics from November 2019 to June 2022, and as Chief Financial Officer of Graybug Vision from December 2017 to October 2019. Prior to these roles, Ms. Wapnick served as Chief Financial Officer of True North Therapeutics and held various positions at Amgen Inc. (Nasdaq: AMGN). Ms. Wapnick received her B.A. in economics from Wellesley College and her MBA in finance from Columbia Business School.

Sarah Noonberg, M.D., Ph.D., has served as our Chief Medical Officer since January 2023. Prior to joining us, Dr. Noonberg served as the Chief Medical Officer at Maze Therapeutics, Nohla Therapeutics and Prothena Corporation plc (Nasdaq: PRTA) from July 2020 to September 2022, May 2018 to May 2019 and May 2017 to May 2018, respectively. Dr. Noonberg served as Group Vice President and Head of Global Clinical Development at BioMarin Pharmaceuticals Inc. (Nasdaq: BMRN) from August 2015 to March 2017. From May 2007 to August 2015, she held several positions at Medivation, Inc., a biopharmaceutical company, culminating in the position of Senior Vice President of Early Development. Dr. Noonberg currently serves on the board of directors of Neurogene Inc. (Nasdaq: NGNE) and Marinus Pharmaceuticals (Nasdaq: MRNS). She has also previously served on the board of directors of Neoleukin Therapeutics (Nasdaq: NLTX) and Protagonist Therapeutics, Inc. (Nasdaq: PTGX) from August 2019 to December 2023 and December 2017 to May 2023, respectively. Dr. Noonberg received her B.S. in engineering at Dartmouth College, her Ph.D. in bioengineering from the University of California, Berkeley and her M.D. from the University of California, San Francisco. Dr. Noonberg is a board-certified internist and completed her residency at Johns Hopkins Hospital.

Simon Harnest, M.Sc., has served as our Chief Investment Officer and Senior Vice President of Strategy since July 2021. Prior to joining us, Mr. Harnest held various positions, most recently as Chief Investment Officer and Senior Vice President of Strategy and Finance, at Cellectis Inc. from April 2015 to July 2021. Mr. Harnest also served as Vice President, Corporate Strategy and Finance at Calyxt from March 2016 to December 2019. Mr. Harnest received his B.Sc in economics from University of Westminster, Westminster Business School and his M.Sc in social studies from London School of Economics, London.

Luis G. Borges, Ph.D., has served as our Chief Scientific Officer since joining Metagenomi in August 2023. Prior to this, Dr. Borges served as Chief Scientific Officer at Century Therapeutics, Inc. (Nasdaq: IPSC) from April 2019 to July 2023 and as Chief Scientific Officer at Cell Medica Limited from August 2017 to March 2019. Dr. Borges

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served in positions of increasing responsibility at Five Prime Therapeutics, Inc. from 2014 to 2017, most recently as Senior Vice President of Research. Dr. Borges also served in positions of increasing responsibility at Amgen Inc. (Nasdaq: AMGN) from 2002 to 2014. Dr. Borges received a B.S. in marine biology from the University of Lisbon and a Ph.D. in pathology from the University of Washington.

Simren Delaney, Ph.D., LL.M., has served as our Vice President of Legal since February 2020 and previously served as our Chief of Staff from January 2022 to December 2022. Prior to joining us, Dr. Delaney was an associate at Wilson Sonsini Goodrich & Rosati from October 2016 to February 2020. Dr. Delaney received her B.Sc in science, LL.B. and Ph.D. in organic chemistry from Deakin University, and her LL.M. from University of California, College of the Law, San Francisco.

Non-Employee Directors

Juergen Eckhardt, M.D., MBA, has served as our Chairman of the Board of Directors since September 2020. Dr. Eckhardt has served as Head of Leaps at Bayer AG since February 2019 and previously served as Head of Venture Investments from September 2016 to February 2019. He currently serves on the boards of Dewpoint Therapeutics, Khoris Biosciences, Oerth Bio, and a few other private biotechnology companies and foundations. Previously, Dr. Eckhardt served as a management consultant and Associate Partner at McKinsey & Co. and a member of McKinsey's Healthcare Leadership Team from 1994 to 2002. Dr. Eckhardt received his M.D. from the University of Basel and his MBA from INSEAD in Fontainebleau, France.

Our board of directors believes that Dr. Eckhardt is qualified to serve as a director because of his extensive experience in strategy, finance, leadership and drug development.

Sebastián Bernales, Ph.D., has served on our board of directors since December 2020 and previously served as a Director of Metagenomi, Inc. from September 2016 to April 2020. Dr. Bernales has been a General Partner at Humboldt Fund since February 2020 and has been a Venture Partner at DROIA Ventures since August 2020. He has served as the Chief Executive Officer of Praxis Biotech LLC since July 2016 and a member of Sake Holdings LLC since May 2020. Dr. Bernales is also the founder of Merken Biotech. Dr. Bernales is a member of the boards of directors of PhageLab, Botanical Solutions, Momentum, Vedra, Alesta, and a few other private biotechnology companies and foundations. Dr. Bernales currently serves as an advisor to NotCo, Levita Magnetics, and Leyden Labs. From 2007 to 2016, Dr. Bernales worked at Medivation Inc., culminating in the position of Vice President of Discovery Biology. He received his B.S. from Catholic University in Chile and his Ph.D. in cell biology at the University of California in San Francisco. He completed his postdoctoral training at the University of California in San Francisco.

Our board of directors believes that Dr. Bernales is qualified to serve as a director because of his significant experience in biotechnology industry.

Risa Stack, Ph.D., has served on our board of directors since April 2022. Dr. Stack has been a Partner at The Production Board since May 2022. Previously, Dr. Stack was a Venture Partner at RA Capital from September 2020 to March 2022. Dr. Stack was a founder and served as Chairperson of Menlo Microsystems from December 2016 to September 2018, and served as a General Manager at General Electric from January 2013 to September 2018. Dr. Stack was a Partner at Kleiner Perkins from June 2003 to December 2012. Before joining Kleiner Perkins, Dr. Stack was a Principal at JP Morgan Partners from September 1996 to May 2003. Dr. Stack currently serves on the Board of Directors of COPD Foundation. Dr. Stack received her B.S. in genetics and development from the University of Illinois and her Ph.D. in immunology from the University of Chicago. Dr. Stack was a member of the second class of Kauffman Fellows.

Our board of directors believes that Dr. Stack is qualified to serve as a director because of her extensive investment experience, knowledge of financial markets and expertise in personalized medicine, therapeutics and platform technology companies.

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Dr. Stack has notified us that she will resign from our board of directors effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

Willard Dere, M.D., has served on our board of directors since August 2021. Dr. Dere currently serves as Chief Advisor and Chief Medical Officer at Angitia since July 2022, and on the board of directors of BioMarin, Seres and Mersana. He also serves on the Scientific Advisory Boards of Surrozen, AliveGen and Heranova Lifesciences. Dr. Dere served as a Professor of Internal Medicine from November 2014 to July 2022 at the University of Utah School of Medicine, and is currently Professor Emeritus, a position he has held since July 2022. Dr. Dere also served as Associate Vice President for Research, Co-Director of The Center for Genomic Medicine and Co-Director of the Utah Clinical and Translational Science Institute at the University of Utah Health Sciences Center during this time period. Before joining the University of Utah, Dr. Dere held various positions at Amgen, Inc., including Senior Vice President of Global Development and Corporate, then International Chief Medical Officer, from July 2003 to October 2014. From 1989 to 2003, Dr. Dere held multiple positions in clinical research, and regulatory affairs and safety at Eli Lilly and Company. He was also an assistant professor from 1989 to 1999 and a clinical associate professor from 1999 to 2009 at the Indiana University School of Medicine. Dr. Dere received his B.A. in history, zoology and M.D. from the University of California, Davis; he completed his postdoctoral training at the University of Utah in internal medicine, and at the University of California, San Francisco in endocrinology and metabolism.

Our board of directors believes that Dr. Dere is qualified to serve as a director because of extensive experience in drug development, and as a board of directors member on several public companies.

Santhosh Palani, Ph.D., has served on our board of directors since January 2022. Dr. Palani is currently an investment partner at PFM Health Sciences since June 2020. He was a Principal at New Enterprise Associates from May 2018 to May 2020. From 2016 to 2018, Dr. Palani was a Vice President at Cowen and Company. He previously served as an Associate Director in Oncology Clinical Development at Pfizer from 2013 to 2016 and as a Scientist in Oncology Preclinical Development at Takeda Pharmaceuticals from 2012 to 2013. Dr. Palani currently serves on the Board of Directors of Turnstone Biologics. Dr. Palani received his B.S. and M.S. in chemical engineering from the University of Madras and Texas A&M University, respectively. Dr. Palani received his Ph.D. in Bioengineering from the University of Pennsylvania and completed his postdoctoral work in biochemistry and molecular biophysics at Columbia University. Dr. Palani is a CFA® Charterholder.

Our board of directors believes that Dr. Palani is qualified to serve as a director because of his strong financial background and significant industry experience in the fields of internal medicine and endocrinology.

Dr. Palani has notified us that he will resign from our board of directors effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

Other Key Personnel

Alan Brooks, Ph.D., has served as our Senior Vice President of Preclinical since January 2023 and previously served as our Director of Preclinical and Vice President of Preclinical from November 2019 to January 2023. Prior to joining us, Dr. Brooks served as a principal scientist at Casebia Therapeutics from August 2017 to August 2019. From October 2007 to August 2017, Dr. Brooks held various positions at Bayer AG, including scientist, senior scientist and principal scientist. Dr. Brooks received his B.Sc in biological sciences from University of Leicester, UK and his Ph.D. in molecular and developmental biology from University of Warwick, UK. He completed his postdoctoral fellowship at the Gladstone Institute/University of California, San Francisco.

Michael Conway, MBA, CPA, has served as our Vice President of Finance since March 2022. Prior to joining us, Mr. Conway served as Senior Director of Financial Planning and Analysis and Vice President of Finance at

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Adamas Pharmaceuticals, Inc. from March 2016 to December 2021, where he was responsible for leading the accounting and financial planning and analysis functions. Mr. Conway received his BBA in management information systems from University of Notre Dame, his MBA from University of Michigan, Ross School of Business, and is a certified public accountant in the state of California.

Christopher T. Brown, Ph.D., has served as our Vice President of Discovery since January 2023 and previously served as our Senior Bioinformatics Scientist, Director of Discovery and Senior Director of Discovery from September 2018 to December 2022. Prior to joining us, Dr. Brown conducted post-doctoral research at the University of California, Berkeley from January 2017 to August 2018. He received his B.Sc in microbiology from the University of Florida and his Ph.D. in plant and microbial biology from the University of California, Berkeley.

Board Composition

Our board of managers currently consists of 6 members, each of whom is a member pursuant to the board composition provisions of our current certificate of incorporation and agreements with our stockholders, which agreements are described in the section of this prospectus entitled "Certain Relationships and Related Person Transactions." These board composition provisions will terminate upon the closing of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nomination and corporate governance committee and our board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees. Our nomination and corporate governance committee's and our board of directors' priority in selecting board members is identification of persons who will further the interests of our stockholders through their established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape, professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until their earlier resignation or removal. Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Staggered Board

In accordance with the terms of our amended and restated certificate of incorporation and our amended and restated bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three staggered classes of directors and each director will be assigned to one of the three classes. At each annual meeting of the stockholders, one class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2024 for Class I directors, 2025 for Class II directors and 2026 for Class III directors.

- Our Class I directors will be ;
- Our Class II directors will be ; and
- Our Class III directors will be .

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering will provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Director Independence

We have applied to list our common stock on the Nasdaq Global Select Market. Under the Nasdaq listing rules, independent directors must comprise a majority of a listed company's board of directors within twelve months from the date of listing. In addition, the Nasdaq listing rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and governance committees be independent within twelve months from the date of listing. Audit committee members must also satisfy additional independence criteria, including those set forth in Rule 10A-3 under the Securities Exchange Act of 1934 (the "Exchange Act"), and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under Nasdaq listing rules, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3 under the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee: (i) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries, other than compensation for board service; or (ii) be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board of directors must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In 2024, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that all members of our board of directors, except [REDACTED], are independent directors, including for purposes of Nasdaq and the SEC rules. In making that determination, our board of directors considered the relationships that each director has with us and all other facts and circumstances the board of directors deemed relevant in determining independence, including the potential deemed beneficial ownership of our capital stock by each director, including non-employee directors that are affiliated with certain of our major stockholders. Upon the completion of this offering, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of Nasdaq and the rules and regulations of the SEC. There are no family relationships among any of our executive officers and directors.

We intend to adopt a policy, subject to and effective upon the effectiveness of the registration statement of which this prospectus forms a part, that outlines a process for our securityholders to send communications to the board of directors.

Board Committees

Our board of directors will establish an audit committee, a compensation committee and a nomination and corporate governance committee, each of which will operate pursuant to a charter to be adopted by our board of directors and will be effective upon the effectiveness of the registration statement of which this prospectus forms a part. We believe that the composition and functioning of all of our committees will comply with the applicable requirements of Nasdaq, the Sarbanes-Oxley Act of 2002 and SEC rules and regulations that will be applicable to us. We intend to comply with future requirements to the extent they become applicable to us.

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Following the consummation of this offering, the full text of our audit committee charter, compensation committee charter and nomination and corporate governance committee charter will be posted on the investor relations portion of our website at <https://www.metagenomi.co>. We do not incorporate the information contained on, or accessible through, our corporate website into this prospectus, and you should not consider it a part of this prospectus.

Audit Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our audit committee will consist of _____ and will be chaired by _____. The functions of the audit committee will include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

All members of our audit committee will meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Nasdaq listing rules. Our board of directors has determined that _____ qualifies as an "audit committee financial expert" within the meaning of applicable SEC regulations. In making this determination, our board of directors considered the nature and scope of experience that _____ has previously had with public reporting companies, including service as _____. Our board of directors has determined that all of the directors that will become members of our audit committee upon the effectiveness of the registration statement of which this prospectus forms a part satisfy the relevant independence requirements for service on the audit committee set forth in the rules of the SEC and the Nasdaq listing rules. Both our independent registered public accounting firm and management will periodically meet privately with our audit committee.

Compensation Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our compensation committee will consist of _____, and will be chaired by _____. The functions of the compensation committee will include:

- annually reviewing and recommending to the board of directors the corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and based on such evaluation (i) reviewing and determining the cash compensation of our Chief Executive Officer and (ii) reviewing and approving grants and awards to our Chief Executive Officer under equity-based plans;
- reviewing and approving the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable Nasdaq listing rules;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and recommending to the board of directors the compensation of our directors;
- preparing our compensation committee report if and when required by SEC rules;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis," if and when required, to be included in our annual proxy statement; and
- reviewing and approving the retention or termination of any consulting firm or outside advisor to assist in the evaluation of compensation matters.

Each member of our compensation committee will be a non-employee director, as defined in Rule 16b-3 promulgated under the Exchange Act, and an outside director, as defined pursuant to Section 162(m) of the Internal Revenue Code of 1986, as amended (the "Code").

Nominating and Corporate Governance Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our nominating and corporate governance committee will consist of _____ and will be chaired by _____. The functions of the nominating and corporate governance committee will include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;

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- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may from time to time establish other committees.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee is, or has at any time during the prior three years been, one of our officers or employees. None of our executive officers currently serve, or have in the past fiscal year served, as a member of the board of directors or compensation committee of any entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee.

Code of Business Conduct and Ethics

Our board of directors intends to adopt, subject to and effective upon the effectiveness of the registration statement of which this prospectus forms a part, a Code of Business Conduct and Ethics in connection with this offering. The Code of Business Conduct and Ethics will apply to all of our employees, officers (including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions), agents and representatives, including directors and consultants.

We intend to disclose future amendments to certain provisions of our Code of Business Conduct and Ethics and our Code of Ethics on our website identified below. Upon the completion of this offering, the full text of our Code of Business Conduct and Ethics and our Code of Ethics will be posted on our website at <https://www.Metagenomi.co>. The inclusion of our website address in this prospectus does not include or incorporate by reference the information on our website into this prospectus, and you should not consider that information a part of this prospectus.

Limitations on Liability and Indemnification Agreements

As permitted by Delaware law, provisions in our amended and restated certificate of incorporation and amended and restated bylaws, both of which will become effective upon the closing of this offering, limit or eliminate the personal liability of directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, a director exercise an informed business judgment based on all material information reasonably available to him or her. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any act related to unlawful stock repurchases, redemptions or other distributions or payments of dividends; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not limit or eliminate our rights or any stockholder's rights to seek non-monetary relief, such as injunctive relief or rescission. These provisions will not alter a director's liability under other laws, such as the federal securities laws or other state or federal laws. Our amended and restated certificate of incorporation that will become effective upon the closing of this offering also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

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As permitted by Delaware law, our amended and restated bylaws to be effective upon the consummation of this offering will provide that:

- we will indemnify our directors, officers, employees and other agents to the fullest extent permitted by law;
- we must advance expenses to our directors and officers, and may advance expenses to our employees and other agents, in connection with a legal proceeding to the fullest extent permitted by law; and
- the rights provided in our amended and restated bylaws are not exclusive.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director or officer, then the liability of our directors or officers will be so eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated bylaws will also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in connection with their services to us, regardless of whether our amended and restated bylaws permit such indemnification. We have obtained such insurance.

In addition to the indemnification that will be provided for in our amended and restated certificate of incorporation and amended and restated bylaws, we plan to enter into separate indemnification agreements with each of our directors and executive officers, which may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements may require us, among other things, to indemnify our directors and executive officers for some expenses, including attorneys' fees, expenses, judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of his service as one of our directors or executive officers or any other company or enterprise to which the person provides services at our request. We believe that these provisions and agreements are necessary to attract and retain qualified individuals to serve as directors and executive officers.

This description of the indemnification provisions of our amended and restated certificate of incorporation, our amended and restated bylaws and our indemnification agreements is qualified in its entirety by reference to these documents, each of which is attached as an exhibit to the registration statement of which this prospectus forms a part.

Insofar as indemnification for liabilities arising under the Securities Act, may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable.

There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

EXECUTIVE COMPENSATION

The following discussion contains forward looking statements that are based on our current plans, considerations, expectations and determinations regarding our future compensation programs. The actual amount and form of compensation and the compensation policies and practices that we adopt in the future may differ materially from currently planned programs as summarized in this discussion.

As an emerging growth company, we have opted to comply with the executive compensation disclosure rules applicable to “smaller reporting companies,” as such term is defined in the rules promulgated under the Securities Act. The compensation provided to our named executive officers for the fiscal year ended December 31, 2023 is detailed in the 2023 Summary Compensation Table and accompanying footnotes and narrative that follow. Our named executive officers for the fiscal year ended December 31, 2023 are:

- Brian C. Thomas, Ph.D., our Chief Executive Officer;
- Jian Irish, Ph.D., MBA, our President and Chief Operating Officer; and
- Sarah Noonberg, M.D., Ph.D., our Chief Medical Officer.

To date, the compensation of our named executive officers has consisted of a combination of base salary, cash bonuses and equity awards in the form of profits interests, as described below. Our named executive officers, like all of our full-time employees, are eligible to participate in our health and welfare benefit plans. As we transition from a private company to a publicly traded company, we intend to evaluate our compensation values and philosophy and compensation plans and arrangements as circumstances require.

2023 Summary Compensation Table

The following table shows the total compensation earned by, or paid to, our named executive officers for services rendered to us in all capacities during the years listed below.

Name and Principal Position	Year	Salary (\$)	Bonus(1) (\$)	Stock Awards(2) (\$)	Non-Equity Incentive Plan Compensation(3) (\$)	All Other Compensation(4) (\$)	Total (\$)
Brian C. Thomas, Ph.D. <i>Chief Executive Officer</i>	2023	516,667	—	6,966,519	—	34,069	7,517,255
	2022	500,000	100,000	1,223,129	318,250	15,250	2,156,629
Jian Irish, Ph.D., MBA <i>President and Chief Operating Officer</i>	2023	465,000	—	1,783,211	—	18,368	2,266,579
	2022	450,000	52,000	313,084	260,354	8,990	1,084,428
Sarah Noonberg, M.D., Ph.D. <i>Chief Medical Officer</i>	2023	388,231	—	1,447,782	—	18,300	1,854,313

(1) The amounts reported in this column reflect one time special bonuses paid to Dr. Thomas and Dr. Irish for performance during the fiscal year ended December 31, 2022.

(2) The amounts reported in this column represent the aggregate grant date fair value of profits interests granted to the named executive officers during the applicable fiscal year, as calculated in accordance with Financial Accounting Standards Board (“FASB”), Accounting Standards Codification (“ASC”), Topic 718. Such grant date value does not take into account any estimated forfeitures related to service-based vesting conditions. On July 31, 2023, as a result of the amendment to the LLC agreement to include a “catch-up” feature, the Company remeasured the fair value of its profits interests as required under ASC 718 resulting in increases to the originally calculated fair values, in the aggregate amount of \$4,564,081. The assumptions used in the grant date fair value of the awards in this column are described in Note 11 – Profits interest plan to our unaudited consolidated financial statements as of September 30, 2023 and for the nine months ended September 30, 2022 and 2023. These assumptions are included elsewhere in this prospectus. These awards are described in more detail under “Narrative Disclosure to Summary Compensation Table – Equity-Based Compensation” below.

(3) The amounts reported represent annual bonuses under our annual cash bonus program based on achievement of company performance and individual performance during the applicable fiscal year. Such amounts for fiscal year 2023 have not yet been determined, but are expected to be determined and paid in the first quarter of 2024 and will be reported at such time as required by SEC rules.

(4) The amounts reported for fiscal year 2023 reflect an employer matching contribution on the employee’s behalf under our 401(k) plan. The amount for Dr. Thomas also includes \$18,102 related to reimbursement of certain legal fees incurred by Dr. Thomas in connection with the negotiation of his employment contract with the Company.

Narrative Disclosure to Summary Compensation Table

2023 Base Salaries

Our named executive officers each receive a base salary to compensate them for services rendered to our Company. The base salary payable to each named executive officer is intended to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities. Base salaries may be adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience. The base salary for Dr. Thomas was adjusted effective as of March 1, 2023 from \$500,000 to \$520,000. The base salary for Dr. Irish was adjusted effective March 1, 2023 from \$450,000 to \$468,000. Dr. Noonberg joined the Company January 30, 2023 and her base salary was not adjusted during the calendar year 2023. As of December 31, 2023, the base salaries for Dr. Thomas, Dr. Irish, and Dr. Noonberg were \$520,000, \$468,000, and \$420,000, respectively.

2023 Cash Bonuses

For the fiscal year ended December 31, 2023, each of the named executive officers is eligible to earn an annual cash bonus determined by our board of directors in its sole discretion, based on achievement of certain individual and corporate performance goals, relating primarily to research and development goals, clinical milestones, business development and organizational goals. The target annual bonus for each of our named executive officers for the fiscal year ended December 31, 2023 was equal to the percentage of the executive's respective annual base salary specified below:

Name	Target Bonus Percentage
Brian C. Thomas	50%
Jian Irish	45%
Sarah Noonberg	40%

The annual cash bonuses earned by each named executive office for the fiscal year ended December 31, 2023 have not yet been determined, but are expected to be determined and paid in the first quarter of 2024 and will be reported at such time as required by SEC rules.

Equity-Based Compensation

Although we do not yet have a formal policy with respect to the grant of equity incentive awards to our executive officers, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our unitholders. We have granted our named executive officers profits interests under our 2019 Equity Incentive Plan (the "2019 Plan"). These profits interests are subject to time-based vesting conditions and are intended to be treated as "profits interests" for U.S. federal income tax purposes.

In connection with the Reorganization, profits interests will be exchanged for shares of common stock and restricted common stock of Metagenomi, Inc.

For additional information regarding outstanding equity awards held by our named executive officers as of December 31, 2023, see the "Outstanding Equity Awards at 2023 Fiscal Year End" table below.

Perquisites/Personal Benefits

Perquisites or other personal benefits are not a significant component of our executive compensation program. Accordingly, we do not provide significant perquisites or other personal benefits to our executive officers, including our named executive officers.

401(k) Plan

We maintain a retirement savings plan ("401(k) plan") that is intended to qualify for favorable tax treatment under Section 401(a) of the Code and contains a cash or deferred feature that is intended to meet the requirements of Section 401(k) of the Code. U.S. employees are generally eligible to participate in the 401(k) plan, subject to certain criteria. Participants may make pre-tax and certain after-tax (Roth) salary deferral contributions to the plan from their eligible earnings up to the statutorily prescribed annual limit under the Code. Participants who are 50 years of age or older may contribute additional amounts based on the statutory limits for catch-up contributions. Participant contributions are held in trust as required by law. We provide employer matching contributions of 100% on the first 5% of participant's compensation contributed to our 401(k) plan.

Outstanding Equity Awards at 2023 Fiscal Year End

The following table lists all outstanding equity awards held by our named executive officers as of December 31, 2023.

Name	Grant Date	Vesting Commencement Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$)(2)	Stock Awards(1)	
					Equity Incentive Plan awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)	Equity Incentive Plan awards: Market Value of Unearned Shares, Units or Other Rights That Have Not Vested (\$)
Brian C. Thomas, Ph.D.(3) <i>Chief Executive Officer</i>	11/2/21 5/26/22 6/26/23	11/1/21 1/21/22 1/20/23	60,604 338,094 590,035			
Jian Irish, Ph.D., MBA(4) <i>President and Chief Operating Officer</i>	1/26/21 11/2/21 5/26/22 6/26/23	1/5/21 11/1/21 1/21/22 1/20/23	130,164 212,110 86,542 151,030			
Sarah Noonberg, M.D.,Ph.D. <i>Chief Medical Officer</i>	3/24/23	1/30/23	200,000			

- (1) All awards in this table consist of profits interests granted under the 2019 Plan that are intended to qualify as "profits interests" for U.S. tax purposes. They do not require the payment of an exercise price and will only obtain value as value of the underlying security rises above its grant date value, which is referred to as the "Threshold Amount." The profits interests vest as follows: 25% vest on the one year anniversary of the vesting commencement date; and then the remaining 75% of the total profits interests vest in substantially equal amounts on each monthly anniversary of the vesting commencement date thereafter, until fully vested on the fourth anniversary of the vesting commencement date, based upon the participant's continued service on each applicable vesting date.
- (2) Represents the fair market value of profits interests that were unvested as of December 31, 2023. The fair market value assumes an initial public offering prior of \$ per share, which is the estimated midpoint of the price range set forth on the cover page of this prospectus.
- (3) Awards held by Dr. Thomas are subject to certain acceleration provisions, as summarized below under "Employment Arrangements in Place Prior to the Offering for Named Executive Officers."
- (4) Awards held by Dr. Irish are subject to certain acceleration provisions, as summarized below under "Employment Arrangements in Place Prior to the Offering for Named Executive Officers."

Executive Compensation Arrangements

We have entered into offer letters and/or employment agreements with each of our named executive officers. Each offer letter or employment agreement provides for “at-will” employment and the compensation and benefits described below.

Employment Arrangements in Place Prior to The Offering for Named Executive Officers

Brian C. Thomas

On March 20, 2023, the Company executed an executive employment agreement with Dr. Thomas (the “Thomas Employment Agreement”), for the position of Chief Executive Officer. The Thomas Employment Agreement provides for Dr. Thomas’s at-will employment. Dr. Thomas’s current base salary is \$520,000 and he is eligible to receive an annual bonus with an annual target amount of 50% of his annual base salary. Dr. Thomas is eligible to participate in the employee benefit plans available to our employees, subject to the terms of such plans.

Upon termination of Dr. Thomas’s employment by us without Cause or his resignation for Good Reason outside of the Change in Control Period, as such terms are defined in the Thomas Employment Agreement, subject to (i) Dr. Thomas resigning from all positions, (ii) signing a general release of claims in favor of the Company and (iii) not breaching any of the post-employment covenants and contractual obligations to the Company, Dr. Thomas shall be entitled to (A) a lump sum payment equal to nine (9) months of his then current base salary and pro-rated target bonus, based on the number of days he was employed in such year, divided by 365, payable within sixty (60) days following his termination, and (B) if Dr. Thomas was participating in the Company’s group health plan immediately prior to the termination date, a monthly cash payment for nine (9) months in an amount equal to Dr. Thomas’s and his eligible dependents monthly COBRA premium. In addition, and subject to the same conditions, upon a termination by us without Cause or his resignation for Good Reason during the Change in Control Period, he shall be entitled to (A) a lump sum payment equal to twelve (12) months of his then current base salary and pro-rated target bonus, based on the number of days he was employed in such year, divided by 365, payable within sixty (60) days following his termination, (B) if Dr. Thomas was participating in the Company’s group health plan immediately prior to the termination date, a monthly cash payment for twelve (12) months in an amount equal to Dr. Thomas’s and his eligible dependents monthly COBRA premium, and (C) full acceleration of his then outstanding and unvested equity awards.

Jian Irish

On January 19, 2021, the Company executed an offer letter with Dr. Irish (the “Irish Offer Letter”), for the position of Chief Operations Officer. The Irish Offer Letter provides for Dr. Irish’s at-will employment. Dr. Irish was promoted to President and Chief Operating Officer effective November 1, 2021. Dr. Irish’s current base salary is \$468,000 and she is eligible to receive an annual bonus with an annual target amount of 45% of her annual salary. Dr. Irish is eligible to participate in the employee benefit plans available to our employees, subject to the terms of such plans. The Irish Offer Letter provides for Dr. Irish’s eligibility to receive a grant of profits interests under the 2019 Plan, which will be subject to full acceleration upon the occurrence of a Change of Control (as defined in the Irish Offer Letter).

Upon a termination of Dr. Irish’s agreement by us without Cause, or her resignation for Good Reason, as such terms are defined in the Irish Offer Letter, she will be eligible to receive six (6) months of base salary, pro-rated annual bonus, and six (6) months vesting acceleration.

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Dr. Irish entered into an Employee Invention Assignment and Confidentiality Agreement that contains various restrictive covenants, including non-solicitation provisions that apply during her employment and for a period of twelve months thereafter.

Sarah Noonberg

On January 30, 2023, the Company executed an offer letter with Dr. Noonberg (the "Noonberg Offer Letter"), for the position of Chief Medical Officer. The Noonberg Offer Letter provides for Dr. Noonberg's at-will employment. Dr. Noonberg's current base salary is \$420,000 and she is eligible to receive an annual bonus with an annual target amount of 40% of her base salary, the target amount for 2023 is prorated given Dr. Noonberg's employment start date in January 2023. Dr. Noonberg is eligible to participate in the employee benefit plans available to our employees, subject to the terms of such plans. The Noonberg Offer Letter provides for Dr. Noonberg's eligibility to receive a grant of profits interests under the 2019 Plan.

Dr. Noonberg entered into an Employee Invention Assignment and Confidentiality Agreement that contains various restrictive covenants, including non-solicitation provisions that apply during his employment and for a period of twelve months thereafter.

Employee Benefit and Equity Compensation Plans

2019 Equity Incentive Plan

The 2019 Plan was initially approved by the board of managers of the Company in March 2019. The 2019 Plan provided for the grant of profits interests, restricted common units, options to purchase common units and restricted equity units to selected employees, officers, directors and consultants of the Company. The total number of common units available for grant and issuance under the 2019 Plan is 14,604,165 common units. Common units that are (i) cancelled, forfeited, settled in cash, used to pay withholding obligations or that expire by their terms at any time and (ii) that are reacquired by the Company pursuant to a right of first refusal or repurchase by the Company, will again become available for issuance under the 2019 Plan. Our board of managers administers the 2019 Plan and has the authority to take any action necessary or advisable for the administration of the 2019 Plan. Our board has the right and discretion to grant awards under the 2019 Plan to participants.

Common units designated as profits interests by the board of managers are intended to meet the definition of a "profits interests" set forth in IRS Revenue Procedures 93-27 and 2001-43. Accordingly, such profits interests do not give the holder a share of the proceeds if the Company's assets were sold at fair market value and the proceeds of such disposition were distributed in a complete liquidation of the Company immediately after the date of grant, but give the holder a right to share in the appreciation in the value of a common unit from the date of receipt to the future, as determined by the applicable provisions of the Company's operating agreement in effect immediately prior to the Reorganization.

Upon a liquidation event, as defined in the 2019 Plan, the board of managers may in its sole discretion, cancel all outstanding and unexercised awards, including profits interests and other unvested awards, in each case, without consideration, as of the date of such liquidation event.

The 2019 Plan will terminate automatically ten (10) years after the later of (i) the date when the board adopted the 2019 Plan and (ii) the date when the board approved the most recent increase in the number of common units reserved under the 2019 Plan, which was also subsequently approved by the members of the company. The board of managers may amend, suspend or terminate the 2019 Plan at any time and for any reason; provided, that any amendment that would materially adversely impact an award shall only be effective with respect to such award if the holder thereof so consents prior to the date of the amendment.

2024 Stock Option and Incentive Plan

Our 2024 Plan was adopted by our board of directors on _____, 2024, approved by our stockholders on _____, 2024, and will become effective upon the date immediately preceding the date on which the registration statement of which this prospectus is part is declared effective by the SEC. The 2024 Plan will replace the 2019 Plan. The 2024 Plan provides flexibility to our compensation committee to use various equity-based incentive awards as compensation tools to motivate our workforce.

We have initially reserved _____ shares of our common stock for the issuance of awards under the 2024 Plan, or the Initial Limit. The 2024 Plan provides that the number of shares reserved and available for issuance under the 2024 Plan will automatically increase on January 1, 2025 and each January 1 thereafter, by _____ 5% of the outstanding number of shares of our common stock on the immediately preceding December 31, or such lesser number of shares as determined by our compensation committee, or the Annual Increase. The number of shares reserved under the 2024 Plan is subject to adjustment in the event of a stock split, stock dividend, or other change in our capitalization.

The shares we issue under the 2024 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards under the 2024 Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without the issuance of stock, or are otherwise terminated (other than by exercise) will be added back to the shares of common stock available for issuance under the 2024 Plan.

The maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the Initial Limit, cumulatively increased on January 1, 2025 and on each January 1 thereafter by the lesser of the Annual Increase for such year or _____ shares of common stock.

The grant date fair value of all awards made under our 2024 Plan and all other cash compensation paid by us to any non-employee director in any calendar year for services as a non-employee director shall not exceed \$800,000; provided, however, that such amount shall be \$1,000,000 for the calendar year in which the applicable non-employee director is initially elected or appointed to the board of directors.

The 2024 Plan will be administered by our compensation committee. Our compensation committee has the full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted and the number of shares subject to such awards, to make any combination of awards to participants, to accelerate at any time the exercisability or vesting of any award, to impose any limitations and/or vesting conditions on each award, and to determine the specific terms and conditions of each award, subject to the provisions of the 2024 Plan. Persons eligible to participate in the 2024 Plan will be those full or part-time officers, employees, non-employee directors, and consultants as selected from time to time by our compensation committee in its discretion.

The 2024 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant unless the option (i) is granted pursuant to a transaction described in, and in a manner consistent with, Section 424(a) of the Code, (ii) is granted to an individual who is not subject to United States income tax, or (iii) complies with Section 409A of the Code. The term of each option will be fixed by our compensation committee and may not exceed ten years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

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Our compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of our common stock on the date of grant unless the stock appreciation right (i) is granted pursuant to a transaction described in, and in a manner consistent with, Section 424(a) of the Code, (ii) is granted to an individual who is not subject to United States income tax, or (iii) complies with Section 409A of the Code. The term of each stock appreciation right will be fixed by our compensation committee and may not exceed ten years from the date of grant. Our compensation committee will determine at what time or times each stock appreciation right may be exercised.

Our compensation committee may award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2024 Plan. Unrestricted stock may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee may grant dividend equivalent rights to participants that entitle the recipient to receive credits for dividends that would be paid if the recipient had held a specified number of shares of our common stock.

Our compensation committee may grant cash bonuses under the 2024 Plan to participants, subject to the achievement of certain performance goals.

The 2024 Plan provides that upon the effectiveness of a "sale event," as defined in the 2024 Plan, an acquirer or successor entity may assume, continue, or substitute outstanding awards under the 2024 Plan. To the extent that awards granted under the 2024 Plan are not assumed, continued, or substituted by the successor entity, upon the effective time of the sale event, such awards shall terminate. In such case, except as may be otherwise provided in the relevant award agreement, all awards with time-based vesting, conditions, or restrictions shall become fully vested and exercisable or nonforfeitable as of the effective time of the sale event, and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and exercisable or nonforfeitable in connection with a sale event in the administrator's discretion or to the extent specified in the relevant award agreement. In the event of such termination, individuals holding options and stock appreciation rights (i) may be permitted to exercise such options and stock appreciation rights (to the extent exercisable) within a specified period of time prior to the sale event or (ii) we may make or provide for a payment, in cash or in kind, to participants holding vested and exercisable options and stock appreciation rights equal to the difference between the per share consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights. In addition, we may make or provide for a payment, in cash or in kind, to participants holding other vested awards.

Our board of directors may amend or discontinue the 2024 Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose but no such action may materially adversely affect rights under an award without the holder's consent. Certain amendments to the 2024 Plan require the approval of our stockholders. The administrator of the 2024 Plan is specifically authorized to exercise its discretion to reduce the exercise price of outstanding stock options and stock appreciation rights or effect the repricing of such awards through cancellation and re-grants without stockholder consent. No awards may be granted under the 2024 Plan after the date that is ten years from the effective date of the 2024 Plan. No awards have been made under the 2024 Plan prior to the date of this prospectus.

2024 Employee Stock Purchase Plan

The 2024 Employee Stock Purchase Plan, or 2024 ESPP, was adopted by our board of directors on _____, 2024, approved by our stockholders on _____, 2024, and will become effective on the date immediately preceding the date on which the registration statement of which this prospectus is part is declared effective by the SEC. The 2024 ESPP includes two components: a Code Section 423 Component, or the 423 Component, and a non-Code Section 423 Component, or the Non-423 Component. The 423 Component is intended to qualify as an "employee stock purchase plan" under Section 423 of the Code. Under the Non-423 Component, which does not qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code, options will be granted pursuant to rules adopted by the administrator of the ESPP designed to achieve tax or securities laws, or other objectives for eligible employees. The 2024 ESPP initially reserves and authorizes the issuance of up to a total of shares of common stock to participating employees. The 2024 ESPP provides that the number of shares reserved and available for issuance will automatically increase on January 1, 2025 and each January thereafter through January 1, 2034, by the least of (i) shares of common stock, (ii) 1% of the outstanding number of shares of our common stock on the immediately preceding December 31, or (iii) such number of shares of common stock as determined by the administrator of the 2023 ESPP. The number of shares reserved under the 2024 ESPP is subject to adjustment in the event of a stock split, stock dividend, or other change in our capitalization.

All individuals classified as employees on the payroll records of the Company or a "designated company," as defined in the 2024 ESPP, as of the first day of the applicable offering period, or the Offering Date, are eligible to participate in the 2024 ESPP; provided that the administrator of the ESPP may determine, in advance of any offering period, that employees are eligible only if, as of the Offering Date, they (a) are customarily employed by us or a Designated Company for more than 20 hours a week, (b) are customarily employed by us or a Designated Company for more than five months per calendar year, and/or (c) have completed at least six months of employment (or other such period as determined by the administrator of the 2024 ESPP, provided such service requirement does not exceed two years of employment). No person who owns or holds, or as a result of participation in the 2024 ESPP would own or hold, common stock or options to purchase common stock, that together equal 5% or more of total outstanding common stock is entitled to participate in the 2024 ESPP. No employee may exercise an option granted under the 2024 ESPP that permits the employee to purchase common stock having a value of more than \$25,000 (determined using the fair market value of our common stock at the time such option is granted) in any calendar year.

We may make one or more offerings each year to our employees to purchase shares under the 2024 ESPP. The first offering period under the ESPP will begin and end on the dates determined by the administrator of the 2024 ESPP. Shares are purchased on the last business day of each offering period. Each eligible employee will be able to elect to participate in any offering by submitting an enrollment form by such deadline as is established by the administrator of the 2024 ESPP.

Each employee who is a participant in the 2024 ESPP will be able to purchase shares by authorizing payroll deductions of up to 15% of such employee's eligible compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, such employee's accumulated payroll deductions will be used to purchase shares of common stock on the last business day of the offering period at a price equal to 85% of the fair market value of the shares on the first business day or the last business day of the offering period, whichever is lower, provided that no more than a number of shares of common stock determined by dividing \$25,000 by the fair market value of the common stock on the first day of the offering may be purchased by any one employee during any offering period.

In the case of and subject to the consummation of a "sale event," as defined in the 2024 ESPP, the administrator of the 2024 ESPP, in its discretion, and on such terms and conditions as it deems appropriate, is

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authorized to take any one or more of the following actions under the 2024 ESPP or with respect to any right under the 2024 ESPP or to facilitate such transactions or events: (a) provide for either (i) termination of any outstanding option in exchange for an amount of cash, if any, equal to the amount that would have been obtained upon the exercise of such option had such option been currently exercisable or (ii) the replacement of such outstanding option with other options or property selected by the administrator of the 2024 ESPP in its sole discretion; (b) provide that the outstanding options under the 2024 ESPP shall be assumed by the successor or survivor corporation, or a parent or subsidiary thereof, or shall be substituted for similar options covering the stock of the successor or survivor corporation, or a parent or subsidiary thereof, with appropriate adjustments as to the number and kind of shares and prices; (c) make adjustments in the number and type of shares of common stock (or other securities or property) subject to outstanding options under the 2024 ESPP and/or in terms and conditions of outstanding options and options that may be granted in the future; (d) provide that the offering with respect to which an option relates will be shortened by setting a new exercise date on which such offering period will end; and (e) provide that all outstanding options shall terminate without being exercised and all amounts in the accounts of participants shall be promptly refunded.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under the 2024 ESPP will terminate upon voluntary withdrawal from the 2024 ESPP or when the employee ceases employment with us for any reason.

The 2024 ESPP may be terminated or amended by our board of directors at any time. An amendment that increases the number of shares of common stock authorized under the 2024 ESPP and certain other amendments will require the approval of our stockholders.

Senior Executive Cash Incentive Bonus Plan

On _____, 2024, our board of directors adopted the Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan. The Bonus Plan provides for cash bonus payments based upon Company and individual performance targets established by our compensation committee. The payment targets will be related to financial and operational measures or objectives with respect to our company, or the Corporate Performance Goals, as well as individual performance objectives.

Our compensation committee may select Corporate Performance Goals from among the following: research, pre-clinical, non-clinical, developmental, publication, clinical or regulatory milestones; scientific or technological advances; R&D capabilities; cash flow (including, but not limited to, operating cash flow and free cash flow); revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of the Company's common stock; economic value-added; acquisitions or strategic transactions; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of the Company's common stock; bookings, new bookings or renewals; sales or market shares; number of customers, number of new customers or customer references; operating income and/or net annual recurring revenue; or any other performance goal selected by the Compensation Committee, any of which may be (A) measured in absolute terms or compared to any incremental increase, (B) measured in terms of growth, (C) compared to another company or companies or to results of a peer group, (D) measured against the market as a whole and/or as compared to applicable market indices and/or (E) measured on a pre-tax or post-tax basis (if applicable). Further, any Corporate Performance Goals may be used to measure the performance of the Company as a whole or a business unit or other segment of the Company, or one or more product lines or specific markets. The Corporate Performance Goals may differ from Covered Executive to Covered Executive and from performance period to performance period.

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Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The Corporate Performance Goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the corporate performance goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period, but not later than 74 days after the end of the fiscal year in which such performance period ends. Subject to any rights contained in any agreement between the executive officer and us, an executive officer shall be required to be employed by us on the bonus payment date to be eligible to receive a bonus payment under the Bonus Plan. The Bonus Plan also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion.

DIRECTOR COMPENSATION

2023 Director Compensation Table

The following table presents the total compensation paid by the Company to non-employee members of our board of managers during the fiscal year ended December 31, 2023. Other than as set forth in the table and described more fully below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of the members of our board of managers in 2023 for their services as members of the board of managers. Dr. Thomas, our Chief Executive Officer, does not receive any compensation from the Company for his service on our board of managers. See the section titled "Executive Compensation" for more information on the compensation paid to or earned by Dr. Thomas as an employee for year ended December 31, 2023.

Name	Year	Fees Earned or Paid in Cash (\$)	All Other Compensation(3) (\$)	Total (\$)
Sebastián Bernales	2023	—	—	—
Willard H. Dere(1)(2)	2023	30,000	19,201	49,201
Juergen Eckhardt	2023	—	—	—
Santosh Palani	2023	—	—	—
Risa Stack(1)	2023	—	—	—

(1) Dr. Dere and Dr. Stack each held 21,080 and 10,540 unvested profits interests granted under the 2019 Plan as of December 31, 2023. None of our other non-employee directors held any equity awards as of December 31, 2023.

(2) We entered into an Independent Manager Offer Letter with Dr. Dere, pursuant to which he is eligible to receive cash compensation of \$30,000 for each calendar year for his services to our board of managers.

(3) The amounts reported in this column represent amounts paid to Dr. Dere in 2023 under his consulting agreement with the Company, which terminated in July 2023.

Non-Employee Director Compensation Policy

In connection with this offering, we intend to adopt a new non-employee director compensation policy that will become effective as of the completion of this offering and will be designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors.

Under the policy, our non-employee directors will be eligible to receive cash retainers (which will be payable quarterly in arrears and prorated for partial years of service) and equity awards as set forth below:

Annual Retainer for Board Membership

for general availability and participation in meetings and conference calls of our Board of Directors \$

Additional Annual Retainer for Committee Membership

Audit Committee Chairperson:	\$
Audit Committee member (other than Chairperson):	\$
Compensation Committee Chairperson:	\$
Compensation Committee member (other than Chairperson):	\$
Nominating and Corporate Governance Committee Chairperson:	\$
Nominating and Corporate Governance Committee member (other than Chairperson):	\$
Science & Technology Committee Chairperson:	\$
Science & Technology Committee member (other than Chairperson):	\$

Additional Retainer for Non-Executive Chairperson of the Board:

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In addition, our policy will provide that, upon initial election or appointment to our board of directors, each new non-employee director will be granted a one-time grant of a non-statutory stock option to purchase shares of our common stock equivalent to \$ _____ in value on the date of such director's election or appointment to the board of directors (the "Director Initial Grant"). The Director Initial Grant will vest subject to the non-employee director's continued services to the us. On the date of each annual meeting of stockholders of our company following the completion of this offering, each non-employee director who will continue as a non-employee director following such meeting will be granted an annual award of a non-statutory stock option to purchase shares of common stock equivalent to \$ _____ in value (the "Director Annual Grant"). The Director Annual Grant will vest in full on the earlier of the one-year anniversary of the grant date or on the date of our next annual meeting of stockholders, subject to the non-employee director's continued services to us. Such awards are subject to full acceleration vesting upon the sale of our company.

The aggregate amount of compensation, including both equity compensation and cash compensation, paid to any non-employee director for service as a non-employee director in a calendar year period will not exceed \$ _____ in the first calendar year such individual becomes a non-employee director and \$ _____ in any other calendar year.

We will reimburse all reasonable out-of-pocket expenses incurred by directors for their attendance at meetings of our board of directors or any committee thereof.

Employee directors will receive no additional compensation for their service as a director.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following is a description of transactions or series of transactions since January 1, 2020, to which we were or will be a party, in which:

- the amount involved in the transaction exceeds, or will exceed, \$120,000; and
- in which any of our executive officers, directors or holder of five percent or more of any class of our capital stock, including their immediate family members or affiliated entities, had or will have a direct or indirect material interest.

Compensation arrangements for our named executive officers and our directors are described elsewhere in this prospectus under “Executive Compensation” and “Director Compensation.”

Series A-4 and Series A-5 Preferred Unit Financings

From 2020 to 2021, we sold an aggregate of 9,861,297 Series A-4 and Series A-5 preferred units in multiple closings, consisting of (i) 8,280,360 Series A-4 preferred units sold at a purchase price of \$4.84875 per unit for an aggregate amount of \$40.1 million and (ii) 1,580,937 Series A-5 preferred units sold at a purchase price of \$6.32536 per unit for an aggregate amount of \$10.0 million, for total aggregate proceeds of \$50.1 million. The following table summarizes purchases of our Series A-4 and Series A-5 preferred units as described above by related persons:

Stockholder	Numbers of Series A-4/Series A-5 preferred units	Total purchase price
Bayer HealthCare LLC(1)	2,062,387	\$9,999,998.97
Humboldt Fund I, LP(2)	2,062,387	\$9,999,998.97
Entities affiliated with RA Capital(3)	1,580,937	\$9,999,995.67
Sake Holdings LLC(4)	929,067	\$4,504,813.62
Entities affiliated with Sozo Ventures(5)	710,907	\$3,447,010.33

- (1) Juergen Eckhardt, a manager on our board of managers, is an affiliate of Bayer Consumer Care AG, which is an affiliate of Bayer HealthCare LLC. Bayer HealthCare LLC holds more than 5 percent of our voting securities.
- (2) Sebastián Bernales, a manager on our board of managers, is an affiliate of Humboldt Fund. Humboldt Fund I, LP is an affiliated fund of Humboldt Fund. Humboldt Fund I, LP holds more than 5 percent of our voting securities.
- (3) Represents 1,343,796 Series A-5 preferred units purchased by RA Capital Healthcare Fund, L.P. and 237,141 Series A-5 preferred units purchased by RA Capital Nexus Fund II, L.P. Entities affiliated with RA Capital collectively hold more than 5 percent of our voting securities.
- (4) Sebastián Bernales, a manager on our board of managers, is an affiliate of Sake Holdings LLC. Sake Holdings LLC holds more than 5 percent of our voting securities.
- (5) Represents 319,908 Series A-4 preferred units purchased by Sozo Ventures – Truebridge Fund II, L.P. and 390,999 Series A-4 preferred units purchased by Sozo Ventures II-S, L.P. Entities affiliated with Sozo Ventures collectively hold more than 5 percent of our voting securities.

Series B Preferred Unit Financing

In 2022 and 2023, we sold an aggregate of 22,162,743 Series B and Series B-1 preferred units in multiple closings, consisting of (i) 15,054,263 Series B preferred units, which includes (a) 12,446,876 Series B preferred units sold at a purchase price of \$11.64951 per unit and (b) 2,607,387 Series B preferred units which converted pursuant to a promissory note with a principal amount of \$30.0 million and accrued interest of \$0.4 million

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between the Company and ModernaTX, Inc., for an aggregate amount of \$175.4 million and (ii) 7,108,480 Series B-1 preferred units sold at a purchase price of \$14.06770 per unit for an aggregate amount of \$100.0 million, for total aggregate proceeds of \$275.4 million. The following table summarizes purchases of our Series B and Series B-1 preferred units by related persons:

Stockholder	Numbers of Series B/Series B-1 preferred units	Total purchase price
ModernaTX, Inc.(1)	2,982,800	\$ 35,655,978.39
Bayer HealthCare LLC(2)	1,920,757	\$ 24,529,689.59
Humboldt Fund I, LP(3)	1,250,532	\$ 14,825,929.39
Entities affiliated with RA Capital(4)	1,000,575	\$ 12,000,002.54
Entities affiliated with Sozo Ventures(5)	816,063	\$ 10,442,237.49

- (1) Represents 2,607,387 Series B preferred units and 375,413 Series B-1 preferred units. ModernaTX, Inc. holds more than 5 percent of our voting securities.
- (2) Represents 1,030,086 Series B preferred units and 890,671 Series B-1 preferred units. Juergen Eckhardt, a manager on our board of managers, is an affiliate of Bayer Consumer Care AG, which is an affiliate of Bayer HealthCare LLC. Bayer HealthCare LLC holds more than 5 percent of our voting securities.
- (3) Represents 1,143,905 Series B preferred units and 106,627 Series B-1 preferred units. Sebastián Bernales, a manager on our board of managers, is an affiliate of Humboldt Fund. Humboldt Fund I, LP is an affiliated fund of Humboldt Fund. Humboldt Fund I, LP holds more than 5 percent of our voting securities.
- (4) Represents 600,883 Series B preferred units and 99,519 Series B-1 preferred units purchased by RA Capital Healthcare Fund, L.P., and 257,522 Series B preferred units and 42,651 Series B-1 preferred units purchased by RA Capital Nexus Fund II, L.P. Entities affiliated with RA Capital collectively hold more than 5 percent of our voting securities.
- (5) Represents 429,202 Series B preferred units and 386,861 Series B-1 preferred units purchased by Sozo Ventures III, L.P. Entities affiliated with Sozo Ventures collectively hold more than 5 percent of our voting securities.

Agreements with Unitholders

In connection with our Series A-1, Series A-2, Series A-3, Series A-4, and Series A-5 preferred unit financings and our Series B preferred unit financing, we entered into investors' rights, voting and right of first refusal and co-sale agreements containing registration rights, information rights, voting rights and rights of first refusal, among other things, with certain holders of our preferred units and certain holders of our common units. These unitholder agreements will terminate upon the closing of this offering, except for the registration rights granted under our investors' rights agreement, as more fully described in "Description of Capital Stock—Registration Rights."

In connection with our Series A-4 preferred unit financing, we entered into a side letter agreement (the "Humboldt Side Letter"), with Humboldt Fund I, LP ("Humboldt"). Pursuant to the Humboldt Side Letter, we represented and warranted to Humboldt regarding certain U.S. tax status and CFIUS matters. We agreed that Humboldt would not be deemed a competitor for any purpose under the financing agreements. We further agreed to use commercially reasonable efforts to comply with all record-keeping, reporting and other reasonable request necessary to comply with any applicable U.S. tax law or to allow Humboldt and its Partners to comply with the applicable provisions of U.S. tax law with respect to the direct or indirect ownership of the Company.

In connection with our Series A-5 preferred unit financing, we entered into a side letter agreement (the "RA Capital Side Letter"), with RA Capital Healthcare Fund, L.P. and RA Capital Nexus Fund II, L.P. (collectively, "RA Capital"). Pursuant to the RA Capital Side Letter, RA Capital is entitled to purchase a portion of the preferred units in the

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event that the Company sells preferred units in a single transaction or series of related transactions following the date of the RA Capital Side Letter, primarily for capital raising purposes, with gross proceeds to the Company in excess of \$10,000,000. In addition, the Series A-5 preferred units held by RA Capital shall not be automatically converted into common units without the prior written approval of RA Capital, but shall remain subject to conversion immediately upon the closing of this offering.

We entered into a research and development master service agreement (the "Bayer R&D Agreement"), with Bayer Healthcare LLC ("Bayer"), in November 2019. Bayer was performing research and development services under the Bayer R&D Agreement in accordance with the statement of works agreed by the parties. Services under the Bayer R&D Agreement were completed as of December 31, 2020, and we accrued \$0.2 million in accrued expenses and other current liabilities as of December 31, 2020. We paid \$0.2 million to Bayer in February and March 2021 in connection with the Bayer R&D Agreement.

Convertible Promissory Note with Affini-T

In December 2020, we entered into a convertible promissory note agreement and a side letter with Affini-T Therapeutics, Inc. ("Affini-T"), a private biotechnology company. We paid cash of \$1.5 million as a principal amount of the promissory note with 6% annual interest and maturity in December 2021. The promissory note was convertible in Affini-T's next qualifying round of financing at a conversion price equal to the lesser of (i) 85% of the price per share paid by other investors (or 80% if the qualified financing occurs after June 24, 2021) or (ii) the price per share obtained by dividing \$30.0 million by the number of shares of common stock of Affini-T outstanding immediately prior to the qualified financing. In accordance with the side letter, we were engaged to perform the certain services for Affini-T. As a consideration for services, we received 1,867,300 shares of Affini-T common stock, of which 10% of such shares were vested at the issuance date and 90% of such shares were subject to forfeiture if no genome editing licensing agreement was finalized between us and Affini-T by October 31, 2021. Effective November 1, 2021, 1,653,570 common stock shares issued to us were forfeited and cancelled as the license agreement was not signed between the parties. When we entered into the convertible promissory note, our chief business officer at the time also served as chief executive officer of Affini-T. Our chief business officer departed the company in November 2021 and Affini-T was no longer a related party of the company as of December 31, 2021.

In March 2022, Affini-T closed a qualified round of financing, and the convertible promissory note and accrued interest were converted into 527,035 shares of Series A convertible preferred stock of Affini-T.

Equity Grants to Executive Officers

We have historically granted profits interests to our named executive officers as more fully described in the section entitled "Executive Compensation".

Indemnification Agreements

In connection with this offering, we intend to enter into new agreements to indemnify our directors and executive officers. These agreements will, among other things, require us to indemnify these individuals for certain expenses (including attorneys' fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our company or that person's status as a member of our board of directors to the maximum extent allowed under Delaware law.

Policies for Approval of Related Party Transactions

Our board of directors reviews and approves transactions with directors, officers, and holders of five percent or more of our voting securities and their affiliates, each a related party. Prior to this offering, the material facts as to the related party's relationship or interest in the transaction were disclosed to our board of directors prior to their consideration of such transaction, and the transaction was not considered approved by our board of directors unless a majority of the directors who are not interested in the transaction approved the transaction. Further, when stockholders are entitled to vote on a transaction with a related party, the material facts of the related party's relationship or interest in the transaction were disclosed to the stockholders, who must approve the transaction in good faith.

In connection with this offering, we expect to adopt a written related party transactions policy that will provide that such transactions must be approved by our audit committee. This policy will become effective on the date on which the registration statement of which this prospectus forms a part is declared effective by the SEC. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving "related party transactions," which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed \$120,000 and in which a related person has or will have a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director, or greater than 5 percent beneficial owner of our common stock, in each case since the beginning of the most recently completed year, and their immediate family members.

PRINCIPAL STOCKHOLDERS

The following table sets forth, as of September 30, 2023, information regarding the beneficial ownership of our common stock by:

- each person, or group of affiliated persons, who is known by us to be the beneficial owner of five percent or more of our outstanding common stock (on an as-converted to common stock basis);
- each of our directors;
- each of our named executive officers; and
- all of our current directors and executive officers as a group.

The information in the following table gives effect to the Reorganization and is calculated based on _____ shares of common stock deemed to be outstanding before this offering and _____ shares of common stock outstanding after this offering, assuming no exercise by the underwriters of their option to purchase additional shares of common stock. The number of shares outstanding is based on the number of shares of common stock outstanding (including _____ shares of unvested restricted common stock) as of September 30, 2023 as adjusted to give effect to:

- the conversion of _____ shares of our redeemable convertible preferred stock outstanding as of September 30, 2023 into an equivalent number of shares of our common stock, which will occur immediately prior to the completion of this offering; and
- the sale of _____ shares of common stock in this offering (assuming no exercise of the underwriters' option to purchase additional shares).

Each individual or entity shown on the table has furnished information with respect to beneficial ownership. Except as otherwise indicated below, the address of each officer, director and five percent stockholder listed below is c/o Metagenomi Technologies, LLC, 1545 Park Avenue, Emeryville, California 94608.

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We have determined beneficial ownership in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities as well as any shares of common stock that the person has the right to acquire within 60 days of September 30, 2023 through the exercise of stock options or other rights. These shares are deemed to be outstanding and beneficially owned by the person holding those options for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them.

	Shares of common stock beneficially owned	Percentage of shares beneficially owned	
		Before offering	After offering
5% or Greater Stockholders			
Bayer HealthCare LLC			
Humboldt Fund I, LP (1)			
ModernaTX, Inc.			
Sake Holdings LLC (2)			
Entities affiliated with Sozo Ventures			
Entities affiliated with RA Capital			
Directors, Named Executive Officers and Other Executive Officers			
Brian C. Thomas, Ph.D.			
Juergen Eckhardt, M.D., MBA			
Sebastián Bernales, Ph.D.			
Risa Stack, Ph.D.			
Willard Dere, M.D.			
Santhosh Palani, Ph.D.			
Jian Irish, Ph.D., MBA			
Simon Harnest, MSc			
All executive officers and directors as a group (12 persons)			

* Less than one percent.

(1) Consists of shares of redeemable convertible preferred stock held by Humboldt Fund I, LP. Humboldt Fund I, LP is solely managed by Humboldt Capital, LLC, which is in turn managed by Sebastian Bernales, Francisco Dopazo and Benjamin Quiroga. As a result, each such individual may be deemed to share voting and dispositive power with respect to the shares held by Humboldt Fund I, LP. Each of Mr. Bernales, Dopazo and Quiroga expressly disclaims beneficial ownership of the shares held by Humboldt Fund I, LP, except to the extent of his pecuniary interest in such shares. The address for Humboldt Fund I, LP is 477 Madison Ave., 6th Floor, New York, NY 10022.

(2) Consists of shares of redeemable convertible preferred stock held by Sake Holdings LLC. Sake Holdings LLC is managed by its board of directors which consists of Sebastian Bernales and Eduardo Ergas. As a result, each such individual may be deemed to share voting and dispositive power with respect to the shares held by Sake Holdings LLC. Each of Mr. Bernales and Mr. Ergas expressly disclaims beneficial ownership of the shares held by Sake Holdings LLC, except to the extent of his pecuniary interest in such shares. The address for Sake Holdings LLC is 1700 Owens Street, Suite 515, San Francisco, CA 94158.

DESCRIPTION OF CAPITAL STOCK

The following descriptions are summaries of the material terms of our amended and restated certificate of incorporation and amended and restated bylaws, which will be effective immediately upon the closing of this offering. The descriptions of the common stock and preferred stock give effect to changes to our capital structure, including the Reorganization, that will occur prior to the effectiveness of this registration statement. We refer in this section to our amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.

General

Upon completion of this offering, our authorized capital stock will consist of _____ shares of common stock, par value \$ _____ per share, and _____ shares of preferred stock, par value \$ _____ per share, all of which shares of preferred stock will be undesignated.

As of September 30, 2023, _____ shares of our common stock were outstanding and held of record by _____ stockholders, after giving effect to the Reorganization. This amount assumes the conversion of _____ shares of our redeemable convertible preferred stock outstanding as of September 30, 2023 into an equivalent number of shares of our common stock, which will occur immediately prior to the closing of this offering.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the common stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Preferred Stock

Immediately prior to the completion of this offering, all outstanding shares of our preferred stock will be converted into shares of our common stock. Upon the closing of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to _____ shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Options

We expect to reserve _____ shares of common stock for future issuance under the 2024 Plan.

Registration Rights

Upon the completion of this offering, the holders of _____ shares of our common stock, including those issuable upon the conversion of preferred stock upon closing of this offering, will be entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of an amended and restated investors' rights agreement between us, certain holders of our common stock and holders of our preferred stock. The amended and restated investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs, and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning 180 days after the effective date of this registration statement, the holders of _____ shares of our common stock, including those issuable upon the conversion of shares of our preferred units upon closing of this offering, are entitled to demand registration rights. Under the terms of the amended and restated investors' rights agreement, we will be required, upon the written request of holders of at least a majority of the securities eligible for registration then outstanding to file a registration statement with respect to at least a majority of the securities eligible for registration then outstanding, we will be required to file a registration statement within 60 days of such request covering all securities eligible for registration that our securityholders request to be included in such registration. We are required to effect only one registration pursuant to this provision of the amended and restated investors' rights agreement in any twelve-month period.

Short-Form Registration Rights

Pursuant to the amended and restated investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of securityholders holding at least twenty percent of the securities eligible for registration then outstanding we will be required to file a Form S-3 registration restatement with respect to outstanding securities of such securityholders having an aggregate price to the public of at least \$5 million. We are required to effect only two registrations in any twelve-month period pursuant to this provision of the amended and restated investors' rights agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the amended and restated investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of our common stock, including those issuable upon the conversion of our preferred units, are entitled to include their shares in the registration. Subject to certain exceptions contained in the amended and restated investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our amended and restated investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements

or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights, and short form registration rights granted under the amended and restated investors' rights agreement will terminate on the earliest to occur of (a) the closing of certain liquidation events, (b) the fifth anniversary of the completion of this offering or (c) at such time after this offering when the holders' shares may be sold without restriction pursuant to Rule 144 under the Securities Act within a three month period.

Expenses

Ordinarily, other than underwriting discounts and commissions, we are generally required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees, and disbursements of a counsel for the selling security holders and blue-sky fees and expenses.

Anti-Takeover Effects of Delaware Law and Certain Provisions of Our Certificate of Incorporation and Bylaws to be in Effect Upon the Completion of this Offering

Some provisions of Delaware law include, and our certificate of incorporation and bylaws to be in effect upon the completion of this offering will include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our certificate of incorporation will provide for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also will provide that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our certificate of incorporation will provide that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our certificate of incorporation and bylaws will provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice

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of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws will limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our bylaws will establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures will provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws will specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our bylaws and certificate of incorporation must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least two-thirds of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our certificate of incorporation will provide for _____ authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation will grant our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Delaware Anti-Takeover Statute

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this

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stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85 percent of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10 percent or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15 percent or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Choice of Forum

Our bylaws will provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (3) any action asserting a claim arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws (including the interpretation, validity or enforceability thereof), or (4) any action asserting a claim that is governed by the internal affairs doctrine; provided, however, that this provision shall not apply to any causes of action arising under the Securities Act or Exchange Act. In addition, our bylaws will provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to these forum provisions. These forum provisions may impose additional costs on stockholders, may limit our stockholders' ability to bring a claim in a forum they find favorable, and the designated courts may reach different judgments or results than other courts. In addition, there is uncertainty as to whether the federal forum provision for Securities Act claims will be enforced, which may impose additional costs on us and our stockholders.

Stock Exchange Listing

We have applied to list our common stock on the Nasdaq Global Select Market under the proposed trading symbol "MGX." The closing of this offering is contingent upon such listing.

Transfer Agent and Registrar

The Transfer Agent and Registrar for our common stock will be

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our shares. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of shares of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares outstanding as of September 30, 2023, upon the completion of this offering and after giving effect to the Reorganization, _____ shares of our common stock will be outstanding, assuming the issuance of _____ shares offered by us in this offering, no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options. Of the outstanding shares, all of the shares sold in this offering will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144 under the Securities Act, may only be sold in compliance with the limitations described below, and restricted shares of common stock are subject to time-based vesting terms. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be "restricted securities" as such term is defined in Rule 144 under the Securities Act. These restricted securities were issued and sold by us in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, summarized below.

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1 percent of the number of shares then outstanding, which will equal approximately _____ shares immediately after this offering, assuming no exercise of the underwriters' option to purchase additional shares, based on the number of shares outstanding as of September 30, 2023; or
- the average weekly trading volume of our common stock on the Nasdaq Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares.

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However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under "Underwriting" included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Lock-Up Agreements

We, all of our directors and officers, and substantially all of our stockholders have agreed not to sell or otherwise transfer or dispose of any of our securities for a period of 180 days from the date of this prospectus, subject to certain exceptions. The representatives of the underwriters may, in their sole discretion, permit early release of shares subject to the lock-up agreements. See the section entitled "Underwriting," included elsewhere in this prospectus for more information.

Registration Rights

Upon completion of this offering, certain holders of our securities will be entitled to various rights with respect to registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section entitled "Description of Capital Stock—Registration Rights" included elsewhere in this prospectus for more information.

Equity Incentive Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register our shares issued or reserved for issuance under our equity incentive plans. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the SEC. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. As of the date of this prospectus, we estimate that such registration statement on Form S-8 will cover approximately shares.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion is a summary of certain material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering, referred to below as "our common stock". For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or other foreign organization taxable as a corporation; or
- a foreign trust or estate the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, the Medicare contribution tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, or any other aspect of any U.S. federal tax other than income taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- "regulated investment companies" and "real estate investment trusts";
- pension plans;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- "qualified foreign pension funds," or entities wholly owned by a "qualified foreign pension fund";

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- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and partners and investors therein);
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who have elected to mark securities to market for U.S. federal income tax purposes;
- persons that hold our common stock as part of a straddle, conversion transaction, synthetic security, or other integrated investment; and
- U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

We have never declared or paid any cash distributions on our members' capital, and we do not anticipate paying cash distributions on our common stock for the foreseeable future. Distributions, if any, on our common stock will generally constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on Sale or Other Taxable Disposition of Our Common Stock." Any such distributions will also be subject to the discussions below under the sections entitled "Backup Withholding and Information Reporting" and "Withholding and Information Reporting Requirements—FATCA."

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30 percent rate or a reduced rate specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30 percent withholding tax if the non-U.S. holder satisfies applicable certification requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30 percent rate or a reduced rate specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Any documentation provided to an applicable withholding agent may need to be updated in certain circumstances. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on Sale or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under "Backup Withholding and Information Reporting" and "Withholding and Information Reporting Requirements—FATCA," a non-U.S. holder generally will not be subject to any U.S. federal income or withholding tax on any gain realized upon such holder's sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for a period or periods aggregating 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30 percent tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," as described below, unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5 percent of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation if the fair market value of its U.S. real property interests, as defined in the Code and applicable Treasury regulations, equals or exceeds 50 percent of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We (or the applicable paying agent) must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. A non-U.S. holder may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through

a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker.

Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements—FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act (FATCA) generally impose a U.S. federal withholding tax at a rate of 30 percent on payments of dividends on, or, subject to the discussion of certain proposed U.S. Treasury regulations below, gross proceeds from the sale or other disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. However, the U.S. Treasury released proposed regulations which, if finalized in their present form, would eliminate the federal withholding tax of 30 percent applicable to the gross proceeds of a sale or other disposition of our common stock. In the preamble to such proposed regulations, the U.S. Treasury stated that taxpayers (including withholding agents) may generally rely on the proposed regulations until final regulations are issued. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30 percent withholding tax under FATCA.

UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Jefferies LLC, Cowen and Company, LLC, Wells Fargo Securities, LLC, and BMO Capital Markets Corp. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares of common stock
J.P. Morgan Securities LLC	
Jefferies LLC	
Cowen and Company, LLC	
Wells Fargo Securities, LLC	
BMO Capital Markets Corp.	
Chardan Capital Markets, LLC	
Total	

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares of common stock. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased, or the offering may be terminated.

The underwriters propose to offer the shares of common stock directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of \$ per share. Any such dealers may resell shares of common stock to certain other brokers or dealers at a discount of up to \$ per share from the initial public offering price. After the initial offering of the shares of common stock to the public, if all of the shares of common stock are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of any shares of common stock made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares of common stock by the underwriters which exceed the number of shares of common stock specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares of common stock. If any shares of common stock are purchased with this option to purchase additional shares of common stock, the underwriters will purchase shares of common stock in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares of common stock on the same terms as those on which the shares of common stock are being offered.

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The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ _____ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

	Without option to purchase additional shares of common stock exercise	With full option to purchase additional shares of common stock exercise
Per Common Share	\$ _____	\$ _____
Total	\$ _____	\$ _____

We estimate that the total expenses of this offering, including registration, filing, and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$ _____ million. We have agreed to reimburse the underwriters for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority, Inc. of up to \$ _____.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares of common stock to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, or submit to, or file with, the SEC a registration statement under the Securities Act relating to, any of our shares of common stock or securities convertible into or exercisable or exchangeable for any of our shares of common stock, or publicly disclose the intention to make any offer, sale, pledge, loan, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of the representatives for a period of 180 days after the date of this prospectus, other than the shares of our common stock to be sold in this offering.

Our directors and executive officers, and substantially all of our stockholders (such persons, the "lock-up parties") have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each lock-up party, with limited exceptions, for a period of 180 days after the date of this prospectus (such period, the "restricted period"), may not (and may not cause any of their direct or indirect affiliates to), without the prior written consent of the representatives, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including without limitation, common stock or such other securities which may be deemed to be beneficially owned by such lock-up parties in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant (collectively with the common stock, the "lock-up securities"), (2) enter into any hedging, swap or other agreement or transaction that transfers, in whole or in part, any of the economic consequences of ownership of the lock-up securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of lock-up securities, in cash or otherwise, (3) make any

demand for, or exercise any right with respect to, the registration of any lock-up securities, or (4) publicly disclose the intention to do any of the foregoing. Such persons or entities have further acknowledged that these undertakings preclude them from engaging in any hedging or other transactions or arrangements (including, without limitation, any short sale or the purchase or sale of, or entry into, any put or call option, or combination thereof, forward, swap or any other derivative transaction or instrument, however described or defined) designed or intended, or which could reasonably be expected to lead to or result in, a sale or disposition or transfer (by any person or entity, whether or not a signatory to such agreement) of any economic consequences of ownership, in whole or in part, directly or indirectly, of any lock-up securities, whether any such transaction or arrangement (or instrument provided for thereunder) would be settled by delivery of lock-up securities, in cash or otherwise.

The restrictions described in the immediately preceding paragraph and contained in the lock-up agreements between the underwriters and the lock-up parties do not apply, subject in certain cases to various conditions, to certain transactions, including (a) transfers or disposals of lock-up securities: (i) as bona fide gifts, or for bona fide estate planning purposes, (ii) by will or intestacy or any other testamentary document, (iii) to any trust for the direct or indirect benefit of the lock-up party or any immediate family member, (iv) to a corporation, partnership, limited liability company, investment fund or other entity (A) of which the lock-up party and/or its immediate family members are the legal and beneficial owner of all of the outstanding equity securities or similar interests, or (B) controlled by, or under common control with, the undersigned or the immediate family of the undersigned (v) to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible under clauses (i) through (iv), (vi) in the case of a corporation, partnership, limited liability company, trust or other business entity, (A) to another corporation, partnership, limited liability company, trust or other business entity that is an affiliate of the lock-up party, or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control with the lock-up party or its affiliates or (B) as part of a distribution to limited members, members or stockholders of the lock-up party; (vii) by operation of law, (viii) to us from an employee upon death, disability or termination of employment of such employee, (ix) as part of a sale of lock-up securities acquired in open market transactions after the completion of this offering, (x) to us in connection with the vesting, settlement or exercise of restricted stock units, options, warrants or other rights to purchase shares of our common stock (including "net" or "cashless" exercise), including for the payment of exercise price and tax and remittance payments, or (xi) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction approved by our board of directors and made to all shareholders involving a change in control, provided that if such transaction is not completed, all such lock-up securities would remain subject to the restrictions in the immediately preceding paragraph; provided that (A) in the case of any transfer or distribution pursuant to clause (a)(i), (ii), (iii), (iv), (v), (vi) and (vii), such transfer shall not involve a disposition for value and each donee, devisee, transferee or distributee shall execute and deliver to the representatives a lock-up letter in the form of the lock-up letter, (B) in the case of any transfer or distribution pursuant to clause (a), (iii), (iv), (v), (vi), (ix) and (x) no filing by any party (donor, donee, devisee, transferor, transferee, distributor or distributee) under the Exchange Act, or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on a Form 5 or a filing required pursuant to Section 13 of the Exchange Act and the rules and regulations promulgated thereunder made after the expiration of the restricted period referred to above) and (C) in the case of any transfer or distribution pursuant to clause (a)(i), (ii), (vi) and (vii) it shall be a condition to such transfer that no public filing, report or announcement shall be voluntarily made and if any filing under Section 16(a) of the Exchange Act, or other public filing, report or announcement shall clearly indicate in the footnotes thereto the nature and conditions of such transfer; (b) exercise of the options, settlement of RSUs or other equity awards, or the exercise of warrants granted pursuant to plans described in in this

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prospectus, provided that any lock-up securities received upon such exercise, vesting or settlement would be subject to restrictions similar to those in the immediately preceding paragraph; (c) the conversion of outstanding preferred stock, warrants to acquire preferred stock, or convertible securities into shares of our common stock or warrants to acquire shares of our common stock, provided that any common stock or warrant received upon such conversion would be subject to restrictions similar to those in the immediately preceding paragraph; and (d) the establishment by lock-up parties of trading plans under Rule 10b5-1 under the Exchange Act, provided that such plan does not provide for the transfer of lock-up securities during the restricted period.

The representatives, in their sole discretion, may release the securities subject to any of the lock-up agreements with the underwriters described above, in whole or in part at any time.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

We have applied to have our common stock approved for listing/quotation on the Nasdaq Global Select Market under the symbol "MGX." The closing of this offering is contingent upon such listing.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional shares of common stock referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares of common stock in the open market. In making this determination, the underwriters will consider, among other things, the price of shares of common stock available for purchase in the open market compared to the price at which the underwriters may purchase shares of common stock through the option to purchase additional shares of common stock. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares of common stock in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares of common stock as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the open market, in the over-the-counter market or otherwise.

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Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our shares of common stock, or that the shares of common stock will trade in the public market at or above the initial public offering price.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each a "Relevant State"), no shares of our common stock have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares of our common stock which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation), except that offers of shares of common stock may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;

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- b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters for any such offer; or
- c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares of common stock shall require the Issuer or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who initially acquires any shares of common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the Company and the underwriters that it is a qualified investor within the meaning of the Prospectus Regulation.

In the case of any shares of common stock being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares of common stock acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in a Relevant State to qualified investors, in circumstances in which the prior consent of the underwriters has been obtained to each such proposed offer or resale.

The Company, the underwriters and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of common stock in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of common stock, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

Notice to Prospective Investors in the United Kingdom

In relation to the United Kingdom (the "UK"), no shares of our common stock have been offered or will be offered pursuant to the offering to the public in the UK prior to the publication of a prospectus in relation to the shares of common stock which has been approved by the Financial Conduct Authority in the UK in accordance with the UK Prospectus Regulation and the FSMA, except that offers of shares of common stock may be made to the public in the UK at any time under the following exemptions under the UK Prospectus Regulation and the FSMA:

- (a) to any legal entity which is a qualified investor as defined under the UK Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the UK Prospectus Regulation), subject to obtaining the prior consent of the underwriters for any such offer; or
- (c) at any time in other circumstances falling within section 86 of the FSMA,

provided that no such offer of shares of common stock shall require the Issuer or any underwriter to publish a prospectus pursuant to Section 85 of the FSMA or Article 3 of the UK Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

Each person in the UK who initially acquires any shares of common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the Company and the underwriters that it is a qualified investor within the meaning of the UK Prospectus Regulation.

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In the case of any shares of common stock being offered to a financial intermediary as that term is used in Article 5(1) of the UK Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares of common stock acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in the UK to qualified investors, in circumstances in which the prior consent of the underwriters has been obtained to each such proposed offer or resale.

The Company, the underwriters and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in the UK means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock, the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018, and the expression "FSMA" means the Financial Services and Markets Act 2000.

This document is for distribution only to persons who (i) have professional experience in matters relating to investments and who qualify as investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the "Financial Promotion Order"), (ii) are persons falling within Article 49(2)(a) to (d) ("high net worth companies, unincorporated associations etc.") of the Financial Promotion Order, (iii) are outside the United Kingdom, or (iv) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as "relevant persons"). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

Notice to Prospective Investors in Canada

The shares of common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts ("NI 33-105"), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in Switzerland

The shares of common stock may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX"), or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares of common stock, or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares of common stock have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares of common stock will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA ("FINMA"), and the offer of shares of common stock has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares of common stock.

Notice to Prospective Investors in Hong Kong

The shares of common stock have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("SFO"), of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong ("CO"), or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares of common stock has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares of common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the SFO and any rules made thereunder.

Notice to Prospective Investors in Singapore

Each joint book-running manager has acknowledged that this prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each joint book-running manager has represented and agreed that it has not offered or sold any shares of common stock or caused the shares of common stock to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares of common stock or cause the shares of common stock to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of common stock, whether directly or indirectly, to any person in Singapore other than:

- (a) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the "SFA")) pursuant to Section 274 of the SFA;
- (b) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or

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(c) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of common stock pursuant to an offer made under Section 275 of the SFA except:
 - (i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
 - (ii) where no consideration is or will be given for the transfer;
 - (iii) where the transfer is by operation of law;
 - (iv) as specified in Section 276(7) of the SFA; or
 - (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of shares of common stock, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the shares of common stock are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Notice to Prospective Investors in Japan

The shares of common stock have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares of common stock nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any "resident" of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to Prospective Investors in the United Arab Emirates

The shares of common stock have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab

Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Notice to Prospective Investors in Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the “Addressed Investors”); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions (the “Qualified Investors”). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. We have not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our shares of common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be offered shares of common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued shares of common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor’s name, address and passport number or Israeli identification number.

Notice to Prospective Investors in Australia

This prospectus:

- (a) does not constitute a disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the “Corporations Act”);
- (b) has not been, and will not be, lodged with the Australian Securities and Investments Commission (“ASIC”), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document for the purposes of the Corporations Act; and
- (c) may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, available under section 708 of the Corporations Act (“Exempt Investors”).

The shares of common stock may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares of common stock may be issued, and no draft or definitive offering

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memorandum, advertisement or other offering material relating to any shares of common stock may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares of common stock, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares of common stock under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the shares of common stock you undertake to us that you will not, for a period of 12 months from the date of issue of the shares of common stock, offer, transfer, assign or otherwise alienate those shares of common stock to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Notice to Prospective Investors in China

This prospectus will not be circulated or distributed in the PRC and the shares of common stock will not be offered or sold, and will not be offered or sold to any person for re-offering or resale directly or indirectly to any residents of the PRC except pursuant to any applicable laws and regulations of the PRC. Neither this prospectus nor any advertisement or other offering material may be distributed or published in the PRC, except under circumstances that will result in compliance with applicable laws and regulations.

Notice to Prospective Investors in Korea

The shares of common stock have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder ("FSCMA"), and the shares of common stock have been and will be offered in Korea as a private placement under the FSCMA. None of the shares of common stock may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder ("FETL"). Furthermore, the purchaser of the shares of common stock shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the shares of common stock. By the purchase of the shares of common stock, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the shares of common stock pursuant to the applicable laws and regulations of Korea.

Notice to Prospective Investors in Saudi Arabia

This document may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority ("CMA"), pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended (the "CMA Regulations"). The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the shares of common stock offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser.

Notice to Prospective Investors in the Dubai International Financial Centre (“DIFC”)

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority (“DFSA”). This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The shares of common stock to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares of common stock offered should conduct their own due diligence on the securities. If you do not understand the contents of this document, you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

Notice to Prospective Investors in Bermuda

Shares of common stock may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

Notice to prospective investors in the British Virgin Islands

The shares of common stock are not being and may not be offered to the public or to any person in the British Virgin Islands for purchase or subscription by or on behalf of us. The shares of common stock may be offered to companies incorporated under the BVI Business Companies Act, 2004 (British Virgin Islands) (BVI Companies), but only where the offer will be made to, and received by, the relevant BVI Company entirely outside of the British Virgin Islands.

Notice to prospective investors in Taiwan

The shares of common stock have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through a public offering or in circumstances which constitutes an offer within the meaning of the Securities and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorized to offer, sell, give advice regarding or otherwise intermediate the offering and sale of the shares of common stock in Taiwan.

Notice to prospective investors in South Africa

Due to restrictions under the securities laws of South Africa, no “offer to the public” (as such term is defined in the South African Companies Act, No. 71 of 2008 (as amended or re-enacted) (the South African Companies Act), is being made in connection with the issue of the shares of common stock in South Africa. Accordingly, this document does not, nor is it intended to, constitute a “registered prospectus” (as that term is defined in the South African Companies Act) prepared and registered under the South African Companies Act and has not been approved by, and/or filed with, the South African Companies and Intellectual Property Commission or any

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other regulatory authority in South Africa. The shares of common stock are not offered, and the offer shall not be transferred, sold, renounced or delivered, in South Africa or to a person with an address in South Africa, unless one or other of the following exemptions stipulated in section 96 (1) applies:

Section 96 (1) (a) the offer, transfer, sale, renunciation or delivery is to:

- (i) persons whose ordinary business, or part of whose ordinary business, is to deal in securities, as principal or agent;
- (ii) the South African Public Investment Corporation;
- (iii) persons or entities regulated by the Reserve Bank of South Africa;
- (iv) authorized financial service providers under South African law;
- (v) financial institutions recognized as such under South African law;
- (vi) a wholly-owned subsidiary of any person or entity contemplated in (iii), (iv) or (v), acting as agent in the capacity of an authorized portfolio manager for a pension fund, or as manager for a collective investment scheme (in each case duly registered as such under South African law); or
- (vii) any combination of the person in (i) to (vi); or

Section 96 (1) (b) the total contemplated acquisition cost of the shares of common stock, for any single addressee acting as principal is equal to or greater than ZAR1,000,000 or such higher amount as may be promulgated by notice in the Government Gazette of South Africa pursuant to section 96(2)(a) of the South African Companies Act.

Information made available in this prospectus should not be considered as "advice" as defined in the South African Financial Advisory and Intermediary Services Act, 2002.

Notice to prospective investors in Malaysia

No prospectus or other offering material or document in connection with the offer and sale of the shares of common stock has been or will be registered with the Securities Commission of Malaysia ("Commission"), for the Commission's approval pursuant to the Capital Markets and Services Act 2007. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of common stock may not be circulated or distributed, nor may the shares of common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Malaysia other than (i) a closed end fund approved by the Commission; (ii) a holder of a Capital Markets Services License; (iii) a person who acquires the shares of common stock, as principal, if the offer is on terms that the shares of common stock may only be acquired at a consideration of not less than RM250,000 (or its equivalent in foreign currencies) for each transaction; (iv) an individual whose total net personal assets or total net joint assets with his or her spouse exceeds RM3 million (or its equivalent in foreign currencies), excluding the value of the primary residence of the individual; (v) an individual who has a gross annual income exceeding RM300,000 (or its equivalent in foreign currencies) per annum in the preceding twelve months; (vi) an individual who, jointly with his or her spouse, has a gross annual income of RM400,000 (or its equivalent in foreign currencies), per annum in the preceding twelve months; (vii) a corporation with total net assets exceeding RM10 million (or its equivalent in a foreign currencies) based on the last audited accounts; (viii) a partnership with total net assets exceeding RM10 million (or its equivalent in foreign currencies); (ix) a bank licensee or insurance licensee as defined in the Labuan Financial Services and Securities Act 2010; (x) an Islamic bank licensee or takaful licensee as defined in the Labuan Financial Services and Securities Act 2010; and (xi) any other person as may be specified by the Commission; provided that, in the each of the preceding categories (i) to (xi), the distribution of the shares of

common stock is made by a holder of a Capital Markets Services License who carries on the business of dealing in securities. The distribution in Malaysia of this prospectus is subject to Malaysian laws. This prospectus does not constitute and may not be used for the purpose of public offering or an issue, offer for subscription or purchase, invitation to subscribe for or purchase any securities requiring the registration of a prospectus with the Commission under the Capital Markets and Services Act 2007.

Notice to prospective investors in Qatar

The shares of common stock described in this prospectus have not been, and will not be, offered, sold or delivered, at any time, directly or indirectly in the State of Qatar in a manner that would constitute a public offering. This prospectus has not been, and will not be, registered with or approved by the Qatar Financial Markets Authority or Qatar Central Bank and may not be publicly distributed. This prospectus is intended for the original recipient only and must not be provided to any other person. It is not for general circulation in the State of Qatar and may not be reproduced or used for any other purpose.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters relating to this offering will be passed upon for the underwriters by Davis Polk & Wardwell LLP, New York, New York.

EXPERTS

The financial statements as of December 31, 2022 and 2021 and for the years then ended included in this Prospectus have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

In connection with their engagement, PricewaterhouseCoopers LLP ("PwC") notified us that a business relationship existed between a PwC member firm and a beneficial owner that has significant influence ("BOSI") over the Company, whereby the BOSI participated in an online platform operated and maintained by the PwC member firm and had access to dedicated space at the PwC member firm's physical location in which the BOSI and other business partners and innovators participated on such platform and/or within the physical location to exchange experiences and ideas, search for technologies, pose challenges to others to provide proposed solutions, make direct contacts and to meet virtually or in person.

The existence of this business relationship identified is inconsistent with SEC and PCAOB auditor independence rules provided in Rule 2-01 of Regulation S-X. The matter was resolved on June 7, 2023, upon the termination of the business relationship between the BOSI and the PwC member firm.

PwC provided an overview of the facts and circumstances surrounding the business relationship to our audit committee and management, including that the entity involved was a BOSI and not an affiliate of the Company, and other relevant facts. The PwC audit engagement team members did not participate in the PwC member firm's activities and engagements with the BOSI or any entity that is part of the PwC member firm's business relationship with the BOSI, and the business relationship was not quantitatively or qualitatively material to the PwC member firm or the BOSI.

Considering the facts presented, our audit committee and PwC have concluded that the business relationship would not impair PwC's application of objective and impartial judgment on any matters encompassed within the audit engagement performed by PwC for our consolidated financial statements as of and for the fiscal years ended December 31, 2022 and 2021, and the review for the interim periods for the nine months ended September 30, 2023 and 2022, and that a reasonable investor with knowledge of all relevant facts and circumstances would conclude that PwC is capable of remaining objective and impartial with respect to the audit and reviews of the Company's consolidated financial statements.

CHANGES IN INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

On September 24, 2021, KPMG, LLP ("KPMG") was engaged as the independent registered public accounting firm to audit our consolidated financial statements for the fiscal year ended December 31, 2020 in accordance with auditing standards generally accepted in the United States.

During the two fiscal years ended December 31, 2020 and 2019 and the subsequent interim period through September 24, 2021 we did not consult with KPMG on (i) matters that involved the application of accounting principles to a specified transaction either completed or proposed, or the type of audit opinion that might be rendered on our consolidated financial statements, and neither a written report nor oral advice was provided to us that KPMG concluded was an important factor considered by us in reaching a decision as to any accounting, auditing or financial reporting issue, or (ii) any matter that was either the subject of a "disagreement" or a "reportable event" (as defined in Item 304(a)(1)(iv) and Item 304(a)(1)(v) of Regulation S-K and the related instructions, respectively).

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On April 28, 2022, our audit committee dismissed KPMG as our independent registered public accounting firm.

KPMG has never issued an audit report on our consolidated financial statements.

During the two fiscal years ended December 31, 2021 and 2020, and the subsequent period through April 28, 2022, (1) there were no disagreements (as that term is used in Item 304(a)(1)(iv) of Regulation S-K and the related instructions) between us and KPMG on any matter of accounting principles or practices, financial statement disclosure, or auditing scope or procedure, which disagreements, if not resolved to the satisfaction of KPMG, would have caused KPMG to make reference thereto in a report on our financial statements for the year ended December 31, 2020 if a report were to be issued, and (2) there were no "reportable events" as such term is defined in Item 304(a)(1)(v) of Regulation S-K.

We have provided KPMG with a copy of the disclosures set forth under the heading "Changes in Independent Registered Public Accounting Firm" and have requested that KPMG furnish a letter addressed to the SEC stating whether or not KPMG agrees with such statements. A copy of the letter is filed as Exhibit 16.1 to the registration statement of which this prospectus forms a part.

On April 28, 2022, PwC was approved as the independent registered public accounting firm for the fiscal year ended December 31, 2021.

During the two most recent fiscal years ended December 31, 2021 and the subsequent interim period through April 28, 2022 we did not consult with PwC on (i) matters that involved the application of accounting principles to a specified transaction either completed or proposed, or the type of audit opinion that might be rendered on our consolidated financial statements, and neither a written report nor oral advice was provided to us that PwC concluded was an important factor considered by us in reaching a decision as to any accounting, auditing or financial reporting issue, or (ii) any matter that was either the subject of a "disagreement" or a "reportable event" (as defined in Item 304(a)(1)(iv) and Item 304(a)(1)(v) of Regulation S-K and the related instructions, respectively).

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (File Number 333-276413) under the Securities Act with respect to the common stock we are offering by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information included in the registration statement. For further information pertaining to us and our common stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

Upon the completion of the offering, we will be subject to the informational requirements of the Exchange Act and will file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. We also maintain a website at <https://www.metagenomi.co> and upon completion of the offering, you may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus.

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Report of Independent Registered Public Accounting Firm

To the Board of Managers and Members of Metagenomi Technologies, LLC

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Metagenomi Technologies, LLC and its subsidiary (the "Company") as of December 31, 2022 and 2021, and the related consolidated statements of operations and comprehensive loss, of redeemable convertible preferred units and members' deficit, and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

San Jose, California
August 3, 2023

We have served as the Company's auditor since 2022.

Consolidated Balance Sheets

(in thousands, except units)

	December 31,	
	2021	2022
Assets		
Current assets:		
Cash and cash equivalents	\$ 39,296	\$ 184,441
Available-for-sale marketable securities	68,858	177,690
Contract assets	—	1,274
Prepaid expenses and other current assets	762	3,494
Total current assets	108,916	366,899
Property and equipment, net	3,862	16,522
Long-term investments	6,417	7,806
Operating lease right-of-use assets	18,028	16,736
Other assets	669	450
Restricted cash	4,100	6,073
Total assets	<u>\$ 141,992</u>	<u>\$ 414,486</u>
Liabilities, redeemable convertible preferred units and members' deficit		
Current liabilities:		
Accounts payable	\$ 1,354	\$ 2,011
Income tax payable	—	1,536
Accrued expenses and other current liabilities	3,531	8,790
Current portion of operating lease liabilities	687	1,515
Collaboration advance	3,559	743
Deferred revenue	16,041	33,942
Total current liabilities	25,172	48,537
Convertible promissory note and accrued interest, net of discount	30,276	—
Non-current portion of operating lease liabilities	17,965	17,056
Collaboration advance, non-current	912	—
Deferred revenue, non-current	23,716	76,185
Other non-current liabilities	—	1,033
Total liabilities	<u>98,041</u>	<u>142,811</u>
Commitments and contingencies (Note 10)		
Redeemable convertible preferred units: 19,650,632 and 41,813,375 units authorized as of December 31, 2021 and 2022, respectively; 19,650,632 and 41,478,621 units issued and outstanding as of December 31, 2021 and 2022, respectively. Liquidation preference \$76,669 and \$347,335 as of December 31, 2021 and 2022, respectively	76,495	346,103
Members' deficit:		
Common units: 32,000,000 and 66,000,000 units authorized as of December 31, 2021 and 2022, respectively; 5,947,500 units issued and outstanding as of December 31, 2021 and 2022	26	26
Profits interests: 6,020,644 and 14,604,165 units authorized as of December 31, 2021 and 2022, respectively; 5,783,758 and 7,516,073 units issued and outstanding as of December 31, 2021 and 2022, respectively	547	2,509
Accumulated other comprehensive loss	(21)	(274)
Accumulated deficit	<u>(33,096)</u>	<u>(76,689)</u>
Total members' deficit	<u>(32,544)</u>	<u>(74,428)</u>
Total liabilities, redeemable convertible preferred units and members' deficit	<u>\$ 141,992</u>	<u>\$ 414,486</u>

The accompanying notes are an integral part of these consolidated financial statements.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except units and per unit data)

	Years ended December 31,	
	2021	2022
Collaboration revenue	\$ 243	\$ 17,200
Operating expenses:		
Research and development	14,478	43,139
General and administrative	9,712	18,701
Total operating expenses	24,190	61,840
Loss from operations	(23,947)	(44,640)
Other income (expense)		
Interest expense	(302)	(98)
Interest income	43	3,419
Change in fair value of long-term investments	2,760	94
Other income, net	4	201
Total other income	2,505	3,616
Net loss before provision for income taxes	(21,442)	(41,024)
Provision for income taxes	—	(2,569)
Net loss	\$ (21,442)	\$ (43,593)
Other comprehensive loss:		
Unrealized loss on available-for-sale marketable securities, net	(21)	(253)
Other comprehensive loss	\$ (21,463)	\$ (43,846)
Net loss per unit attributable to common unitholders, basic and diluted	\$ (3.77)	\$ (7.34)
Weighted average common units outstanding, basic and diluted	5,691,431	5,938,654

The accompanying notes are an integral part of these consolidated financial statements.

Consolidated Statements of Redeemable Convertible Preferred Units and Members' Deficit

(in thousands, except units)

	Redeemable Convertible Preferred Units		Common Units		Profits Interests		Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Members' Deficit
	Units	Amount	Units	Amount	Units	Amount			
		\$		\$		\$			
BALANCE—January 1, 2021	18,069,695	\$ 66,547	5,947,500	\$ 26	2,302,239	\$ 172	\$ -	(11,654)	\$ (11,456)
Issuance of Series A-5 redeemable convertible preferred units, net of issuance costs of \$52	1,580,937	9,948	-	-	-	-	-	-	-
Issuance of profits interests	-	-	-	-	3,550,854	-	-	-	-
Cancellation and forfeiture of profits interests	-	-	-	-	(69,335)	-	-	-	-
Unit-based compensation expense	-	-	-	-	-	375	-	-	375
Other comprehensive loss	-	-	-	-	-	-	(21)	-	(21)
Net loss	-	-	-	-	-	-	-	(21,442)	(21,442)
BALANCE—December 31, 2021	19,650,632	\$ 76,495	5,947,500	\$ 26	5,783,758	\$ 547	\$ (21)	(33,096)	\$ (32,544)
Issuance of Series B redeemable convertible preferred units for cash, net of issuance costs of \$697	12,446,876	144,304	-	-	-	-	-	-	-
Issuance of Series B redeemable convertible preferred units upon conversion of convertible note and accrued interest	2,607,387	30,374	-	-	-	-	-	-	-
Issuance of Series B-1 redeemable convertible preferred units, net of issuance costs of \$361	6,773,726	94,930	-	-	-	-	-	-	-
Issuance of profits interests	-	-	-	-	2,763,356	-	-	-	-
Cancellation and forfeiture of profits interests	-	-	-	-	(1,031,041)	-	-	-	-
Unit-based compensation expense	-	-	-	-	-	1,962	-	-	1,962
Other comprehensive loss	-	-	-	-	-	-	(253)	-	(253)
Net loss	-	-	-	-	-	-	-	(43,593)	(43,593)
BALANCE—December 31, 2022	41,478,621	\$ 346,103	5,947,500	\$ 26	7,516,073	\$ 2,509	\$ (274)	(76,689)	\$ (74,428)

The accompanying notes are an integral part of these consolidated financial statements.

Consolidated Statements of Cash Flows

(in thousands)

	Years ended December 31,	
	2021	2022
Cash flows from operating activities		
Net loss	\$ (21,442)	\$ (43,593)
Adjustments to reconcile net loss to net cash provided by operating activities		
Unit-based compensation expense	375	1,962
Depreciation and amortization	387	1,733
Loss on fixed assets write-off	—	282
Non-cash lease expense	937	1,292
Amortization of premiums and discounts on available-for-sale marketable securities, net	203	(1,129)
Amortization of non-cash collaboration revenue	—	(314)
Non-cash interest expense	302	98
Change in fair value of long-term investments	(2,760)	(94)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(502)	(2,465)
Contract assets	—	(1,274)
Other assets	68	(173)
Accounts payable	695	721
Income tax payable	—	1,536
Deferred revenue and collaboration advance	44,228	65,661
Accrued expenses and other current liabilities	1,854	4,529
Operating lease liabilities	(88)	(81)
Other non-current liabilities	—	1,033
Net cash provided by operating activities	<u>24,257</u>	<u>29,724</u>
Cash flows from investing activities		
Purchases of property and equipment	(2,903)	(13,977)
Purchases of available-for-sale marketable securities	(69,258)	(214,850)
Purchases of long-term investments	(2,155)	—
Maturities and sales of available-for-sale marketable securities	—	106,627
Net cash used in investing activities	<u>(74,316)</u>	<u>(122,200)</u>
Cash flows from financing activities		
Proceeds from issuance of redeemable convertible preferred units, net of issuance costs	9,948	239,594
Proceeds from issuance of convertible promissory note, net of issuance costs	29,974	—
Net cash provided by financing activities	<u>39,922</u>	<u>239,594</u>
Net change in cash, cash equivalents and restricted cash	(10,137)	147,118
Cash, cash equivalents and restricted cash at the beginning of the period	53,533	43,396
Cash, cash equivalents and restricted cash at the end of the period	<u>\$ 43,396</u>	<u>\$ 190,514</u>
Reconciliation of cash, cash equivalents and restricted cash		
Cash and cash equivalents	\$ 39,296	\$ 184,441
Restricted cash	4,100	6,073
Cash, cash equivalents and restricted cash at the end of the period	<u>\$ 43,396</u>	<u>\$ 190,514</u>

The accompanying notes are an integral part of these consolidated financial statements.

Consolidated Statements of Cash Flows (Continued)
(in thousands)

	Years ended December 31,	
	2021	2022
Supplemental cash flow information		
Issuance of Series B redeemable convertible preferred units upon conversion of convertible promissory note and accrued interest	\$ —	\$ 30,374
Common shares of Affini-T received for collaboration revenue	\$ —	\$ 1,295
Operating lease right-of-use assets obtained in exchange for new lease liabilities	\$ 18,659	\$ —
Non-cash expense related to a lease modification	\$ 2,059	\$ —
Deferred finance issuance costs included in other assets	\$ 143	\$ —
Unpaid finance issuance costs included in accounts payable and accrued expenses	\$ —	\$ 360
Purchases of property and equipment included in accounts payable and accrued expenses	\$ 725	\$ 1,247

The accompanying notes are an integral part of these consolidated financial statements.

Notes to the consolidated financial statements

1. Description of business, organization and liquidity

Organization and business

Metagenomi Technologies, LLC ("Metagenomi"), together with its wholly owned subsidiary Metagenomi, Inc. ("Metagenomi Inc.") (together, the "Company") is a gene editing biotechnology company developing therapeutics by leveraging a toolbox of next-generation gene editing systems to accurately edit DNA.

Formation and group reorganizations

Metagenomi.co was incorporated in September 2016 in the State of Delaware and is headquartered in Emeryville, California. In September 2018, Metagenomi.co formed a subsidiary, Metagenomi Technologies, LLC, as its sole member. In November 2018, the two companies completed a reorganization where Metagenomi Technologies, LLC became the parent of Metagenomi.co. The reorganization was a transaction of entities under common control and did not change the group.

In December 2018, Metagenomi formed another wholly owned subsidiary, Metagenomi IP Technologies, LLC. Metagenomi IP Technologies, LLC did not have any operations except for the initial transfer of IP from Metagenomi.co and an ongoing license of its technology to Metagenomi.co. Key activities of Metagenomi were raising capital to support operations of Metagenomi.co.

In April 2020, Metagenomi.co changed its name to Metagenomi, Inc.

In December 2021, the group completed another tax-free reorganization, whereby Metagenomi IP Technologies, LLC merged with and into Metagenomi, Inc. As of December 31, 2022, the group consisted of two entities: Metagenomi Technologies, LLC and its subsidiary, Metagenomi Inc. Both 2018 and 2021 reorganizations were accounted as transactions under common control at historical carrying values.

Liquidity and going concern

The Company has incurred significant losses from operations since its inception. During the years ended December 31, 2021 and 2022, the Company incurred net losses of \$21.4 million and \$43.6 million, respectively. As of December 31, 2022, the Company had an accumulated deficit of \$76.7 million.

The Company has historically financed its operations primarily through issuance of redeemable convertible preferred units, convertible promissory notes and its collaboration agreements with Moderna, Affini-T and Ionis (see Note 7). The Company expects to continue to incur substantial losses, and its ability to achieve and sustain profitability will depend on the successful development, approval, and commercialization of any product candidates it may develop, and on the achievement of sufficient revenue to support its cost structure. The Company may never achieve profitability and, unless and until it does, it will need to continue to raise additional capital. Management expects that existing cash and cash equivalents and available-for-sale marketable securities of \$362.1 million as of December 31, 2022, will be sufficient to fund its current operating plan for at least the next 12 months from the date of issuance of these consolidated financial statements.

2. Summary of significant accounting policies

Basis of presentation

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). The accompanying consolidated financial statements

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include the accounts of Metagenomi and Metagenomi Inc., a wholly owned subsidiary. All intercompany balances and transactions have been eliminated in consolidation.

Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of expenses during the reporting period. On an ongoing basis, the Company evaluates estimates and assumptions, including but not limited to those related to revenue recognition under its collaboration agreements, the fair value of its common and redeemable convertible preferred units, the fair value of derivative liabilities, unit-based compensation expense, accruals for research and development expenses, the fair value of long-term investments and convertible promissory notes in private companies, the valuation of deferred tax assets, and uncertain income tax positions. Management bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from those estimates.

Segment and geographical information

The Company operates and manages its business as one reportable and operating segment, which is the business of developing next generation gene-editing technologies and therapies. The chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance. All of the Company's long-lived assets are located in the United States.

Risks and uncertainties

The Company is subject to certain risks and uncertainties, including, but not limited to, changes in any of the following areas that the Company believes could have a material adverse effect on the future financial position or results of operations: the Company's ability to advance the development of its next generation gene-editing platform, timing and ability to advance any product candidates it may develop into and through pre-clinical and clinical development; costs and timelines associated with the manufacturing of clinical supplies of any product candidates the Company may develop; regulatory approval, market acceptance of, and reimbursement for any product candidates the Company may develop; performance of third-party vendors; competition from pharmaceutical or other gene-editing companies with greater financial resources or expertise; protection of intellectual property; litigation or claims against the Company based on intellectual property or other factors; and its ability to attract and retain employees necessary to support its growth.

The Company's business and operations may be affected by worldwide economic conditions, which may continue to be impacted by global macroeconomic challenges such as the effects of the ongoing geopolitical conflicts in Ukraine, tensions in U.S.-China relations, the COVID-19 pandemic, uncertainty in the markets, including disruptions in the banking industry, and inflationary trends. Fiscal year 2022 was marked by significant market uncertainty, increasing inflationary pressures. These market dynamics may continue into 2023 and these and similar adverse market conditions may negatively impact the Company's operations and financial position.

Cash and cash equivalents

Cash equivalents are defined as short-term, highly liquid investments with original maturities of 90 days or less at the date of purchase. As of December 31, 2021 and 2022, the Company's cash and cash equivalents consisted of deposit accounts and investments in money market funds.

Marketable securities

Investments with original maturities of greater than 90 days are classified as available-for-sale marketable securities on the consolidated balance sheets and consist primarily of U.S. Treasury, corporate debt obligations, commercial paper, government agency obligations and asset-backed securities. As the Company's entire investment portfolio is considered available for use in current operations, the Company classifies all investments as available-for-sale and as current assets, even though the stated maturity may be more than one year from the current consolidated balance sheets date. Available-for-sale securities are carried at fair value, with unrealized gains and losses reported in accumulated other comprehensive loss, which is a separate component of members' deficit in the consolidated balance sheets.

The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity, which are both recorded to interest income in the consolidated statements of operations and comprehensive loss.

Changes in the fair value of available-for-sale securities are reflected within unrealized loss on available-for-sale marketable securities, net in the consolidated statements of operations and comprehensive loss. Realized gains and losses on the sale of securities are determined by specific identification of each security's cost basis. The Company regularly reviews its investment portfolio to determine if any security is impaired, which would require it to record an allowance for credit losses or an impairment charge in the period any such determination is made. In making this judgment, the Company evaluates, among other things, the extent to which the fair value of a security is less than its amortized cost, its intent to sell or whether it is more likely than not that the Company will be required to sell the security before recovery of its amortized cost basis, the financial condition of the issuer and any changes thereto, and, as necessary, the portion of a decline in fair value that is credit-related. This assessment could change in the future due to new developments or changes in assumptions related to any particular security. Realized gains and losses, allowances for credit losses and impairments on available-for-sale securities, if any, are recorded to interest expense, net in the consolidated statements of operations and comprehensive loss.

Long-term investments

The Company determines at the inception of each arrangement whether an investment or other interest is considered a variable interest entity ("VIE"). If the investment or other interest is determined to be a VIE, the Company evaluates whether it is considered the primary beneficiary. The primary beneficiary of a VIE is the party that meets both of the following criteria: (i) has the power to direct the activities that most significantly impact the VIE's economic performance; and (ii) has the obligation to absorb losses or the right to receive benefits from the VIE. For investments in VIEs in which the Company is considered the primary beneficiary, the assets, liabilities and results of operations of the VIE are included in the Company's consolidated financial statements. As of December 31, 2021 and 2022, there were no VIEs for which the Company was the primary beneficiary.

If the Company concludes that it exercises significant influence over an investee's operations, it may account for its investment either using the equity method of accounting or fair value method. The election to account for an investment at fair value is irrevocable unless an event occurs creating a new election date. If the

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Company does not have a significant influence, it accounts for its investment at fair value and may elect to account for an equity security without a readily determinable fair value using the measurement alternative method. The measurement alternative method allows the Company to measure the equity investment at its cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. Changes in fair value and impairment losses are recognized as other income (expenses) in the consolidated statements of operations and comprehensive loss.

Restricted cash

Restricted cash of \$4.1 million and \$6.1 million as of December 31, 2021 and 2022, respectively, represents security deposits in the form of a letter of credit issued in connection with the Company's leases (see Note 10).

Concentration of credit risk

Cash and cash equivalents, marketable securities and investments in convertible promissory notes are financial instruments that potentially subject the Company to concentrations of credit risk. As of December 31, 2021 and 2022, cash consists of cash deposited with one financial institution, Silicon Valley Bank ("SVB"), and account balances exceed federally insured limits.

On March 10, 2023, SVB was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. On March 12, 2023 the FDIC transferred all deposits, both insured and uninsured, and substantially all assets from the former SVB to a newly created, full-service FDIC-operated "bridge bank", Silicon Valley Bridge Bank, N.A. ("SVBB") and the FDIC, Treasury Department, and Federal Reserve announced that all deposits will be fully protected, whether or not they had been insured by the FDIC. On March 27, 2023, First-Citizens Bank & Trust Company assumed all of SVBB's customer deposits and certain other liabilities and acquired substantially all of SVBB's loans and certain other assets from the FDIC. As of the date of the issuance of these consolidated financial statements, the Company has full access to and control over all its cash, cash equivalents and available-for-sale marketable securities.

The Company also has investments in money market funds, U.S. Treasuries, corporate debt obligations, commercial paper, government agency obligations and asset-backed securities, which can be subject to certain credit risks. The Company mitigates the risks by investing in high-grade instruments, limiting its exposure to any one issuer and monitoring the ongoing creditworthiness of the financial institutions and issuers. The Company has not experienced any losses on its financial instruments.

Concentration of collaboration revenue and contract assets

The following table summarizes the percentages of collaboration revenues and of contract assets from each of the Company's customers that individually accounted for 10% or more of its collaboration revenues:

	Collaboration revenue		Contract assets
	Year ended December 31,		December 31,
	2021	2022	2022
Customer A	100%	84%	—
Customer B	—	15%	100%
	100%	99%	100%

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The Company reviews its contract assets for impairment. No contract asset impairment was recorded as of December 31, 2022.

Fair value measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The carrying amounts of cash equivalents, prepaid expenses and other current assets, accounts payable, accrued expenses and other liabilities, approximate fair value due to their short-term maturities. Financial instruments, such as money market funds, marketable securities and certain equity and long-term investments are measured at fair value at each reporting date (see Note 3).

Deferred finance issuance costs

Deferred finance issuance costs, consisting of legal fees relating to in-process equity financings or offerings are capitalized. The deferred finance issuance costs will be offset against offering proceeds upon the completion of the financing or the offering. In the event the financing or the offering is terminated or delayed, deferred finance issuance costs will be expensed immediately as a charge to general and administrative expenses in the consolidated statements of operations and comprehensive loss. As of December 31, 2021, the Company capitalized and recorded \$0.1 million in issuance costs related to its Series B preferred unit financing in other assets in the consolidated balance sheets, which closed in January 2022. There were no deferred finance issuance costs as of December 31, 2022.

Property and equipment, net

Property and equipment are recorded at cost, less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, generally three to five years, and leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset. Repairs and maintenance expenditures, which are not considered improvements and do not extend the useful life of property and equipment, are expensed as incurred. When assets are retired or otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the consolidated balance sheets and the resulting gain or loss is reflected in the consolidated statements of operations and comprehensive loss in the period realized.

Leases

The Company determines whether an arrangement is or contains a lease at the inception of the arrangement and whether such a lease should be classified as a financing lease or operating lease at the commencement date of the lease. Leases with a term greater than one year are recognized on the consolidated balance sheets as operating right-of-use asset ("ROU asset") and operating lease liabilities. We elected not to recognize the right-of-use assets and lease liabilities for leases with lease terms of one year or less (short-term leases). Lease liabilities and their corresponding ROU assets are recorded based on the present value of lease payments over the lease term. The Company considers the lease term to be the noncancelable period that it has the right to use the underlying asset, together with any periods where it is reasonably certain it will exercise an option to extend (or not terminate) the lease. As the interest rate implicit in the Company's lease contracts is not readily determinable, the Company utilizes its incremental borrowing rate ("IBR") based on the information available at the commencement date to determine the present value of lease payments.

Rent expense for operating leases is recognized on a straight-line basis over the lease term. The Company has elected to not separate lease and non-lease components for its real estate leases and instead accounts for each

separate lease component and the non-lease components associated with that lease component as a single lease component. Variable lease payments are recognized as incurred.

As of December 31, 2021 and 2022, the Company had no finance leases.

Impairment of long-lived assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparing the carrying amount to the future undiscounted net cash flows which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows generated by the assets. There have been no such impairments of long-lived assets in the years ended December 31, 2021 and 2022.

Redeemable convertible preferred units

The Company records redeemable convertible preferred units at their respective fair values on the dates of issuance, net of issuance costs. The redeemable convertible preferred units are recorded outside of permanent equity because while it is not mandatory, redemption is contingent upon the occurrence of certain events considered not solely within the Company's control. The Company has not adjusted the carrying values of the redeemable convertible preferred units to the liquidation preferences of such units because it is uncertain whether or when a deemed liquidation event would occur that would obligate the Company to pay the liquidation preferences to holders of redeemable convertible preferred units. Subsequent adjustments to the carrying values to the liquidation preferences will be made only when it becomes probable that such a deemed liquidation event will occur.

Collaboration arrangements and revenue recognition

At the inception of an agreement, the Company evaluates if an agreement is a collaborative arrangement within the scope of ASC 808, *Collaborative Arrangements* ("ASC 808"). For collaborative arrangements that fall within the scope of ASC 808, the Company first determines which elements of the collaboration are deemed to be a performance obligation with a customer within the scope of ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). For elements of collaboration arrangements that are accounted for pursuant to ASC 808 and are not subject to the guidance in ASC 606, the Company applies the revenue recognition model under ASC 606 or other guidance, as deemed appropriate.

The Company re-evaluates whether the license agreement continues to be a collaborative arrangement, or whether the license agreement becomes a collaborative arrangement, whenever there is a change in either the roles of the participants in the arrangement or the participants' exposure to significant risks and rewards dependent on the ultimate commercial success of the endeavor.

Under ASC 606, the Company recognizes revenue when the Company's customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods and services. To determine revenue recognition for arrangements within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including the constraint on variable consideration; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when or as the Company satisfies a performance obligation.

The Company's revenue is primarily derived through its license, research, development and option agreements. These agreements may include the following types of promised goods or services: (i) grants of licenses,

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(ii) performance of research and development services, and (iii) participation on joint research and/or development committees. They also may include options to obtain licenses to the Company's intellectual property or to extend the term of the research activities. Payments to the Company under these arrangements typically include one or more of the following: non-refundable upfront payments; reimbursement for research services; research, development or regulatory milestone payments; profit-sharing arrangements; and royalty and commercial sales milestone payments. The event-based milestone payments, royalties and cost reimbursements represent variable consideration. The Company evaluates the probability that the event-based milestones will be achieved and estimates the amount to be included in the transaction price using the most likely amount method. The Company includes cost reimbursement in the transaction price using the expected value method.

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC 606. The Company allocates the total transaction price, including variable consideration that is not constrained, to each performance obligation based on the estimated standalone selling price and recognizes revenue when, or as, the performance obligation is satisfied. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur. At the end of each reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price.

The Company's collaboration and license agreements include contingent payments related to sales-based milestones and royalties. Sales-based milestones and royalties are typically payable when annual sales of a covered product reach specified levels and sales occur. When intellectual property license is determined to be a predominant promise in the arrangement, sales-based milestones and royalties are recognized at the later of when the associated performance obligation has been satisfied or when the sales occur. Unlike other contingency payments, such as regulatory milestones, sales-based milestones and royalties are not included in the transaction price based on estimates at the inception of the contract, but rather, are included when the sales or usage occur.

In cases when upfront payment contains a material right for the optional services the Company may provide in the future, the material right is treated as a separate performance obligation. The value allocated to such material right is deferred and recognized as revenue when the performance obligation is satisfied, and the optional services are provided, or when the right expires.

Contract assets and contract liabilities

A contract asset is a right to consideration in exchange for goods or services that the Company has transferred to a customer when that right is conditional and is not just subject to the passage of time. A receivable is recorded on the consolidated balance sheets when the Company has unconditional rights to consideration. As of December 31, 2022, the contract asset balance of \$1.3 million related to revenue recognized and unbilled under the Affini-T Agreement (Note 7).

A contract liability is an obligation to transfer goods or services for which the Company has received consideration, or for which an amount of consideration is due from the customer. Contract liabilities consist of deferred revenue and relate to amounts invoiced to, or advance consideration received from, licensees that precede the Company's satisfaction of the associated performance obligations. The Company's deferred revenue primarily results from upfront payments received relating to the performance obligations that are satisfied over time under the Company's revenue arrangements (Note 7).

The Company's contract balances are reported in a net contract asset or liability position on a contract-by-contract basis at the end of each reporting period. Changes in the contract assets and the contract

liabilities balances during the period are the result of the issuance of invoices, receipts of non-refundable upfront payments and recognition of deferred revenues.

Research and development expenses

Research and development costs are expensed as incurred. Research and development costs include salaries, unit-based compensation, and benefits for employees performing research and development activities, an allocation of facility and overhead expenses, expenses incurred under agreements with consultants, third-party organizations and vendors that conduct research and pre-clinical activities, regulatory support activities, manufacturing process development activities and provide supplies.

Research and development expenses accruals are estimated based on the level of services performed, progress of the work orders, including the phase or completion of events, and contracted costs. The estimated costs of research and development services provided, but not yet invoiced, are included in accrued expenses and other current liabilities in the consolidated balance sheets. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. To date, there have been no material differences between estimates of such expenses and the amounts actually incurred.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized and recorded in prepaid expenses and other current assets, and then expensed as the related goods are delivered or the services are performed.

Patent costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty of the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Unit-based compensation expense

The Company's unit-based equity awards include issuance of profits interests that are granted to employees and consultants under the 2019 Equity Incentive Plan. Profits interests usually vest over four years and are a separate class of equity with defined rights within the LLC Agreement. A profits interest is an interest in the increase in the value of the Company over the threshold amount, as determined at the time of grant on a per unit basis. The holder, therefore, has the right to participate in distributions of profits only in excess of the threshold amount. The threshold amount is based on the valuation of the common units on or around the grant date.

The Company accounts for profits interests granted in accordance with ASC 718, *Compensation-Stock Compensation* (ASC 718). In accordance with ASC 718, compensation expense is measured at the estimated fair value of the profits interest using the Black-Scholes option-pricing model and is included as compensation expense over the vesting period during which an employee or a consultant provides service in exchange for the award. Unit-based compensation expense is recognized over the awards' vesting period on a straight-line basis and recorded as either research and development or general and administrative expenses in the consolidated statements of operations and comprehensive loss based on the function to which the related services are provided. Forfeitures are accounted for as they occur.

Income taxes

Metagenomi is taxed under the provisions of Sub chapter K- Partners and Partnerships of the Internal Revenue Code. Under those provisions, Metagenomi does not pay federal or state corporate income taxes on its taxable income. Instead, each member includes net operating income or loss for Metagenomi on its individual return.

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Metagenomi Inc. uses the liability method to account for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts of existing assets and liabilities and their tax bases. Deferred tax assets and liabilities are measured using enacted tax rates applied to taxable income in the years in which those temporary differences are expected to be recovered or settled. A valuation allowance is established when necessary to reduce deferred tax assets to the amount expected to be realized.

Metagenomi Inc. assesses the likelihood of deferred tax assets being realized. It provides a valuation allowance when it is more likely than not that some portion or all of a deferred tax asset will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Tax positions that meet the more-likely-than-not threshold are measured at the largest amount of tax benefit that is greater than 50% likely of being realized upon settlement with the taxing authority. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Net loss per unit

The Company calculates basic and diluted net loss per unit in conformity with the two-class method required for participating securities. Under the two-class method, basic net loss per unit is computed by dividing the net loss by the weighted average number of common units outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per unit is computed by dividing the net loss by the sum of the weighted average number of common units outstanding during the period plus the dilutive effects of potentially dilutive securities outstanding during the period. Potentially dilutive securities include incentive units, unvested restricted common units and redeemable convertible preferred units. The dilutive effect of incentive units and unvested restricted common units is computed using the treasury stock method and the dilutive effect of redeemable convertible preferred units is calculated using the if-converted method. For all periods presented, diluted net loss per unit is the same as basic net loss per unit since the effect of including potential dilutive securities is anti-dilutive and incentive units' participation thresholds were not met.

Comprehensive loss

Comprehensive income (loss) is defined as a change in equity of a business enterprise during a period resulting from transactions from non-owner sources. The Company's other comprehensive income (loss) is comprised solely of unrealized gains (losses) on available-for-sale marketable securities. The Company has not recorded any reclassifications from other comprehensive income (loss) to net loss during the periods presented.

Recently issued accounting pronouncements

The Company noted no recently issued accounting pronouncements that will impact its consolidated financial statements and were not adopted by the Company. No new accounting pronouncements were adopted during the year ended December 31, 2022.

3. Fair value measurements

Assets and liabilities recorded at fair value on a recurring basis in the consolidated balance sheets, are categorized based upon the level of judgment associated with inputs used to measure their fair values. The accounting guidance for fair value provides a framework for measuring fair value and requires certain

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disclosures about how fair value is determined. The accounting guidance establishes a three-level valuation hierarchy that prioritizes the inputs to valuation techniques used to measure fair value based upon whether such inputs are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions made by the reporting entity. The three-level hierarchy for the inputs to valuation techniques is briefly summarized as follows:

Level 1 — Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2 — Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3 — Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. An assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. Changes in the ability to observe valuation inputs may result in a reclassification of levels of certain securities within the fair value hierarchy. The Company recognizes transfers into and out of levels within the fair value hierarchy in the period in which the actual event or change in circumstances that caused the transfer occurs.

The Company's financial instruments measured at fair value on a recurring basis consist of Level 1, Level 2, and Level 3 financial instruments. Usually, marketable securities are considered Level 2 when their fair values are determined using inputs that are observable in the market or can be derived principally from or corroborated by observable market data such as pricing for similar securities, recently executed transactions, cash flow models with yield curves, and benchmark securities. In addition, Level 2 financial instruments are valued using comparisons to like-kind financial instruments and models that use readily observable market data as their basis. U.S. Government bonds, corporate debt obligations, commercial paper, government agency obligations and asset-backed securities are valued primarily using market prices of comparable securities, bid/ask quotes, interest rate yields and prepayment spreads and are included in Level 2.

Financial assets and liabilities are considered Level 3 when their fair values are determined using pricing models, discounted cash flow methodologies, or similar techniques, and at least one significant model assumption or input is unobservable. The Company's investments in a convertible promissory note, preferred stock shares and restricted common stock of Affini-T Therapeutics Inc. ("Affini-T") (see Note 5) are Level 3 financial assets.

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The following table summarizes the estimated fair value of the financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy as of December 31, 2021 (in thousands):

	December 31, 2021			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds (included in cash and cash equivalents)	\$ 34,940	\$ 34,940	\$ —	\$ —
U.S. Treasury bills	2,989	2,989	—	—
Government agency obligations	3,028	—	3,028	—
Corporate debt obligations	20,070	—	20,070	—
Commercial paper	29,719	—	29,719	—
Asset-backed securities	13,052	—	13,052	—
Long-term investments (Note 5)	4,262	—	—	4,262
Total fair value of assets	\$ 108,060	\$ 37,929	\$ 65,869	\$ 4,262

In addition, restricted cash of \$4.1 million as of December 31, 2021, collateralized by the Company's cash equivalents, are financial assets measured at fair value and is a Level 1 financial instruments under the fair value hierarchy.

The following table summarizes the estimated fair value of the financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy as of December 31, 2022 (in thousands):

	December 31, 2022			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds (included in cash and cash equivalents)	\$ 182,441	\$ 182,441	\$ —	\$ —
U.S. Treasury bills	14,821	14,821	—	—
U.S. Government bonds	14,651	—	14,651	—
Government agency obligations	22,468	—	22,468	—
Corporate debt obligations	25,900	—	25,900	—
Commercial paper	88,447	—	88,447	—
Asset-backed securities	11,403	—	11,403	—
Long-term investments (Note 5)	5,651	—	—	5,651
Total fair value of assets	\$ 365,782	\$ 197,262	\$ 162,869	\$ 5,651

In addition, restricted cash of \$6.1 million as of December 31, 2022, collateralized by the Company's cash equivalents, are financial assets measured at fair value and is a Level 1 financial instruments under the fair value hierarchy.

In December 2020, the Company entered into a convertible promissory note agreement and a side letter with Affini-T (see Note 5), and recorded an aggregate \$1.5 million investment in Affini-T within long-term investments on the consolidated balance sheet related to (i) the Affini-T Convertible Promissory Note and (ii) shares of Affini-T's common stock. The Company concluded it exercised significant influence over Affini-T, and the Company elected the fair value method to account for the investment in Affini-T. The fair value of

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common stock shares was estimated by the Company's management, considering the most recent third-party valuation, which was based on an option-pricing model and Affini-T's most recent round of financing.

During the year ended December 31, 2021, the Company recognized an aggregate \$2.8 million change in fair value of its investment in Affini-T within the change in fair value of long-term investments in the consolidated statement of operations and comprehensive loss consisting of a \$2.5 million change in fair value of the Affini-T Convertible Promissory Note and a \$0.3 million change in fair value of the shares of Affini-T common stock. As of December 31, 2021, the aggregate fair value of the Company's investment in Affini-T was \$4.3 million, of which \$4.0 million related to the Affini-T Convertible Promissory Note and \$0.3 million related to the shares of Affini-T common stock.

In March 2022, the Company's investment in the Affini-T Convertible Promissory Note was converted into shares of convertible preferred stock, resulting in no convertible note outstanding as of December 31, 2022 (see Note 5). The fair value of the convertible preferred stock shares was based on cash paid per share by third party investors. During the year ended December 31, 2022, the Company recognized a change in fair value of the Affini-T Convertible Promissory Note of \$0.1 million within the change in fair value of long-term investments in the consolidated statement of operations and comprehensive loss. There was no change in the fair value of the shares of Affini-T common stock during the year ended December 31, 2022.

As of December 31, 2021, the fair value of the Affini-T Convertible Promissory Note was estimated using the fair value of preferred stock using Affini-T's recent valuation and future payments discounted at a rate of 6%. As of the date of the conversion, the fair value was estimated as \$4.1 million, which was the fair value of the convertible preferred stock issued upon the conversion and as of December 31, 2022.

There were no transfers between Level 1 and Level 2 categories in the years ended December 31, 2021 and 2022. As of December 31, 2021 and 2022, the Company's investments in Affini-T were accounted as Level 3 investments and recorded at fair value.

4. Available-for-sale marketable securities

The following table summarizes the amortized cost, unrealized gains (losses) and estimated fair value of the available-for-sale marketable securities as of December 31, 2021 (in thousands):

	Amortized cost	Unrealized gains	Unrealized losses	Estimated fair value
Money market funds	\$ 34,940	\$ —	\$ —	\$ 34,940
U.S. Treasury obligations	2,989	—	—	2,989
Government agency obligations	3,031	—	(3)	3,028
Corporate debt obligations	20,083	—	(13)	20,070
Commercial paper	29,719	—	—	29,719
Asset-backed securities	13,057	—	(5)	13,052
Total	103,819	—	(21)	103,798
Less: amounts classified as cash equivalents	(34,940)	—	—	(34,940)
Total available-for-sale marketable securities	\$ 68,879	\$ —	\$ (21)	\$ 68,858

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The following table summarizes the amortized cost, unrealized gains (losses) and estimated fair value of the available-for-sale marketable securities as of December 31, 2022 (in thousands):

	Amortized cost	Unrealized gains	Unrealized losses	Estimated fair value
Money market funds	\$ 182,441	\$ —	\$ —	\$ 182,441
U.S. Treasury bills	14,818	3	—	14,821
U.S. Government bonds	14,720	—	(69)	14,651
Government agency obligations	22,431	41	(4)	22,468
Corporate debt obligations	26,041	10	(151)	25,900
Commercial paper	88,447	—	—	88,447
Asset-backed securities	11,508	—	(105)	11,403
Total	360,406	54	(329)	360,131
Less: amounts classified as cash equivalents	(182,441)	—	—	(182,441)
Total available-for-sale marketable securities	\$ 177,965	\$ 54	\$ (329)	\$ 177,690

As of December 31, 2021 and 2022, no significant facts or circumstances were present to indicate a deterioration in the creditworthiness of the issuers of the available-for-sale securities, and the Company has no requirement or intention to sell these securities before maturity or recovery of their amortized cost basis. The Company considered the current and expected future economic and market conditions and determined that its investments were not significantly impacted. For all securities with a fair value less than its amortized cost basis, the Company determined the decline in fair value below amortized cost basis to be immaterial and non-credit related, and therefore no allowance for losses has been recorded. During the years ended December 31, 2021 and 2022, the Company did not recognize any impairment losses on its investments.

The Company's policy is to exclude the applicable accrued interest from both the fair value and the amortized cost basis of its available-for-sale securities for purposes of identifying and measuring an impairment. The Company presents accrued interest receivable related to the available-for-sale securities in prepaid expenses and other current assets, separate from available-for-sale marketable securities in the consolidated balance sheets. As of December 31, 2021 and 2022, accrued interest receivable was \$0.2 million and \$0.3 million, respectively. The Company's accounting policy is to not measure an allowance for credit losses for accrued interest receivables and to write-off any uncollectible accrued interest receivable as a reversal of interest income in a timely manner, which it considers to be in the period in which the Company determines the accrued interest will not be collected. The Company has not written off any accrued interest receivables for the years ended December 31, 2021 and 2022.

The amortized cost and fair value of available-for-sale marketable securities by contractual maturity were as follows as of December 31, 2021 (in thousands):

	Amortized cost	Estimated fair value
Maturing within one year	\$ 67,318	\$ 67,298
Maturing in one to five years	1,561	1,560
Total available-for-sale marketable securities	\$ 68,879	\$ 68,858

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The amortized cost and fair value of available-for-sale marketable securities by contractual maturity were as follows as of December 31, 2022 (in thousands):

	Amortized cost	Estimated fair value
Maturing within one year	\$ 163,259	\$ 163,030
Maturing in one to five years	14,706	14,660
Total available-for-sale marketable securities	<u>\$ 177,965</u>	<u>\$ 177,690</u>

5. Long-term investments

Affini-T investment

In December 2020, the Company entered into a convertible promissory note agreement and a side letter with Affini-T, a private biotechnology company. The Company participated with other investors in Affini-T's convertible notes financing and paid cash of \$1.5 million as a principal amount of a convertible promissory note with 6% annual interest and maturity in December 2021. The Affini-T Convertible Promissory Note was convertible in Affini-T's next qualifying round of financing at a conversion price equal to the lesser of (i) 85% of the price per share paid by other investors (or 80% if the qualified financing occurs after June 24, 2021) or (ii) the price per share obtained by dividing \$30.0 million by the number of shares of common stock of Affini-T outstanding immediately prior to the qualified financing. In accordance with the side letter, the Company was engaged to perform the testing of its gene editing system to knock-in T-cell receptor ("TCR") targets in primary T-cells as selected by Affini-T. As consideration for services, the Company received 1,867,300 shares of restricted common stock of Affini-T, of which 10% of the shares vested on the issuance date and 90% shares were subject to forfeiture if no gene editing licensing agreement was finalized between the Company and Affini-T by October 31, 2021. Effective November 1, 2021, 1,653,570 shares of restricted common stock issued to the Company were forfeited and cancelled as a license agreement was not signed between the parties.

In March 2022, Affini-T closed a qualifying round of financing, and the Affini-T Convertible Promissory Note and accrued interest were converted into 527,035 Series A convertible preferred stock shares of Affini-T. The Company accounted for its investments in the Affini-T Convertible Promissory Note and convertible preferred stock at fair value (see Note 3).

The Company performed a VIE analysis and concluded that it was not a primary beneficiary of Affini-T. The Company concluded that it exercised significant influence over Affini-T until November 2021, when shares of restricted common stock were forfeited and the Company's former chief business officer, who was also the founder and chief executive officer of Affini-T, resigned. The Company accounted for its investment in 213,730 shares of Affini-T common stock at fair value of \$0.3 million for each of the periods ending December 31, 2021 and 2022 (see Note 3).

In June 2022, the Company entered into a Development, Option and License Agreement with Affini-T to perform research and development activities (see Note 7). The Company received an upfront equity consideration of 719,920 shares of Affini-T's common stock with an estimated fair value of \$1.3 million in June 2022. The fair value of common shares was estimated by the Company's management, considering the most recent third-party valuation. No impairment loss was recognized on the Company's investment in Affini-T as of December 31, 2021 and 2022.

ViTToria investment

The Company purchased 603,262 Series Seed-2 convertible preferred stock shares of ViTToria Biotherapeutics, Inc. ("Vittoria"), a private biotechnology company, for a total of \$2.2 million cash in July and December 2021.

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During the years ended December 31, 2021 and 2022, the Company did not have a board seat and owned less than 20% of outstanding voting shares of Vittoria. The investment in Vittoria does not provide the Company the ability to control or have significant influence over Vittoria's operations. The Company accounted for the investment in Vittoria's Series Seed-2 convertible preferred stock using the measurement alternative method. The fair value of the investment was estimated by management using per share price of \$3.57, which was the price paid for convertible preferred stock shares by other investors. As of December 31, 2021 and 2022, the carrying value of Vittoria's investment was \$2.2 million and no impairment was recognized.

6. Consolidated balance sheets components

Property and equipment, net consists of the following (in thousands):

	Useful life	December 31,	
		2021	2022
Laboratory equipment	5	\$ 3,029	\$ 13,455
Leasehold improvements	lesser of useful life or the lease term	293	3,531
Furniture and fixtures	3	190	328
Computers and related equipment	3	16	54
Construction in progress		887	1,402
Total property and equipment		4,415	18,770
Less: Accumulated depreciation and amortization		(553)	(2,248)
Total property and equipment, net		\$ 3,862	\$ 16,522

The depreciation and amortization expense was \$0.4 million and \$1.7 million for the years ended December 31, 2021 and 2022, respectively.

Prepaid expenses and other current assets consist of the following (in thousands):

	December 31,	
	2021	2022
Payroll tax credit	\$ 300	\$ 289
Interest receivable on available-for-sale marketable securities	190	261
Prepaid research and development expenses	—	685
Grant income receivable	—	125
Other prepaid expenses and other current assets	272	2,134
Total prepaid expenses and other current assets	\$ 762	\$ 3,494

Other assets consist of the following (in thousands):

	December 31,	
	2021	2022
Operating lease deposit	\$ 276	\$ 237
Prepaid property and equipment	250	—
Long-term prepaid services	—	213
Deferred finance issuance costs	143	—
Total other assets	\$ 669	\$ 450

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Accrued expenses and other current liabilities consist of the following (in thousands):

	December 31,	
	2021	2022
Accrued personnel related expenses	\$ 2,244	\$ 4,819
Accrued legal and professional services	414	1,200
Accrued purchases of property and equipment	382	896
Accrued research and development expenses	147	1,684
Other accrued liabilities	344	191
Total accrued expenses and other current liabilities	\$ 3,531	\$ 8,790

7. Significant agreements

Moderna strategic collaboration and license agreement

Terms of the agreement

On October 29, 2021, the effective date, the Company entered into a Strategic Collaboration and License Agreement (the "Moderna Agreement") with ModernaTX, Inc. ("Moderna"). The parties will collaborate on the research and development of *in vivo* genome editing therapies directed at certain targets and the commercialization of such genome editing therapies. The collaboration provides Moderna with exclusive access to the Company's technology platform during the research period in (1) the field of *in vivo* gene editing technology for a therapeutic, ameliorative or prophylactic application by way of knock-out through InDel formation or base editing or insertion of an exogenous DNA template (such field, "DT Field") and (2) the field of *in vivo* gene editing technology for a therapeutic, ameliorative or prophylactic application outside the use of (a) DNA donor templates and (b) no exogenous template at all but including (c) correction by base editing (such field, "RT Field"). The parties formed a joint steering committee, a joint research subcommittee and a joint patent subcommittee to oversee the collaboration activities.

Under the terms of the Moderna Agreement, the parties will collaborate on one or more programs in the RT Field (the "Moderna RT program") and two programs in the DT Field (the "Moderna DT program" and the "DT Co-Co program").

With respect to the Moderna RT and Moderna DT programs, the parties will collaborate on the research and development of product candidates under the approved research plans. The initial research term of the Moderna RT program is four years, which may be extended by Moderna for an additional three years upon written notice and a payment of extension fees. The initial research term of the Moderna DT program is four years. The Company granted to Moderna an option to obtain an exclusive license to develop, manufacture and commercialize up to ten Moderna RT program candidates and up to two Moderna DT program candidates at any time during the research term and prior to filing of an investigational new drug ("IND") application with the Food Drug and Administration ("FDA") or any similar application filed with a regulatory authority in a country other than the United States ("U.S."), subject to Moderna's payment of an option exercise fee of \$10.0 million per target.

With respect to the DT Co-Co program, the parties will work together on the co-development and commercialization of products and share costs and profits equally. The Company maintains commercialization rights in the U.S. (subject to Moderna's right to appoint up to 50% of the U.S. sales force for the DT Co-Co program), while Moderna maintains these rights in countries other than the U.S. The initial research term for the DT Co-Co program is four years, and each party has a right to opt-out of the DT Co-Co program at any time, at which point the other party has the right to solely continue the development and commercialization activities. If there is no development candidate nomination by the end of the initial research term, the DT Co-Co program will expire, unless the parties have mutually agreed to continue the program.

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During the year ended December 31, 2021, the Company received a non-refundable upfront payment of \$40.0 million and a \$5.0 million payment for the first year of research costs. Concurrent with the Moderna Collaboration Agreement, Moderna also provided \$30.0 million in cash in the form of a convertible promissory note (see Note 9) pursuant to a convertible promissory note agreement dated October 29, 2021 (the "Moderna Convertible Promissory Note Agreement"). Moderna will reimburse the Company up to \$5.0 million in annual research and development costs related to the Moderna DT and Moderna RT programs, or up to the agreed amount of expenses per the budget.

For the Moderna RT and Moderna DT programs, the Company is eligible to receive (i) technology milestone fees related to the achievement of certain preclinical research objectives of up to \$75.0 million, (ii) development and regulatory milestones of up to \$100.0 million per target, (iii) sales milestones of up to \$200.0 million per target, and (iv) royalties ranging from a mid-single digit to a low-teens percentage of annual net sales of a licensed product. Any profits and losses from the co-development and commercialization of the DT Co-Co program are shared equally between the Company and Moderna. With respect to the DT Co-Co program for which the opt-out party has exercised its opt-out right, the continuing party will pay to the opt-out party, certain development, regulatory and sales milestone payments that will not exceed an aggregate \$239.0 million per DT Co-Co target, and opt-out royalties ranging from a high-single digit to a low-teens percentage of annual net sales of a licensed product.

The term of the Moderna Agreement will continue on a licensed product-by-licensed product and country-by-country basis, until the expiration of the applicable royalty term. The royalty term commences on the first commercial sale of a licensed product and terminates on the latest of: (a) the expiration or abandonment of the last valid claim of a patent within the licensed Moderna DT or RT technology; (b) 10 years after the first commercial sale of a licensed product; and (c) expiration of the regulatory exclusivity. Upon the expiration of the term of a licensed product in the Moderna DT or Moderna RT program, the licenses granted to Moderna will survive and become perpetual, fully paid and royalty-free. Each party may terminate the Moderna Agreement on a program-by-program basis upon written notice to the other party for an uncured material breach or insolvency. The Company may terminate the Moderna Agreement upon written notice to Moderna for a patent challenge. Additionally, Moderna may terminate the agreement at its convenience with respect to Moderna DT or Moderna RT programs for any reason upon at least: (a) 60 days' prior written notice if a first commercial sale has not occurred for the products in such program, or (b) 180 days' prior written notice if a first commercial sale of a product in such program has occurred.

Accounting analysis and revenue recognition

The Company concluded that the Moderna DT and Moderna RT programs are in the scope of ASC 606. The Company determined that the licenses granted to Moderna, and its participation in the joint steering committee are not capable of being distinct from the preclinical research and development services and therefore concluded that there are two performance obligations: (1) the Moderna RT program and (2) the Moderna DT program. The Company also concluded that the option to obtain an exclusive license and options to extend Moderna RT program term do not include significant incremental discounts, and as such, the options do not provide material rights.

The Company concluded the DT Co-Co program research activities are within the scope of ASC 808, as the Company and Moderna are both active participants in the research, development and commercialization activities, are exposed to significant risks and rewards that are dependent on the success of the DT Co-Co program activities and share costs and profits equally. The Company determined that the guidance in ASC 730, *Research and Development*, was appropriate to apply to the DT Co-Co program research activities by analogy, based on the nature of the cost sharing provisions of the agreement. The Company concluded that DT Co-Co

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program is one unit of accounting, as the co-exclusive license is not distinct from the research and development and the participation in joint steering committee activities. The Company recognizes payments to or from Moderna related to the DT Co-Co program cost sharing research activities as an increase to or reduction of research and development expenses, respectively.

The Company concluded that the Moderna Collaboration Agreement and the Moderna Convertible Promissory Note Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. The Company estimated the contract consideration to be \$90.0 million, which consisted of: 1) the non-refundable upfront collaboration payment of \$40.0 million received in 2021, 2) \$30.0 million in cash received in 2021 in exchange for the convertible promissory note and 3) the estimated cost reimbursements for Moderna DT and Moderna RT programs of \$20.0 million. The Company constrained future milestones, as it assessed that it is probable that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in future periods. During the year ended December 31, 2021, the Company recorded \$30.0 million of the contract consideration for the convertible promissory note based on the fair value (see Note 9) and allocated the transaction price of \$60.0 million to each of the following programs on a relative standalone selling price basis: 1) \$49.5 million to the Moderna RT program, 2) \$5.5 million to the Moderna DT program, and 3) \$5.0 million to the DT Co-Co program.

The variable consideration is reevaluated at each reporting period and as changes in circumstances occur. The Company recognizes revenue for each of the Moderna DT and Moderna RT programs as collaboration revenue based on the measure of progress using an estimated cost-based input method each reporting period. The Company also amortizes the allocation consideration for the DT Co-Co program of \$5.0 million as a credit to research and development expenses during the discovery and lead optimization phases for the DT Co-Co program.

The Company recognized collaboration revenue of \$0.2 million and \$14.5 million in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2021 and 2022, respectively. As of December 31, 2021 and 2022, deferred revenue related to Moderna was \$39.7 million and \$30.2 million, respectively. Collaboration revenue recognized during the year ended December 31, 2022 included \$14.5 million that was included in deferred revenue as of December 31, 2021. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligations was approximately \$41.9 million as of December 31, 2022, which the Company expects to recognize as revenue over the next three-to-four years.

The Company recognized \$0.2 million and \$0.3 million in credits to research and development expenses related to cost sharing allocation and amortization of the collaboration advance, respectively, within research and development expenses in the consolidated statement of operations and comprehensive loss during the year ended December 31, 2021. The Company recognized \$0.9 million and \$3.5 million in credits to research and development expenses related to cost sharing allocation and amortization of the collaboration advance, respectively, during the year ended December 31, 2022. As of December 31, 2021, the collaboration advance balance was \$4.7 million, partially offset by the cost-sharing receivable balance of \$0.2 million, which was presented as a collaboration advance on the Company's consolidated balance sheet. As of December 31, 2022, the collaboration advance balance was \$1.1 million, partially offset by the cost-sharing receivable balance of \$0.4 million, which was presented as a collaboration advance on the Company's consolidated balance sheet.

Affini-T development, option and license agreement

Terms of the agreement

On June 14, 2022, the effective date, the Company entered into a Development, Option and License Agreement (the "Affini-T Agreement") with Affini-T. Pursuant to the Affini-T Agreement, the parties have agreed to identify,

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develop or optimize certain reagents using the Company's proprietary technology for Affini-T to use such reagents to develop and commercialize gene edited T-cell receptor ("TCR")-based therapeutic products exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with any engineered primary TCR alpha/beta T cells and non-exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with certain other engineered immune cells worldwide. A joint steering committee was established by both parties to assign alliance managers and project leaders to oversee the collaboration activities.

Pursuant to the Affini-T Agreement, the Company granted Affini-T options to receive, on a pre-specified target-by-pre-specified target basis, for up to six pre-specified targets, either (i) an exclusive, royalty-bearing, sublicensable worldwide license under all of the Company's applicable intellectual property to research, develop, manufacture, use, commercialize and otherwise exploit any TCR-based therapy, preventative treatment, or diagnostic for humans that is directed to such pre-specified target, contains or comprises Primary TCR alpha/beta T Cells and is derived from *ex vivo* application of a Company reagent (the "Exclusive Option") or (ii) a non-exclusive, royalty-bearing, sublicensable worldwide license under all of the Company's applicable intellectual property to research, develop, manufacture, use, commercialize and otherwise exploit any TCR-based therapy, preventative treatment, or diagnostic for humans that is directed to such pre-specified target, contains or comprises TCR natural killer ("NK") cells derived from iPSC immune cells or TCR T cells derived from donor-derived or iPSC immune cells. Affini-T can exercise its options for either an exclusive license or a non-exclusive license, or both, for each pre-specified target by providing written notice prior to the earlier of (x) the end of the Affini-T Agreement term or (y) 90 days following the filing of an IND for a licensed product directed to a pre-specified target, subject to the payment of certain fees per each option exercised. After the option exercise, Affini-T has agreed to use commercially reasonable efforts to conduct all development and commercialization activities for a licensed product, and development and commercialization of all licensed products will be at Affini-T's sole cost and expense.

In connection with the Affini-T Agreement, the Company received upfront equity consideration of 719,920 shares of Affini-T's common stock with an estimated fair value of \$1.3 million in June 2022. The fair value of Affini-T's shares of common stock was estimated by the Company's management, considering the most recent third-party valuation. Affini-T has also agreed to reimburse the Company for expenses incurred while performing research activities under the research plans. Additionally, the Company is eligible to receive (i) 933,650 shares of Affini-T's common stock upon the achievement of a regulatory milestone, which is the earlier of a submission of a drug master file to the FDA or an acceptance of an IND filing for a licensed product by the FDA, (ii) up to \$18.8 million in future developmental milestone payments depending on the completion of or the number of patients dosed in, the relevant human clinical trial, or the initiation of a pivotal trial, and \$40.6 million in future regulatory approval milestone payments, which include regulatory approvals in the U.S. and other markets for licensed products directed to a pre-specified target if options for both exclusive and non-exclusive licenses are exercised with respect to such target, (iii) up to \$250.0 million in sales-based milestones for aggregate sales of all licensed products directed to a given pre-specified target and (iv) royalties ranging from a low-single digit to high-single digit percentage of worldwide annual net sales of licensed products.

The initial term of the Affini-T Agreement is five years from the effective date. If Affini-T exercises an Exclusive Option with respect to any pre-specified target during the initial term, the initial term will be extended by an additional five years. Following the expiration of the extended term, if any, the agreement will continue on a target-by-target basis and expire with respect to such target upon the expiration of the royalty term for all licensed products directed to such target. The Affini-T Agreement may be terminated during the term by either party for an uncured material breach by, or bankruptcy of, the other party. Additionally, Affini-T may terminate the Affini-T Agreement for convenience, in its entirety, on a research plan-by-research plan basis, on a target-by-target basis or on a licensed product-by-licensed product basis, by providing prior written notice.

Accounting analysis and revenue recognition

The Company concluded that the Affini-T Agreement is in the scope of ASC 606 and that there is one performance obligation to perform research activities under the Affini-T Agreement. Exclusive and non-exclusive licenses are optional contingent purchases that do not include significant incremental discounts, and therefore do not provide a material right.

At the effective date, the transaction price consisted of the upfront equity consideration with an estimated fair value of \$1.3 million and estimated research reimbursement costs. Research reimbursement costs represent variable consideration, and the Company's management estimates what portion to include in total consideration at the end of each reporting period. Other payments under the Affini-T Agreement, including additional equity consideration and development and regulatory milestones, also represent variable consideration, and are constrained to the extent that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in future periods. As of December 31, 2022, additional equity consideration and future development and regulatory milestone payments were excluded from the estimated total transaction price as they were considered constrained. The transaction price is reevaluated in each reporting period and as changes in circumstances occur. The Company recognizes revenue each reporting period based on the measure of progress using an estimated cost-based input method.

The Company recognized \$2.6 million in collaboration revenue in the consolidated statements of operations and comprehensive loss during the year ended December 31, 2022. As of December 31, 2022, the Company recorded \$1.3 million in contract assets on the consolidated balance sheet, related to services performed but not invoiced. There was no deferred revenue related to the Affini-T Agreement as of December 31, 2022. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligation was approximately \$8.0 million as of December 31, 2022, which the Company expects to recognize as revenue over the next five-to-six years. In June 2023, the joint steering committee approved the budget for estimated research reimbursement costs for the Affini-T Agreement, which resulted in a \$2.4 million reduction to variable consideration.

Ionis collaboration and license agreement

Terms of the agreement

On November 10, 2022, the effective date, the Company entered into a Collaboration and License Agreement (the "Ionis Agreement") with Ionis Pharmaceuticals, Inc. ("Ionis") to collaborate on drug discovery and exploratory research activities to advance new medicines using gene editing strategies, with the goal of discovering novel medicines. Pursuant to the terms of the Ionis Agreement, the Company granted Ionis and its affiliates a worldwide exclusive, royalty-bearing license, with the right to grant sublicenses, to use all licensed systems and licensed products in the field of *in vivo* gene editing for all therapeutic, prophylactic, palliative, and analgesic uses in humans. In connection with the Ionis Agreement, the Company also has the right to exercise an exclusive option to co-develop and co-commercialize certain products under a drug discovery program. A joint steering committee was established by both parties to coordinate, oversee, and monitor the research and drug discovery activities under the Ionis Agreement.

The parties will collaborate to discover therapeutic products under a drug discovery program and develop a drug discovery plan for each target, selected by Ionis. The target selection is divided into two waves: up to four targets in Wave 1 and up to four targets in Wave 2. For each drug discovery program, once the parties identify a development candidate that is suitable for further development, Ionis will be responsible for the development and commercialization of products resulting from such program. Per the terms of the Ionis Agreement, at any time prior to the designation of a development candidate for a drug discovery program and for any reason, Ionis may replace the collaboration target, provided such target has not previously been substituted out. Ionis may substitute (i) up to two Wave 1 targets and (ii) up to two Wave 2 targets.

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The drug discovery activities for a program commence on the selection of a target and expire upon the earlier of (a) completion of all drug discovery activities for such program, (b) the fifth anniversary of the effective date and (c) selection of a development candidate for such drug discovery program. If one or more Wave 2 targets become collaboration targets as a result of the parties achieving enabled delivery and less than two years are remaining in the drug discovery term, then the term will be extended to the earlier of (i) the time that the Company completes all of its activities under the applicable drug discovery plan and (ii) the seventh anniversary of the effective date, subject to the Company's consent.

The parties will also conduct an exploratory research program, and will jointly optimize gRNA and select delivery technologies and other activities. The exploratory research activities commence on the effective date and expire upon the earlier of (a) completion of all exploratory research activities established in the exploratory research plan, and (b) the fifth anniversary of the effective date.

The Company has the exclusive option to co-develop and co-commercialize the licensed products under a drug discovery program (the "Co-Co Option") with Ionis. The Co-Co Option may be exercised for (a) the initial Wave 1 target ("Target 1"), (b) no more than one of the other three discovery programs for the Wave 1 targets, and (c) no more than two drug discovery programs for the Wave 2 targets that become collaboration targets. If the Company exercises the Co-Co Option for a particular drug discovery program, that drug discovery program will automatically be deemed a "Co-Co Program", all corresponding licensed products be deemed "Co-Co Products," the Company will be obligated to pay Ionis an option exercise fee, and the parties will enter into a separate co-development and co-commercialization agreement. The Co-Co Option exercise fee will equal 50% of Ionis' internal costs and out-of-pocket costs incurred in the conduct of the drug discovery activities prior to the exercise of the Co-Co Option and be reduced by 50% of the Company's corresponding costs incurred. Future development and commercialization costs will be shared equally. The Company may elect to reduce its cost-share percentage anywhere between 50% and 25% on a go-forward basis, provided the Company will continue to bear 50% of the costs of any clinical trials ongoing at the time of the election through the completion of the clinical trials.

The Company will manufacture all licensed systems and certain components of the applicable licensed products that are needed by Ionis for use in its development activities and all of the Company's manufactured components needed by Ionis for use in its commercialization activities. The Company will provide the manufactured components at a price that represents the cost of goods plus 15%.

Pursuant to the terms of the Ionis Agreement, the Company has also been granted an option to obtain a non-exclusive, royalty-bearing license, with the right to grant sublicenses, for certain Ionis' background technology to use in up to eight therapeutic products discovered by the Company in the field of *in vivo* gene editing and directed to a Collaboration Target (each such product, a "Metagenomi Product" and each such option an "Ionis IP Option"), but subject to encumbrance checks with respect to particular targets. A Collaboration Target is a target that is selected by Ionis, and, with respect to the Company is not the subject of discussions with a third party, is not the subject of a contractual grant of rights to a third party nor the subject of a Company bona fide research and development program. If the Company exercises its Ionis IP Option, the Company will pay to Ionis up to several million dollars per Metagenomi Product upon achievement of certain clinical and regulatory milestones. The Company is also obligated to pay Ionis royalties in an amount equal to a low single-digit royalty on the net sales of the applicable Metagenomi Product on product-by-product and country-by-country basis.

In November 2022, the Company received an \$80.0 million upfront payment from Ionis for the Wave 1 drug discovery research collaboration and selected Target 1. Ionis selected its second target ("Target 2") in Wave 1 in December 2022, and will select two final additional Wave 1 targets ("Target 3" and "Target 4") within the 12 months from the effective date, as permitted under the arrangement. Ionis has an option to select up to four

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Wave 2 targets at any time during the drug discovery term, if (a) an IND for any licensed product directed to a Wave 1 target is filed with the applicable regulatory authority or (b) the parties achieve enabled delivery for a non-liver target under the exploratory research activities, by providing written notice and by paying a Wave 2 target selection fee of \$15.0 million or \$30.0 million, depending on and per the selected target.

Ionis is obligated to reimburse the Company for all internal costs and out-of-pocket costs incurred in the performance of the exploratory research activities, up to an aggregate of \$10.0 million, which is payable in quarterly installments of \$0.5 million during the exploratory research term. The Company is also eligible to receive (a) up to \$29.0 million in future development milestone payments for each licensed product; (b) up to \$60.0 million in future regulatory milestone payments for each licensed product; (c) up to \$250.0 million in sales-based milestones for each licensed product; and (d) royalties on annual net sales of licensed products from a mid-single-digit to low-teens percentage, subject to customary reductions.

The term of the Ionis Agreement will continue (i) with respect to the drug discovery programs, until the expiration of all applicable royalty terms for a licensed product, (ii) with respect to the Co-Co Programs, until the parties cease all exploitation for the Co-Co Products that are the subject to such Co-Co Program, and (iii) with respect to the Metagenomi Products, until the expiration of the royalty term for a Metagenomi Product. The royalty term ends on the latest of the following two dates: (i) the expiration of (A) the last claim of any issued and unexpired patent, or (B) a claim within a patent application that has not been pending for more than seven years from the earliest date to which the claim or applicable patent application is entitled to claim priority and which claim has not been revoked, cancelled, withdrawn, held invalid, or abandoned, or (ii) 12 years following the first commercial sale of a licensed product.

The Ionis Agreement may be terminated during the term by either party for an uncured material breach or bankruptcy by the other party. Additionally, Ionis may terminate the Ionis Agreement for convenience and without penalty, in its entirety or on a licensed product-by-licensed product basis, by providing 90 days' written notice.

Accounting analysis and revenue recognition

The Company concluded that the Ionis Agreement is in the scope of ASC 606 at the effective date and until the Company exercises its Co-Co Option for any drug discovery program, which was determined to not be probable at the effective date and as of December 31, 2022. The Company also concluded that exclusive licenses and participation in a joint steering committee are not distinct from discovery research services and should thus be combined into one performance obligation (the "discovery program"). The Company also concluded that exploratory research services are a separate and distinct performance obligation (the "exploratory program"). As the Ionis options for Wave 2 targets are optional purchases and do not have significant incremental discounts, as such, the options do not provide material rights.

The Company allocated the total estimated transaction price of \$90.0 million, which consisted of an \$80.0 million upfront payment received in November 2022 and a \$10.0 million reimbursement for research costs, into two performance obligations, and was determined based on their estimated standalone selling prices. The Company concluded that future development and commercial supply agreements are at market terms, as the terms were consistent with industry standards as of the effective date. The Company constrains future milestone payments under the arrangement to the extent that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in future periods. The Company constrained all development and regulatory milestone payments at the effective date and as of December 31, 2022. The Company is recognizing revenue of \$80.0 million related to the discovery program and of \$10.0 million related to exploratory program over the research terms using an estimated cost-based input method as a measure of progress for each obligation.

The Company recognized \$0.1 million in collaboration revenue in the consolidated statements of operations and comprehensive loss during the year ended December 31, 2022. As of December 31, 2022, deferred revenue

related to the Ionis Agreement was \$79.9 million. The value of the transaction price allocated to the remaining performance obligations was approximately \$89.9 million as of December 31, 2022, which the Company expects to recognize as revenue over the next five-to-six years.

8. Cystic fibrosis foundation grant income

In April 2021, the Company received an award of \$0.6 million to finance a development program (the "CFF Grant Letter"), to discover and use novel gene-editing systems to correct cystic fibrosis transmembrane conductance regulator mutations, from Cystic Fibrosis Foundation ("CFF"), a non-profit organization. In accordance with CFF Grant Letter, the Company received \$0.4 million upon initiation of the development program in June 2021 and expects to receive \$0.2 million upon the program completion in 2023 fiscal year. The award was provided to the Company without a provision for financial return to CFF. However, in the event that CFF provides additional funding to the Company, pursuant to a separate agreement between CFF and the Company (a "Future Funding Agreement"), CFF may receive royalty rights, an equity interest, a debt instrument or other consideration of economic value that is based on the amount of funding CFF has provided to the Company, the award amount actually paid to the Company under the current award will be treated as an advance towards, and included in, the award amount, investment amount, principal amount or other similar term representing the amount of funding provided by CFF to the Company under the Future Funding Agreement. The Company does not expect to receive any future funding from CFF and concluded that funds received are non-refundable. The Company recognized \$0.2 million and \$0.3 million related to the progress of a development program during the years ended December 31, 2021 and 2022, respectively, as other income (expense), net, in the consolidated statements of operations and comprehensive loss, as this grant is not considered an ongoing major and central operation of the Company's business. The Company recognized \$0.2 million and zero of deferred grant income in accrued expenses and other current liabilities in the consolidated balance sheet as of December 31, 2021 and December 31, 2022, respectively. The Company recognized \$0.1 million of grant income receivable in prepaid expenses and other current assets in the consolidated balance sheets as of December 31, 2022.

9. Convertible promissory note

In October 2021, together with the Moderna Agreement, the Company issued a convertible promissory note for \$30.0 million to Moderna with 6.0% annual interest payable upon the note maturity in April 2023. The Company cannot prepay the convertible promissory note without Moderna's consent. The outstanding principal amount and any unpaid accrued interest is automatically convertible into redeemable convertible preferred units sold in a private financing with total gross cash proceeds of not less than \$50.0 million (the "Qualified Financing") at a conversion price equal to the purchase price per unit that depends on the timing of the qualified financing: i) 100% of the lowest price paid per unit by investors in the qualified financing, if the qualified financing occurs within three months from the note issuance date; ii) 95% of the lowest price paid per unit by investors in the qualified financing, if the qualified financing occurs between three and six months from the note issuance date; iii) 90% of the lowest price paid per unit by investors in the qualified financing, if the qualified financing occurs between six and twelve months from the note issuance date; iv) 85% of the lowest price paid per unit by investors in the qualified financing, if the qualified financing occurs after twelve months from the note issuance date.

Moderna also had an option to convert the note on similar terms in the event of a non-qualified financing using the conversion price upon a qualified financing. Upon maturity, the outstanding principal and accrued interest is either due and payable in full or converted in the Series A-5 redeemable convertible preferred units (or the most senior redeemable convertible preferred units of the Company then outstanding) at a conversion price equal to the original issue price of the Series A-5 redeemable convertible preferred units (or the most senior units of the Company then outstanding). Principal and accrued interest of the note were payable in cash in an

event of default. In a deemed liquidation event the outstanding principal and accrued and unpaid interest is either due and payable in full, plus 50% on the outstanding principal amount of the note or were convertible into the common units of the Company at a conversion price equal to the original issue price of the Series A-5 redeemable convertible preferred units (or the most senior units of the Company then outstanding). In the event that the Company closes its initial public offering of its common units or common stock or other equity securities with total gross proceeds of not less than \$50.0 million ("Qualified IPO"), the principal and unpaid accrued interest then outstanding is convertible automatically into the same type of the Company's securities issued upon IPO at 90% of the lowest purchase price paid per equity securities in the Qualified IPO.

The convertible promissory note is carried at amortized cost, which management estimates approximates its fair value. On the issuance date of the convertible promissory note, the Company concluded that certain embedded unit-settled conversion put features, qualified IPO features and deemed liquidation put features were derivatives that required bifurcation. The Company estimated the fair value of embedded derivatives was minimal due to the low probability of settlement events for these features. The Company recognized \$34,000 of issuance costs as a debt discount related to legal fees, which was amortized to interest expense over the term of the note using effective interest method. The Company recognized \$0.3 million and \$0.1 million of accrued interest expense in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2021 and 2022, respectively.

The convertible promissory note and all accrued interest were converted, upon the Qualified Financing, into 2,607,387 Series B redeemable convertible preferred units without any discount in January 2022 (see Note 11) and no gain or loss was recognized on the conversion.

10. Commitments and contingencies

Operating leases

In November 2019, the Company entered into a 5-year operating lease for laboratory and office space in Emeryville, California. In conjunction with signing the lease, the Company secured a letter of credit in favor of the lessor in the amount of \$0.2 million. The lease agreement includes a renewal provision allowing the Company to extend this lease for an additional 5 years at the prevailing rental rate, which the Company was not reasonably certain to exercise. In addition to base rent, the Company was obligated to pay variable costs related to its share of operating expenses and taxes as well as parking fees for unreserved parking spaces in a shared lot. In March 2021, this lease was modified to shorten the lease term to terminate in April 2021. Lease payments made related to this lease in 2021 totaled \$0.1 million. In May 2021, the letter of credit related to this lease was canceled.

In January 2021, the Company entered into a ten-year operating lease for laboratory and office space in Emeryville, California. The lease commencement date was in February 2021. In conjunction with signing this lease, the Company secured a letter of credit for \$3.3 million, which is recorded as noncurrent restricted cash in the consolidated balance sheets. The lease agreement includes a renewal provision allowing the Company to extend this lease for an additional five years, which the Company is not reasonably certain to exercise. In addition to base rent, the Company pays variable costs related to operating expenses and taxes, which are recognized as incurred.

In September 2021, the Company entered into a 9.25-year operating lease for office space in Emeryville, California, with a lease commencement date in November 2021. In conjunction with signing the lease, the Company secured a letter of credit for \$0.8 million, which is recorded as noncurrent restricted cash in the consolidated balance sheets. In addition to base rent, the Company will pay variable costs related to operating expenses and taxes, which are recognized as incurred.

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In November 2022, the Company entered into an 8.25-year sublease for office, research and laboratory space in Emeryville, California, with a lease commencement date in January 2023. In conjunction with signing the lease, the Company secured a letter of credit for \$2.0 million, which is recorded as restricted cash in the consolidated balance sheet as of December 31, 2022. Payments for base rent required under this lease are expected to total approximately \$49.3 million over the term, of which \$2.9 million is payable within the 12 months. In addition to base rent, the Company will pay variable costs related to its share of operating expenses and taxes. As this lease has not yet commenced as of December 31, 2022, no right-of use asset or lease liability is recorded.

Operating lease cost for the years ended December 31, 2021 and 2022, totaled \$2.2 million and \$3.5 million, respectively, including \$0.5 million and \$0.4 million of variable lease cost, respectively.

Supplemental information related to the Company's operating leases is as follows (in thousands):

	Years ended December 31	
	2021	2022
Cash paid for amounts included in the measurement of lease liabilities	\$ 1,453	\$ 2,158
Weighted average remaining lease term (in years)	9.1	8.1
Weighted-average discount rate	10.1%	10.1%

The following table summarizes a maturity analysis of the Company's operating lease liabilities showing the aggregate lease payments as of December 31, 2022 (in thousands):

2023	\$ 3,279
2024	3,122
2025	3,216
2026	3,313
2027	3,412
Thereafter	10,862
Total future lease payments	27,204
Less imputed interest	(8,633)
Total lease liability balance(1)	18,571
Less: current operating lease liabilities	(1,515)
Non-current operating lease liabilities	\$ 17,056

(1) Total lease liability as of December 31, 2022 excludes lease payments of \$49.3 million for a lease signed but not yet commenced.

Legal contingencies

From time to time, the Company may become involved in legal proceedings arising from the ordinary course of business. The Company records a liability for such matters when it is probable that future losses will be incurred and that such losses can be reasonably estimated. Significant judgment by the Company is required to determine both probability and the estimated amount. Management is currently not aware of any legal matters that could have a material adverse effect on the Company's financial position, results of operations or cash flows.

Guarantees and indemnifications

In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. Its exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To the extent permitted under Delaware law, the

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Company has agreed to indemnify its directors and officers for certain events or occurrences while the director or officer is, or was serving, at a request in such capacity. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2021 and 2022, the Company did not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded related liabilities.

11. Redeemable convertible preferred units

On March 15, 2021, the Company closed the Series A-5 financing and issued 1,580,937 shares of the Series A-5 redeemable convertible preferred units for gross cash proceeds of \$10.0 million. The Company incurred \$0.1 million in issuance costs.

On January 21, 2022, the Company closed the Series B financing and issued 12,446,876 shares of the Series B redeemable convertible preferred units for gross cash proceeds of \$145.0 million. The Company incurred \$0.7 million in issuance costs. Concurrently with the closing of the Series B financing, the outstanding Moderna convertible promissory note and accrued interest of \$30.4 million was converted into 2,607,387 Series B Preferred Units, at a conversion price equal to the price per unit paid by the Series B investors.

On December 20, 2022, the Company entered into Series B-1 redeemable convertible preferred unit purchase agreement to sell up to 7,108,480 Series B redeemable convertible preferred units at the purchase price of \$14.06770. In December 2022, the Company sold and issued 6,773,726 shares of the Series B-1 redeemable convertible preferred units for gross cash proceeds of \$95.3 million in the initial closing. The Company incurred \$0.4 million issuance costs. Additional shares may be sold within 90 days of the initial closing.

As of December 31, 2022, the Company operated under the Amended and Restated Limited Liability Company Agreement dated December 20, 2022 (the "LLC Agreement"). The LLC Agreement provides for eight classes of units: common units, Series A-1 redeemable convertible preferred units (Series A-1), Series A-2 redeemable convertible preferred units (Series A-2), Series A-3 redeemable convertible preferred units (Series A-3), Series A-4 redeemable convertible preferred units (Series A-4), Series A-5 redeemable convertible preferred units (Series A-5), Series B redeemable convertible preferred units (Series B) and Series B-1 redeemable convertible preferred units (Series B-1).

The redeemable convertible preferred units as of December 31, 2021, consisted of the following (in thousands, except unit data):

	Units authorized	Units issued and outstanding	Aggregate liquidation preference	Net carrying value
Series A-1	7,501,002	7,501,002	\$ 24,247	\$ 24,067
Series A-2	774,473	774,473	500	581
Series A-3	1,513,860	1,513,860	1,773	1,892
Series A-4	8,280,360	8,280,360	40,149	40,007
Series A-5	1,580,937	1,580,937	10,000	9,948
	<u>19,650,632</u>	<u>19,650,632</u>	<u>\$ 76,669</u>	<u>\$ 76,495</u>

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The redeemable convertible preferred units as of December 31, 2022, consisted of the following (in thousands, except unit data):

	Units authorized	Units issued and outstanding	Aggregate liquidation preference	Net carrying value
Series A-1	7,501,002	7,501,002	\$ 24,247	\$ 24,067
Series A-2	774,473	774,473	500	581
Series A-3	1,513,860	1,513,860	1,773	1,892
Series A-4	8,280,360	8,280,360	40,149	40,007
Series A-5	1,580,937	1,580,937	10,000	9,948
Series B	15,054,263	15,054,263	175,375	174,678
Series B-1	7,108,480	6,773,726	95,291	94,930
	<u>41,813,375</u>	<u>41,478,621</u>	<u>\$ 347,335</u>	<u>\$ 346,103</u>

The holders of the redeemable convertible preferred units have various rights and preference as follows:

Voting rights

Each redeemable convertible preferred unit is entitled to one vote for each common unit into which such redeemable convertible preferred unit is then convertible. The redeemable convertible preferred unit holders and the common unit holders vote together on all matters as a single class, except as otherwise provided by law or the provisions of the LLC Agreement.

The Board of Managers consists of up to seven individuals. As long as at least 618,716 Series A-1 redeemable convertible preferred units, Series A-2 redeemable convertible preferred units and/or Series A-3 redeemable convertible preferred units remain outstanding, the members holding a majority of the outstanding Series A-1 redeemable convertible preferred units, Series A-2 redeemable convertible preferred units and Series A-3 redeemable convertible preferred units, voting together as a single class on an as-converted basis, are entitled to elect one manager. As long as at least 1,654,555 Series A-4 redeemable convertible preferred units remain outstanding, the members holding a majority of the Series A-4 redeemable convertible preferred units, voting as a single class, are entitled to elect one manager. As long as at least 316,187 Series A-5 redeemable convertible preferred units remain outstanding, the members holding a majority of the Series A-5 redeemable convertible preferred units, voting as a single class, are entitled to elect one manager. As long as at least 3,010,852 Series B redeemable convertible preferred units remain outstanding, the members holding a majority of the Series B redeemable convertible preferred units, voting as a single class, are entitled to elect one manager. The members holding a majority of the common units, voting as a single class are entitled to elect one manager. The members holding a majority of the units then outstanding, voting together as a single class on an as-converted to common units basis are entitled to elect any remaining managers. As of December 31, 2021 and 2022, respectively, the Company's Board of Managers consisted of five and six individuals, respectively.

Conversion

Each redeemable convertible preferred unit is convertible into common units at the option of a holder at the then applicable conversion price, which is equal the original purchase price, subject to adjustments for recapitalization and others. The original purchase price is equal to \$3.2325 per Series A-1 Preferred Unit, \$0.6456 per Series A-2 Preferred Unit, \$1.1713 per Series A-3 Preferred Unit, \$4.84875 per Series A-4 Preferred Unit, \$6.32536 per Series A-5 Preferred Unit, \$11.64951 per Series B Preferred Unit, and \$14.06770 per Series B-1 Preferred Unit. As of December 31, 2021 and 2022, the redeemable convertible preferred units were convertible into common units at a one-for-one conversion ratio.

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Each redeemable convertible preferred unit is automatically convertible into common units (or shares of common stock, if the Company is converted into a corporation), based on the then-effective applicable conversion rate (A) at any time upon the affirmative vote or written consent of (i) the members holding a majority of the redeemable convertible preferred units then outstanding, (ii) the members holding a majority of the Series B redeemable convertible preferred units then outstanding, and (iii) the members holding a majority of the Series B-1 redeemable convertible preferred units then outstanding, or (B) immediately upon the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common units (or other common securities) with the gross cash proceeds to the Company, before underwriting discounts, commissions and offering expenses, are at least \$100.0 million, or (C) the closing of a merger, acquisition or other business combination involving the Company and a publicly traded special purpose acquisition company ("SPAC") or its subsidiary or affiliate in which the surviving public company has available immediately cash of at least \$100.0 million in the aggregate greater than the cash on the Company's consolidated balance sheets as of immediately prior to such merger, acquisition or other business combination (including proceeds of a private investment in public equity transaction that is substantially contemporaneous with or conditioned on such merger, acquisition or other business combination, and any redemptions from the SPAC's trust account).

Anti-dilution and other protective provisions

The holders of the redeemable convertible preferred units have proportional anti-dilution protection right for unit splits, unit dividends and similar recapitalizations, subject to certain exclusions, anti-dilution price protection for additional sales of securities by the Company for consideration per unit less than the applicable conversion price per unit of any series of the redeemable convertible preferred units, on a broad-based weighted average basis.

The holders of the redeemable convertible preferred units have certain protective rights. The Company shall not, either directly or by amendment, merger, consolidation or otherwise, without the prior written approval of members holding a majority of the redeemable convertible preferred units then outstanding to alter or change the rights, preferences or privileges of the redeemable convertible preferred units; consummate a liquidation or a deemed liquidation event; change the Company's LLC Agreement; authorize or create any new class or series of units or other equity security; increase or decrease the authorized number of the common units or the redeemable convertible preferred units or any series; redeem, acquire or repurchase any, or make any distribution on, any common units or redeemable convertible preferred units; change the compensation or equity awards granted to executive officers of the Company, unless such transaction is approved by the Board of Managers; increase or decrease the authorized number of managers constituting the Board of Managers and amend other rights or enter into certain transactions.

Liquidation preference

In the event of a liquidation, a deemed liquidation event (including a consolidation, merger or reorganization or a sale, lease, transfer, exclusive irrevocable license or other disposition of all or substantially all of the assets of the Company), dissolution or winding-up of the Company, the funds are distributed first to the members holding the redeemable convertible preferred units in proportion to and to the extent of their unreturned original purchase price per redeemable convertible preferred unit, until each member holding the redeemable convertible preferred units has received cumulative distributions in an amount equal to the unreturned original purchase price for each of such member's redeemable convertible preferred unit. Second, to the members holding common units and the redeemable convertible preferred units pro rata based on the number of units held by each such holder, assuming for this purpose that all the redeemable convertible preferred units have been converted into common units as of the date of such operating distribution or distribution of net proceeds.

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or assets available for distribution, whether in cash or in other property. Third, the amounts that would otherwise be distributed to any redeemable convertible preferred unit holder pursuant to the liquidation preference on as-converted to common units basis will be reduced by an amount equal to the remaining preferred participation threshold amount for such redeemable convertible preferred unit. The preferred participation threshold amount for a redeemable convertible preferred unit is equal to the original purchase price, reduced by distributions paid.

Distributions preference

Distributions, when determined by the Board of Managers, are payable to the members holding the redeemable convertible preferred units, pro rata in proportion to the liquidation preference amounts in respect of the redeemable convertible preferred units held by such members; thereafter, to the members in proportion to the number of shares held by such members, on as converted basis. No distributions were declared or made from inception and during the years ended December 31, 2021 and 2022.

Redemption

The redeemable convertible preferred units are not redeemable except in the event of certain effected deemed liquidation events, that are not in the Company's control.

12. Common units

As of December 31, 2021 and 2022, the Company was authorized to issue 32,000,000 and 66,000,000 common units, respectively. Each common unit is entitled to cast one vote. The holders of common units are also entitled to receive distributions whenever funds are legally available and when declared by the Company's Board of Managers, subject to prior rights of the holders of the redeemable convertible preferred units. No distributions have been declared from inception to date.

As of December 31, 2021 and 2022, the Company reserved common units for future issuance as follows:

	2021	December 31, 2022
Outstanding redeemable convertible preferred units	19,650,632	41,478,621
Outstanding profits interests	5,783,758	7,516,073
Units available for grants under 2019 Equity Incentive Plan	236,886	7,088,092
Total common units reserved for future issuance	<u>25,671,276</u>	<u>56,082,786</u>

Founders and investors common units

In June 2017, Metagenomi Inc. issued 4,687,500 shares of its common stock at a purchase price of \$0.0001 per share to its founders and investors for services, which was an estimated fair value determined by the Board of Managers at the issuance date. Pursuant to the terms of the stock purchase agreements, 25% of the shares vested on the first anniversary of the vesting start date and monthly over the next 36 months. Vesting of shares is accelerated upon a change of control event (including an acquisition of the Company by another entity by means of any transaction or series of related transactions, or a sale of all or substantially all of the assets of the Company). The Company has a right to repurchase unvested shares upon termination of services provided by the founders to the Company at the price lower of i) the purchase price or ii) the fair value at the date of

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repurchase. In November 2018, in connection with the reorganization, common stock issued by Metagenomi Inc. was exchanged for common units of Metagenomi with the same terms. The estimated fair value of common unit at the modification date was determined to be \$0.02 per unit, based on the Company's recent common unit valuation, and the modification expense was immaterial.

In March 2019, the Company issued 1,260,000 common units to an investor for services with a purchase price of \$0.02 per unit, which was based on the recent Company's common stock valuation. As long as the investor continues to provide services, 25% of the shares vested immediately and the remainder vested monthly over the next 36 months. Vesting of shares is accelerated upon a change of control event. The Company has a right to repurchase unvested shares upon termination of services provided by the founders to the Company at the price lower of i) the purchase price or ii) the fair value at the date of repurchase.

The Company accounts for issued common units as unit-based compensation to founders and investors as service providers and recognizes unit-based compensation expense of \$0.1 million over the vesting period. The Company had 494,689 and 78,750 common units vested during the years ended December 31, 2021 and December 31, 2022, respectively, each having fair value of less than \$0.1 million. 78,750 and zero common units were unvested as of December 31, 2021 and 2022, respectively.

The following table provides a summary of common units with vesting conditions activity during the year ended December 31, 2022:

	Number of common units unvested	Weighted- average grant date fair value
Unvested as of January 1, 2022	78,750	\$ 0.03
Common Units vested	(78,750)	\$ 0.03
Unvested as of December 31, 2022	—	\$ —

13. Profits interests plan

The Company grants profits interests under the 2019 Equity Incentive Plan, adopted on March 13, 2019 (the "2019 Plan"). The Company may grant profits interests with a threshold amount, which may be zero, established by the Board of Managers on the date of issuance. Accordingly, such profits interests do not give a holder a share of the proceeds if the Company's assets were sold at fair market value and the proceeds of such disposition were distributed in complete liquidation of the Company immediately after the date of grant but give a holder a right to share in the appreciation in the value of a common unit from the date of receipt to the future, as specifically provided in the LLC Agreement. The 2019 Plan allows for grants of profits interests to the Company's officers, employees, directors and consultants. Profits interests generally vest monthly over four years, with or without one- year cliff vesting in the first year. In the event of a profits interest holder's termination, the unvested portion of such profits interest is automatically forfeited and cancelled without any additional consideration. Additionally, the Company has the right to repurchase the vested portion of such profits interest at its fair market value, which is based on the fair market value of a common unit (as determined by the Board of Managers), less the applicable profits interest threshold amount, at any time during the 12-month period after termination of a profits interest holder's service to the Company.

The number of common units reserved for issuance under the 2019 Plan was 6,020,644 and 14,604,165 at December 31, 2021, and 2022, respectively.

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The table below presents a summary of activities and a reconciliation of common units authorized and remaining for grant under the 2019 Plan during the year ended December 31, 2022:

	Units available for grants	Profits interests	Weighted- average threshold amount	Aggregate intrinsic value (in thousands)
Outstanding as of January 1, 2022	236,886	5,783,758	\$ 0.27	\$ 1,372
Authorized	8,583,521	—	\$ —	
Profits interests granted	(2,763,356)	2,763,356	\$ 3.20	
Forfeited and expired	1,031,041	(1,031,041)	\$ 1.55	
Outstanding as of December 31, 2022	7,088,092	7,516,073	\$ 1.17	\$ 34,398
Vested and expected to vest	7,088,092	7,516,073	\$ 1.17	\$ 34,398

The aggregate intrinsic value is calculated as the positive difference between the threshold amount of the profits interests and the fair value of the Company's common unit as of December 31, 2021 and 2022.

During the years ended December 31, 2021 and 2022, the Company granted 3,550,854 and 2,763,356 profits interests with a weighted average grant date fair value of \$1.03 and \$1.90, respectively. The total fair value of the profits interests vested during the years ended December 31, 2021 and 2022 was \$0.2 million and \$1.1 million, respectively.

Unit-based compensation expense

The Company estimated the fair value of profits interests on the grant date using the Black-Scholes option-pricing model based on the following assumptions for the years ended December 31, 2021 and 2022:

	Years ended December 31	
	2021	2022
Expected volatility	79.62% — 91.19%	79.57% — 82.60%
Expected dividend yield	0%	0%
Expected term (in years)	2.66 — 6.63	3.51 — 4.00
Risk-free interest rate	0.18% — 0.94%	2.65% — 4.33%
Threshold range	\$ 0.34 — \$0.51	\$ 3.20

Expected volatility—The Company is a private company and lacks company-specific historical and implied volatility information. Therefore, the Company estimates its expected unit's volatility based on the historical volatility of a publicly traded set of peer companies and expect to continue to do so until the Company has adequate historical data regarding the volatility of the Company's traded unit or stock price.

Expected term—The expected term of profits interests has been determined based on the expected time to liquidity and expected vesting term.

Risk-free interest rate—The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award.

Dividends—Expected dividend yield is zero because the Company does not pay cash dividends on common units and does not expect to pay any cash dividends in the foreseeable future.

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The grant date fair value of common units utilized in the Black-Scholes model is determined by the Company's Board of Managers with the assistance of management. The grant date fair value of common units is determined using valuation methodologies which utilizes certain assumptions including probability weighting of expected exit events, volatility, time to liquidation, a risk-free interest rate and an assumption for a discount for lack of marketability. In determining the fair value of the common units, the methodologies used to estimate the enterprise value were performed using methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

The following table presents the classification of unit -based compensation expense for the years ended December 31, 2021 and 2022 (in thousands):

	Years ended December 31,	
	2021	2022
Research and development expenses	\$ 90	\$ 754
General and administrative expenses	285	1,208
Total unit-based compensation expense	<u>\$ 375</u>	<u>\$ 1,962</u>

The above unit-based compensation expense related to the following unit-based awards for the years ended December 31, 2021 and 2022 (in thousands):

	Years ended December 31,	
	2021	2022
Profits Interests	\$ 365	\$ 1,960
Common Units	10	2
Total unit-based compensation expense	<u>\$ 375</u>	<u>\$ 1,962</u>

There was \$3.3 million and \$5.7 million in unrecognized unit-based compensation expense related to the profits interests as of December 31, 2021 and 2022, respectively, that was expected to be recognized over a weighted-average period of 3.81 and 3.03 years, respectively. There was less than \$0.1 million unrecognized unit-based compensation expense related to the common units with vesting conditions as of December 31, 2021, that was expected to be recognized over a weighted-average period of 0.2 years. As of December 31, 2022, there was no unrecognized expense related to the common units with vesting conditions.

14. Related party transactions

The Company's former chief business officer was a founder, and a chief executive officer of Affini-T. Affini-T was a related party when the Company exercised significant influence until November 2021. In November 2021, certain common stock shares were forfeited, and the chief business officer resigned from the Company. As of December 31, 2021, Affini-T is no longer a related party of the Company (see Note 5).

Bayer Healthcare LLC ("Bayer") is a significant investor in the Company and has a Board seat. The Company and Bayer entered into a research and development master service agreement in November 2019. Bayer was performing research and development services under the agreement in accordance with the statement of works agreed by the parties. Services under this agreement were completed as of December 31, 2020, and the Company accrued \$0.2 million in accrued expenses and other current liabilities as of December 31, 2020. The Company paid \$0.2 million to Bayer in February and March 2021 and there were no other services provided by Bayer to the Company during the years ended December 31, 2021 and December 31, 2022.

In connection with Series B and Series B-1 financings, the Company reimbursed certain investors for finance issuance costs that they incurred totaling \$0.4 million. As of December 31, 2022, \$0.1 million of Series B-1 financing costs reimbursable to investors is recorded in accrued expenses and other current liabilities in the consolidated balance sheets.

15. Income taxes

Metagenomi is treated as a partnership for tax purposes, and thus, is not subject to income taxes. It is the responsibility of the LLC members to report their proportionate share of any taxable income or loss generated by Metagenomi to the appropriate taxing authorities and pay the associated taxes, if any. With respect to the Company's subsidiary, Metagenomi Inc. is a corporation for tax purposes and is subject to income taxes which have been included in the consolidated financial statements. All pre-tax losses have been incurred in the United States.

During the year ended December 31, 2022, income tax expense consisted of the following (in thousands):

Current:	
Federal	\$ 2,569
State	—
Total current tax expense	2,569
Deferred:	
Federal	—
State	—
Total deferred tax expense	—
Total tax expense	<u>\$ 2,569</u>

The Company recognized an income tax provision of \$2.6 million for the year ended December 31, 2022 as a result of their taxable income related to an upfront payment received under the Moderna Agreement and capitalization of their research and development expenses under the newly enacted Internal Revenue Code Section 174 ("Section 174"), which became effective on January 1, 2022. Section 174 changed the tax treatment of research and experimentation (R&E) expenditures, which requires the capitalization of R&E expenditures over a period of five years for R&E paid or incurred in the United States and 15 years for R&E paid or incurred outside of the United States.

During the year ended December 31, 2021, the Company had no income tax expense, and all losses were from the U.S.

The effective tax rate of the Company's provision for income taxes differs from the federal statutory rate of 21% for the years ended December 31, 2021 and 2022, is as follows:

	Years ended December 31,	
	2021	2022
Statutory rate	21.00 %	21.00 %
Nontaxable LLC losses	(15.99)%	(0.13)%
State tax rate	1.60 %	9.73 %
Permanent and other adjustments	(0.12)%	(1.31)%
Change in valuation allowance	(6.49)%	(41.02)%
Research credits	0.00 %	5.47 %
Total	<u>0.00 %</u>	<u>(6.26)%</u>

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Significant components of the deferred tax assets for federal and state income taxes as of December 31, 2021 and 2022, are as follows (in thousands):

	Years ended December 31,	
	2021	2022
Deferred Tax Assets:		
Net operating loss carry forwards	\$ 1,601	\$ 655
Research credits	232	1,568
Reserves and accruals	618	1,326
Lease liability	5,226	5,199
Deferred revenue	—	8,465
Capitalized research and development expenses	—	8,901
Total deferred tax assets	<u>7,677</u>	<u>26,114</u>
Deferred Tax Liabilities:		
Property and equipment	(607)	(2,583)
Right-of-use asset	(5,051)	(4,685)
Total gross deferred tax liabilities	<u>(5,658)</u>	<u>(7,268)</u>
Less: Valuation allowance	(2,019)	(18,846)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

A valuation allowance is required to be established when it is more likely than not that all or a portion of a deferred tax asset will not be realized. Realization of deferred tax assets is dependent upon future earnings, the timing and amount of which are uncertain. Metagenomi Inc. believes that, based on a number of factors such as the history of operating losses, it is more likely than not that the deferred tax assets will not be fully realized, such that a full valuation allowance has been recorded. The valuation allowance increased by \$1.4 million and \$16.8 million for the years ended December 31, 2021 and 2022, respectively, primarily due to the increase in deferred revenue and capitalization of research and development expenses under newly enacted Section 174.

As of December 31, 2022, Metagenomi Inc. had \$0.02 million and \$8.3 million of net operating loss carryforwards for federal and state income tax purposes, respectively. Federal net operating loss carryforwards do not expire. State net operating loss carryforwards begin expiring in 2037.

As of December 31, 2022, Metagenomi Inc. had \$0 and \$2.8 million of research credit carryforwards for federal and state income tax purposes, respectively. State research credit carryforwards do not expire and can be carried forward indefinitely.

Utilization of some of the federal and state net operating losses and credit carryforwards may be subject to annual limitations due to the change in ownership provisions of the Internal Revenue Code of 1986 ("Internal Revenue Code") and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization. As of December 31, 2022, the Company has completed an IRC Section 382 analysis from inception through the year ended December 31, 2022. The Company experienced two ownership changes in August 2019 and January 2022. Net operating losses generated prior to December 31, 2017, of \$0.3 million are permanently limited for federal tax purposes. Net federal operating losses generated after December 31, 2017 are not limited as they can be carried forward indefinitely, subject to an 80% income limitation. Net operating losses of \$0.1 million are permanently limited for California tax purposes.

Metagenomi Inc. uses the "more likely than not" criterion for recognizing the income tax benefit of uncertain income tax positions and establishing measurement criteria for income tax benefits. Although it is reasonably

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possible that certain unrecognized tax benefits may increase or decrease within the next twelve months due to tax examination changes, settlement activities, expirations of statute of limitations, or the impact on recognition and measurement considerations related to the results of published tax cases or other similar activities, Metagenomi Inc. does not anticipate significant changes to unrecognized tax benefits over the next 12 months. During the years ended December 31, 2021 and 2022, no interest or penalties were recognized relating to unrecognized tax benefits. In the event Metagenomi Inc. should need to recognize interest and penalties related to unrecognized income tax liabilities, this amount will be recorded as an accrued liability and an increase to income tax expense.

The changes in the balance of gross unrecognized tax benefits, which excludes interest and penalties, for the years ended December 31, 2021 and 2022, are as follows (in thousands):

	Years ended December 31,	
	2021	2022
Beginning balance	\$ 131	\$ 131
Gross increases—tax position in current period	—	1,231
Gross increases—tax position in prior periods	—	426
Reductions for tax positions of prior years	—	(33)
Ending balance	\$ 131	\$ 1,755

Metagenomi Inc. files tax returns in the U.S. and California. Metagenomi Inc. is not currently under examination in any of these jurisdictions and all its tax years remain effectively open to examination due to net operating losses from inception. Metagenomi Inc. recognized \$1.0 million of uncertain tax positions as other non-current liabilities and \$0.8 million was netted against deferred tax assets.

In accordance with the Tax Cuts and Jobs Act of 2017, research and experimental (R&E) expenses under Internal Revenue Code Section 174 are required to be capitalized beginning in 2022. R&E expenses are required to be amortized over a period of 5 years for domestic expenses and 15 years for foreign expenses.

On August 16, 2022, President Biden signed into law the Inflation Reduction Act of 2022, which includes an Alternative Minimum Tax based on the Adjusted Financial Statement Income of Applicable Corporations. Based on an initial evaluation, the Company does not believe the Inflation Reduction Act will have a material impact on the income tax provision and cash taxes. The Company will continue to monitor the changes in tax laws and regulations to evaluate their potential impact on the business.

16. Net loss per unit

Basic and diluted net loss per unit attributable to common unitholders is calculated as follows (in thousands except share and per share amounts):

	Years ended December 31	
	2021	2022
Numerator:		
Net loss attributable to common members	\$ (21,442)	\$ (43,593)
Denominator:		
Weighted average common units outstanding	5,947,500	5,947,500
Less: Weighted-average unvested common units subject to repurchase	(256,069)	(8,846)
Weighted average units used to computing basic and diluted net loss per share	5,691,431	5,938,654
Net loss per unit attributable to common unitholders—basic and diluted:	\$ (3.77)	\$ (7.34)

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The following outstanding potentially dilutive securities have been excluded from the calculation of diluted net loss per unit, as their effect is anti-dilutive:

	Years ended December 31,	
	2021	2022
Redeemable convertible preferred units	19,650,632	41,478,621
Profits interests	5,783,758	7,516,073
Unvested common units	78,750	—
Total	25,513,140	48,994,694

17. Employee retirement plan

The Company has a defined contribution plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"), covering its employees. Employees may contribute a percentage of their annual compensation to this plan, subject to the maximum allowable amount set by the Internal Revenue Service. The 401(k) Plan provides that the Company matches each participant's contribution at 100% up to the first 5% of the employee's eligible compensation. The Company's contributions to the 401(k) Plan were \$0.2 million and \$0.6 million for the years ended December 31, 2021 and 2022, respectively.

18. Subsequent events

The Company has reviewed and evaluated subsequent events through August 3, 2023, the date that the consolidated financial statements were available to be issued.

In January 2023, the Company sold an additional 334,754 Series B-1 redeemable convertible preferred units in accordance with the Series B-1 purchase agreement and received gross cash proceeds of \$4.7 million.

In March and June 2023, the Company granted 450,860 and 1,530,523 profits interests to officers, employees and consultants with a threshold amount of \$5.75 and \$7.40, respectively. These profits interests vest over a period of two to four years.

19. Subsequent events (unaudited)

The Company has reviewed and evaluated subsequent events through December 8, 2023, the date that the consolidated financial statements were available to be reissued.

Profits Interests Grants

In September 2023, the Company granted 274,830 profits interests awards to officers, employees and consultants with a threshold amount of \$11.84. In July and September 2023, the Company canceled and re-issued 781,312 profits interests awards with thresholds of \$7.40 and \$11.84. Issued profits interests vest over a period of two to four years.

Amendment to the LLC Agreement

The Company's LLC Agreement was amended on July 31, 2023 to provide for "catch-up" distributions for profits interests once the applicable catch-up threshold amount for such profits interests was met (the "Amendment to the LLC Agreement").

The LLC Agreement provides each profits interest with a distribution threshold amount, which is determined on the date of issuance and represents the amount that would be distributed if, immediately after issuance, the

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Company sold all of its assets at fair market value and distributed the net proceeds in liquidation. A profits interest does not participate in Company distributions until an amount equal to its distribution threshold amount has been distributed to other members of the Company with units that either have a lower threshold amount or no threshold amount.

Once the applicable distribution threshold amount has been met for a particular profits interest, such profits interest will participate in Company distributions on a pro rata basis until the catchup threshold amount has been met. Once the catch-up threshold amount has been met, subsequent "catch-up" distributions will be made solely to holders of profits interests until such holders have received an amount equal to the amount such holders would have received had the distribution threshold not existed. Once the profits interest holders have received distributions in an amount equal to what they would have received had the distribution threshold not existed, all subsequent distributions are made on a pro rata basis with common unitholders.

The catch-up threshold amount of \$11.84 per unit reflected the estimated fair value of the Company's common unit as of July 31, 2023, as determined by the Company's board of managers, with input from management, and considering the Company's most recently available third-party valuations of common units. The amendment to the LLC Agreement resulted in a change to the fair value of the profits interests and will be accounted for as a modification of the profits interests' awards.

Ionis Agreement

In November 2023, Ionis selected its third target ("Target 3") in Wave 1 and the Company agreed to extend the period during which the Company expects Ionis will select its fourth target ("Target 4") in Wave 1 by an additional three months from the 12-month anniversary of the effective date, as permitted under the arrangement.

Condensed Consolidated Balance Sheets

(in thousands, except units)
(unaudited)

	December 31, 2022	September 30, 2023
Assets		
Current assets:		
Cash and cash equivalents	\$ 184,441	\$ 101,897
Available-for-sale marketable securities	177,690	191,030
Accounts receivable	—	3,924
Contract assets	1,274	—
Prepaid expenses and other current assets	3,494	3,152
Total current assets	366,899	300,003
Property and equipment, net	16,522	21,213
Long-term investments	7,806	10,676
Operating lease right-of-use assets	16,736	44,475
Other assets	450	4,818
Restricted cash	6,073	5,248
Total assets	\$ 414,486	\$ 386,433
Liabilities, redeemable convertible preferred units and members' deficit		
Current liabilities:		
Accounts payable	\$ 2,011	\$ 4,893
Income tax payable	1,536	2,168
Accrued expenses and other current liabilities	8,790	10,799
Current portion of operating lease liabilities	1,515	2,269
Collaboration advance	743	430
Deferred revenue	33,942	48,223
Total current liabilities	48,537	68,782
Non-current portion of operating lease liabilities	17,056	45,938
Deferred revenue, non-current	76,185	36,524
Other non-current liabilities	1,033	3,452
Total liabilities	142,811	154,696
Commitments and contingencies (Note 8)		
Redeemable convertible preferred units: 41,813,375 units authorized as of December 31, 2022 and September 30, 2023; 41,478,621 and 41,813,375 units issued and outstanding as of December 31, 2022 and September 30, 2023, respectively. Liquidation preference \$347,335 and \$352,044 as of December 31, 2022 and September 30, 2023, respectively	346,103	350,758
Members' deficit:		
Common units: 66,000,000 units authorized as of December 31, 2022 and September 30, 2023; 5,947,500 units issued and outstanding as of December 31, 2022 and September 30, 2023	26	26
Profits interests: 14,604,165 units authorized as of December 31, 2022 and September 30, 2023; 7,516,073 and 9,556,687 units issued and outstanding as of December 31, 2022 and September 30, 2023, respectively	2,509	6,962
Accumulated other comprehensive loss	(274)	(359)
Accumulated deficit	(76,689)	(125,650)
Total members' deficit	(74,428)	(119,021)
Total liabilities, redeemable convertible preferred units and members' deficit	\$ 414,486	\$ 386,433

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

Condensed Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except units and per unit data)
(unaudited)

	Nine Months Ended September 30,	
	2022	2023
Collaboration revenue	\$ 11,605	\$ 32,357
Operating expenses:		
Research and development	28,082	69,648
General and administrative	12,397	21,005
Total operating expenses	40,479	90,653
Loss from operations	(28,874)	(58,296)
Other income (expense)		
Interest expense	(98)	—
Interest income	1,489	11,836
Change in fair value of long-term investments	94	2,870
Other income (expense), net	146	(70)
Total other income, net	1,631	14,636
Net loss before provision for income taxes	(27,243)	(43,660)
Provision for income taxes	(1,723)	(5,301)
Net loss	\$ (28,966)	\$ (48,961)
Other comprehensive loss:		
Unrealized loss on available-for-sale marketable securities, net	(301)	(85)
Other comprehensive loss	\$ (29,267)	\$ (49,046)
Net loss per unit attributable to common unitholders, basic and diluted	\$ (4.88)	\$ (8.23)
Weighted average common units outstanding, basic and diluted	5,935,673	5,947,500

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

Condensed Consolidated Statements of Redeemable Convertible Preferred Units and Members' Deficit

(in thousands, except units)
(unaudited)

	Redeemable Convertible Preferred Units		Common Units		Profits Interests		Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Members' Deficit
	Units	Amount	Units	Amount	Units	Amount			
BALANCE—January 1, 2022	19,650,632	\$ 76,495	5,947,500	\$ 26	5,783,758	\$ 547	\$ (21)	\$ (33,096)	\$ (32,544)
Issuance of Series B redeemable convertible preferred units for cash, net of issuance costs of \$697	12,446,876	144,304	—	—	—	—	—	—	—
Issuance of Series B redeemable convertible preferred units upon conversion of convertible note and accrued interest	2,607,387	30,374	—	—	—	—	—	—	—
Issuance of profits interests	—	—	—	—	2,244,356	—	—	—	—
Cancellation and forfeiture of profits interests	—	—	—	—	(942,677)	—	—	—	—
Unit-based compensation expense	—	—	—	—	—	1,391	—	—	1,391
Other comprehensive loss	—	—	—	—	—	—	(301)	—	(301)
Net loss	—	—	—	—	—	—	—	(28,966)	(28,966)
BALANCE—September 30, 2022	34,704,895	\$ 251,173	5,947,500	\$ 26	7,085,437	\$ 1,938	\$ (322)	\$ (62,062)	\$ (60,420)
BALANCE—January 1, 2023	41,478,621	\$ 346,103	5,947,500	\$ 26	7,516,073	\$ 2,509	\$ (274)	\$ (76,689)	\$ (74,428)
Issuance of Series B-1 redeemable convertible preferred units, net of issuance costs of \$54	334,754	4,655	—	—	—	—	—	—	—
Issuance of profits interests	—	—	—	—	2,267,813	—	—	—	—
Cancellation and forfeiture of profits interests	—	—	—	—	(227,199)	—	—	—	—
Unit-based compensation expense	—	—	—	—	—	4,453	—	—	4,453
Other comprehensive loss	—	—	—	—	—	—	(85)	—	(85)
Net loss	—	—	—	—	—	—	—	(48,961)	(48,961)
BALANCE—September 30, 2023	41,813,375	\$ 350,758	5,947,500	\$ 26	9,556,687	\$ 6,962	\$ (359)	\$ (125,650)	\$ (119,021)

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

Condensed Consolidated Statements of Cash Flows

(in thousands)
(unaudited)

	Nine Months Ended September 30,	
	2022	2023
Cash flows from operating activities		
Net loss	\$ (28,966)	\$ (48,961)
Adjustments to reconcile net loss to net cash used in operating activities		
Unit-based compensation expense	1,391	4,453
Depreciation and amortization	1,014	3,006
Loss on fixed assets write-off	269	9
Non-cash lease expense	967	3,107
Amortization of premiums and discounts on available-for-sale marketable securities	(216)	(6,852)
Amortization of non-cash collaboration revenue	(265)	(654)
Non-cash interest expense	98	—
Change in fair value of long-term investments	(94)	(2,870)
Changes in operating assets and liabilities:		
Accounts receivable	—	(3,924)
Contract assets	—	1,274
Prepaid expenses and other current assets	(1,398)	352
Other assets	(13)	37
Accounts payable	(192)	2,439
Income tax payable	1,029	632
Deferred revenue and collaboration advance	(14,330)	(25,039)
Accrued expenses and other current liabilities	2,050	727
Operating lease liabilities	(45)	(972)
Other non-current liabilities	692	2,419
Net cash used in operating activities	<u>(38,009)</u>	<u>(70,817)</u>
Cash flows from investing activities		
Purchases of property and equipment	(10,469)	(8,077)
Purchases of available-for-sale marketable securities	(136,634)	(168,977)
Maturities and sales of available-for-sale marketable securities	63,777	162,156
Net cash used in investing activities	<u>(83,326)</u>	<u>(14,898)</u>
Cash flows from financing activities		
Payments of initial public offering costs	—	(1,949)
Proceeds from issuance of redeemable convertible preferred units, net of issuance costs	144,304	4,295
Net cash provided by financing activities	<u>144,304</u>	<u>2,346</u>
Net change in cash, cash equivalents and restricted cash	22,969	(83,369)
Cash, cash equivalents and restricted cash at the beginning of the period	43,396	190,514
Cash, cash equivalents and restricted cash at the end of the period	<u>\$ 66,365</u>	<u>\$ 107,145</u>
Reconciliation of cash, cash equivalents and restricted cash		
Cash and cash equivalents	\$ 62,265	\$ 101,897
Restricted cash	4,100	5,248
Cash, cash equivalents and restricted cash at the end of the period	<u>\$ 66,365</u>	<u>\$ 107,145</u>

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements

Condensed Consolidated Statements of Cash Flows (continued)

(in thousands)

(unaudited)

	Nine Months Ended	
	September 30,	
	2022	2023
Supplemental cash flow information		
Issuance of Series B redeemable convertible preferred units upon conversion of convertible promissory note and accrued interest	\$ 30,374	\$ —
Common shares of Affini-T received for collaboration revenue	\$ 1,295	\$ —
Purchases of property and equipment included in accounts payable and accrued expenses and other current liabilities	\$ 1,470	\$ 876
Operating lease right-of-use assets obtained in exchange for new lease liabilities	\$ —	\$ 30,608
Deferred initial public offering costs included in accounts payable and accrued expenses and other current liabilities	\$ —	\$ 2,456

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

Notes to the Unaudited Condensed Consolidated Financial Statements

1. Description of business, organization and liquidity

Organization and business

Metagenomi Technologies, LLC ("Metagenomi"), together with its wholly owned subsidiary Metagenomi, Inc. ("Metagenomi Inc.") (together, the "Company") is a gene editing biotechnology company developing therapeutics by leveraging a toolbox of next-generation gene editing systems to accurately edit DNA.

Liquidity and going concern

The Company has incurred significant losses from operations since its inception. During the nine months ended September 30, 2022 and 2023, the Company incurred net losses of \$29.0 million and \$49.0 million, respectively. As of September 30, 2023, the Company had an accumulated deficit of \$125.7 million.

The Company has historically financed its operations primarily through issuance of redeemable convertible preferred units, convertible promissory notes and its collaboration agreements with Moderna, Affini-T and Ionis (see Note 7). The Company expects to continue to incur substantial losses, and its ability to achieve and sustain profitability will depend on the successful development, approval, and commercialization of any product candidates it may develop, and on the achievement of sufficient revenue to support its cost structure. The Company may never achieve profitability and, unless and until it does, it will need to continue to raise additional capital. Management expects that existing cash, cash equivalents and available-for-sale marketable securities of \$292.9 million as of September 30, 2023, will be sufficient to fund its current operating plan for at least the next 12 months from the date of issuance of these condensed consolidated financial statements.

2. Summary of significant accounting policies

Basis of presentation

These condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") and pursuant to the rules and regulations of the Securities and Exchange Commission ("SEC") regarding interim financial reporting. The accompanying condensed consolidated financial statements include the accounts of Metagenomi and Metagenomi Inc., a wholly owned subsidiary. All intercompany balances and transactions have been eliminated in consolidation.

The interim condensed consolidated balance sheet as of September 30, 2023, and the condensed consolidated statements of operations and comprehensive loss, and cash flows for the nine months ended September 30, 2022 and 2023 are unaudited. The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the annual consolidated financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for the fair statement of the Company's financial position as of September 30, 2023 and its results of operations and cash flows for the nine months ended September 30, 2022 and 2023. The financial data and the other financial information disclosed in these notes to the condensed consolidated financial statements related to the nine-month periods are also unaudited. The results of operations for the nine months ended September 30, 2023 are not necessarily indicative of the results to be expected for the year ending December 31, 2023, or for any other future annual or interim period. The condensed consolidated balance sheet as of December 31, 2022, included herein was derived from the audited consolidated financial statements as of that date. Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been

Notes to the Unaudited Condensed Consolidated Financial Statements

condensed or omitted from these interim condensed consolidated financial statements. These unaudited condensed financial statements should be read in conjunction with the Company's audited consolidated financial statements included elsewhere in this prospectus.

Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of expenses during the reporting period. On an ongoing basis, the Company evaluates estimates and assumptions, including but not limited to those related to revenue recognition under its collaboration agreements, the fair value of its common and redeemable convertible preferred units, the fair value of derivative liabilities, unit-based compensation expense, accruals for research and development expenses, the fair value of long-term investments, the valuation of deferred tax assets and uncertain income tax positions. Management bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from those estimates.

Risks and uncertainties

The Company is subject to certain risks and uncertainties, including, but not limited to, changes in any of the following areas that the Company believes could have a material adverse effect on the future financial position or results of operations: the Company's ability to advance the development of its next generation gene-editing platform, timing and ability to advance any product candidates it may develop into and through pre-clinical and clinical development; costs and timelines associated with the manufacturing of clinical supplies of any product candidates the Company may develop; regulatory approval, market acceptance of, and reimbursement for any product candidates the Company may develop; performance of third-party vendors; competition from pharmaceutical or other gene-editing companies with greater financial resources or expertise; protection of intellectual property; litigation or claims against the Company based on intellectual property or other factors; and its ability to attract and retain employees necessary to support its growth.

The Company's business and operations may be affected by worldwide economic conditions, which may continue to be impacted by global macroeconomic challenges such as the effects of the ongoing geopolitical conflict in Ukraine and the Israel-Hamas war, tensions in U.S.-China relations, the COVID-19 pandemic, uncertainty in the markets, including disruptions in the banking industry, and inflationary trends. Fiscal year 2022 was marked by significant market uncertainty, increasing inflationary pressures. These market dynamics may continue into 2023 and these and similar adverse market conditions may negatively impact the Company's operations and financial position.

Concentration of credit risk

Cash and cash equivalents, available-for-sale marketable securities and preferred and common stock shares related to our investment in Affini-T (Note 5) are financial instruments that potentially subject the Company to

Notes to the Unaudited Condensed Consolidated Financial Statements

concentrations of credit risk. As of December 31, 2022 and September 30, 2023, cash consists of cash deposited with three financial institutions, and account balances exceed federally insured limits.

On March 10, 2023, SVB was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. On March 12, 2023 the FDIC transferred all deposits, both insured and uninsured, and substantially all assets from the former SVB to a newly created, full-service FDIC-operated "bridge bank", Silicon Valley Bridge Bank, N.A. ("SVBB") and the FDIC, Treasury Department, and Federal Reserve announced that all deposits will be fully protected, whether or not they had been insured by the FDIC. On March 27, 2023, First-Citizens Bank & Trust Company assumed all of SVBB's customer deposits and certain other liabilities and acquired substantially all of SVBB's loans and certain other assets from the FDIC. As of September 30, 2023, the Company's held cash and cash equivalents of \$6.7 million at SVB. As of the date of the issuance of these condensed consolidated financial statements, the Company has full access to and control over all its cash, cash equivalents and available-for-sale marketable securities.

The Company also has investments in money market funds, U.S. Treasuries, corporate debt obligations, commercial paper, government agency obligations and asset-backed securities, which can be subject to certain credit risks. The Company mitigates the risks by investing in high-grade instruments, limiting its exposure to any one issuer and monitoring the ongoing creditworthiness of the financial institutions and issuers. The Company has not experienced any losses on its financial instruments.

Concentration of collaboration revenue, accounts receivable and contract assets

The following table summarizes the percentages of collaboration revenues, accounts receivable and contract assets from each of the Company's customers that individually accounted for 10% or more of its collaboration revenues, accounts receivable and contract assets:

	Collaboration revenue	
	Nine months ended September 30,	
	2022	2023
Customer A	92%	44%
Customer B	*	12%
Customer C	*	44%
	92%	100%

	Contract assets	
	December 31, 2022	September 30, 2023
Customer B	100%	*
	100%	*

Notes to the Unaudited Condensed Consolidated Financial Statements

	Accounts receivable	
	December 31, 2022	September 30, 2023
Customer A	*	38%
Customer B	*	62%
	*	100%

* *the customer did not account for 10% or more of the Company's collaboration revenues, accounts receivable or contract assets during the respective fiscal period*

The Company reviews its accounts receivable and contract assets for impairment and credit loss allowance. No impairment or credit loss allowance was recorded as of December 31, 2022 and September 30, 2023.

Deferred finance issuance costs

Deferred finance issuance costs, consisting of legal fees relating to in-process equity financings and initial public offering are capitalized. The deferred finance issuance costs will be offset against offering proceeds upon the completion of the financing or the offering. In the event the financing or the offering is terminated or delayed, deferred finance issuance costs will be expensed immediately as a charge to general and administrative expenses in the condensed consolidated statements of operations and comprehensive loss. The Company had no deferred finance issuance costs capitalized and \$4.4 million of deferred finance issuance costs as of December 31, 2022 and September 30, 2023, respectively, included in other assets in the condensed consolidated balance sheets.

Recently issued accounting pronouncements

The Company noted no recently issued accounting pronouncements that will impact its condensed consolidated financial statements and were not adopted by the Company. No new accounting pronouncements were adopted during the nine months ended September 30, 2023.

3. Fair value measurements

Assets and liabilities recorded at fair value on a recurring basis in the condensed consolidated balance sheets, are categorized based upon the level of judgment associated with inputs used to measure their fair values. The accounting guidance for fair value provides a framework for measuring fair value and requires certain disclosures about how fair value is determined. The accounting guidance establishes a three-level valuation hierarchy that prioritizes the inputs to valuation techniques used to measure fair value based upon whether such inputs are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions made by the reporting entity. The three-level hierarchy for the inputs to valuation techniques is briefly summarized as follows:

Level 1 — Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2 — Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Notes to the Unaudited Condensed Consolidated Financial Statements

Level 3 — Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. An assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. Changes in the ability to observe valuation inputs may result in a reclassification of levels of certain securities within the fair value hierarchy. The Company recognizes transfers into and out of levels within the fair value hierarchy in the period in which the actual event or change in circumstances that caused the transfer occurs.

The Company's financial instruments measured at fair value on a recurring basis consist of Level 1, Level 2, and Level 3 financial instruments. Usually, marketable securities are considered Level 2 when their fair values are determined using inputs that are observable in the market or can be derived principally from or corroborated by observable market data such as pricing for similar securities, recently executed transactions, cash flow models with yield curves, and benchmark securities. In addition, Level 2 financial instruments are valued using comparisons to like-kind financial instruments and models that use readily observable market data as their basis. U.S. Government bonds, corporate debt obligations, commercial paper, government agency obligations and asset-backed securities are valued primarily using market prices of comparable securities, bid/ask quotes, interest rate yields and prepayment spreads and are included in Level 2.

Financial assets and liabilities are considered Level 3 when their fair values are determined using pricing models, discounted cash flow methodologies, or similar techniques, and at least one significant model assumption or input is unobservable. The Company's investments in preferred stock and common stock shares of Affini-T Therapeutics Inc. ("Affini-T") (see Note 5) are Level 3 financial assets.

The following table summarizes the estimated fair value of the financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy as of December 31, 2022 (in thousands):

	December 31, 2022			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds (included in cash and cash equivalents)	\$ 182,441	\$ 182,441	\$ —	\$ —
U.S. Treasury bills(1)	14,821	—	14,821	—
U.S. Government bonds	14,651	—	14,651	—
Government agency obligations	22,468	—	22,468	—
Corporate debt obligations	25,900	—	25,900	—
Commercial paper	88,447	—	88,447	—
Asset-backed securities	11,403	—	11,403	—
Long-term investments (Note 5)	5,651	—	—	5,651
Total fair value of assets	<u>\$ 365,782</u>	<u>\$ 182,441</u>	<u>\$ 177,690</u>	<u>\$ 5,651</u>

(1) Certain prior period amounts have been reclassified to conform to the current period presentation

Notes to the Unaudited Condensed Consolidated Financial Statements

The following table summarizes the estimated fair value of the financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy as of September 30, 2023 (in thousands):

	September 30, 2023			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds (included in cash and cash equivalents)	\$ 95,753	\$ 95,753	\$ —	\$ —
U.S. Treasury bills	50,622	—	50,622	—
U.S. Government bonds	2,970	—	2,970	—
Government agency obligations	44,615	—	44,615	—
Corporate debt obligations	22,812	—	22,812	—
Commercial paper	63,263	—	63,263	—
Asset-backed securities	3,302	—	3,302	—
Foreign debt securities	3,446	—	3,446	—
Long-term investments (Note 5)	8,521	—	—	8,521
Total fair value of assets	\$ 295,304	\$ 95,753	\$ 191,030	\$ 8,521

In addition, restricted cash of \$6.1 million and \$5.2 million as of December 31, 2022 and September 30, 2023, respectively, collateralized by the Company's cash equivalents, are financial assets measured at fair value and are Level 1 financial instruments under the fair value hierarchy.

The Company's investments in shares of Affini-T common stock and preferred stock are accounted at fair value and are Level 3 investments. The fair value is estimated based on information available to management including recent financing transactions, capitalization and rights and preferences of outstanding securities and is based on option-pricing model. The estimated fair value of the Company's investment in Affini-T was \$5.7 million and \$8.5 million as of December 31, 2022 and September 30, 2023, respectively.

The following table sets forth a summary of the changes in the fair value of the Company's Level 3 financial assets (in thousands):

	2022	2023
Fair value as of January 1	\$ 4,262	\$ 5,651
Change in fair value included in other income (expense)	94	2,870
Fair value of investment received as collaboration consideration (Note 7)	1,295	—
Fair value as of September 30	\$ 5,651	\$ 8,521

There were no transfers within the fair value hierarchy during the nine months ended September 30, 2022 and 2023.

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4. Available-for-sale marketable securities

The following table summarizes the amortized cost, unrealized gains (losses) and estimated fair value of the available-for-sale marketable securities as of December 31, 2022 (in thousands):

	Amortized cost	Unrealized gains	Unrealized losses	Estimated fair value
Money market funds	\$ 182,441	\$ —	\$ —	\$ 182,441
U.S. Treasury bills	14,818	3	—	14,821
U.S. Government bonds	14,720	—	(69)	14,651
Government agency obligations	22,431	41	(4)	22,468
Corporate debt obligations	26,041	10	(151)	25,900
Commercial paper	88,447	—	—	88,447
Asset-backed securities	11,508	—	(105)	11,403
Total	360,406	54	(329)	360,131
Less: amounts classified as cash equivalents	(182,441)	—	—	(182,441)
Total available-for-sale marketable securities	\$ 177,965	\$ 54	\$ (329)	\$ 177,690

The following table summarizes the amortized cost, unrealized gains (losses) and estimated fair value of the available-for-sale marketable securities as of September 30, 2023 (in thousands):

	Amortized cost	Unrealized gains	Unrealized losses	Estimated fair value
Money market funds	\$ 95,753	\$ —	\$ —	\$ 95,753
U.S. Treasury bills	50,630	1	(9)	50,622
U.S. Government bonds	3,007	—	(37)	2,970
Government agency obligations	44,732	—	(117)	44,615
Corporate debt obligations	22,906	—	(94)	22,812
Commercial paper	63,333	1	(71)	63,263
Asset-backed securities	3,319	—	(17)	3,302
Foreign debt securities	3,462	—	(16)	3,446
Total	287,142	2	(361)	286,783
Less: amounts classified as cash equivalents	(95,753)	—	—	(95,753)
Total available-for-sale marketable securities	\$ 191,389	\$ 2	\$ (361)	\$ 191,030

As of December 31, 2022 and September 30, 2023, no significant facts or circumstances were present to indicate a deterioration in the creditworthiness of the issuers of the available-for-sale securities, and the Company has no requirement or intention to sell these securities before maturity or recovery of their amortized cost basis. The Company considered the current and expected future economic and market conditions and determined that its investments were not significantly impacted. For all securities with a fair value less than its amortized cost basis, the Company determined the decline in fair value below amortized cost basis to be immaterial and non-credit related, and therefore no allowance for losses has been recorded. During the nine months ended September 30, 2022 and 2023, the Company did not recognize any impairment losses on its investments.

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The Company's policy is to exclude the applicable accrued interest from both the fair value and the amortized cost basis of its available-for-sale securities for purposes of identifying and measuring an impairment. The Company presents accrued interest receivable related to the available-for-sale securities in prepaid expenses and other current assets, separate from available-for-sale marketable securities in the condensed consolidated balance sheets. As of December 31, 2022 and September 30, 2023, accrued interest receivable was \$0.3 million and \$0.7 million, respectively. The Company's accounting policy is to not measure an allowance for credit losses for accrued interest receivable and to write-off any uncollectible accrued interest receivable as a reversal of interest income in a timely manner, which it considers to be in the period in which the Company determines the accrued interest will not be collected. The Company has not written off any accrued interest receivable for the nine months ended September 30, 2022 and 2023.

The amortized cost and fair value of available-for-sale marketable securities by contractual maturity were as follows as of December 31, 2022 (in thousands):

	Amortized cost	Estimated fair value
Maturing within one year	\$ 163,259	\$ 163,030
Maturing in one to five years	14,706	14,660
Total available-for-sale marketable securities	\$ 177,965	\$ 177,690

The amortized cost and fair value of available-for-sale marketable securities by contractual maturity were as follows as of September 30, 2023 (in thousands):

	Amortized cost	Estimated fair value
Maturing within one year	\$ 187,332	\$ 187,014
Maturing in one to five years	4,057	4,016
Total available-for-sale marketable securities	\$ 191,389	\$ 191,030

5. Long-term investments

Affini-T investment

As of December 31, 2022 and September 30, 2023, the Company had investments in shares of preferred stock and common stock of Affini-T. The Company performed a VIE analysis and concluded that it was not a primary beneficiary of Affini-T as of December 31, 2022 and September 30, 2023. The Company is using the fair value method to account for its investments in Affini-T with changes in fair value recorded to the condensed consolidated statements of operations and other comprehensive loss (see Note 3).

As of December 31, 2022, the fair value of common stock shares was estimated by management, considering the most recent third-party valuation, and the fair value of preferred stock shares was estimated based on recent sales of similar preferred stock to another investor for cash. As of June 30, 2023, the fair values of common stock and preferred stock shares were estimated by management using an option-pricing valuation model and recent financing transactions at Affini-T. The Company noted no changes in estimated fair value of Affini-T preferred and common stock from June 30, 2023 to September 30, 2023. The Company recognized changes in fair value of \$0.1 million and of \$2.9 million for the nine months ended September 30, 2022 and 2023, respectively.

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No impairment loss was recognized on the Company's investment in Affini-T as of December 31, 2022 or September 30, 2023.

VITtoria investment

As of December 31, 2022 and September 30, 2023, the Company had investment in shares of preferred stock of VITtoria Biotherapeutics, Inc. ("Vittoria"), a private biotechnology company. The Company accounts for its investment in Vittoria using the measurement alternative method. As of December 31, 2022 and September 30, 2023, the carrying value of Vittoria's investment was \$2.2 million and no impairment was recognized.

6. Condensed consolidated balance sheets components

Property and equipment, net consists of the following (in thousands):

		December 31, 2022	September 30, 2023
Laboratory equipment	Useful life 5	\$ 13,455	\$ 20,239
Leasehold improvements	lesser of useful life or the lease term	3,531	3,810
Furniture and fixtures	3-5	328	374
Computers and related equipment	3-5	54	602
Construction in progress		1,402	1,422
Total property and equipment		18,770	26,447
Less: Accumulated depreciation and amortization		(2,248)	(5,234)
Total property and equipment, net		\$ 16,522	\$ 21,213

Depreciation and amortization expense was \$1.0 million and \$3.0 million for the nine months ended September 30, 2022 and 2023, respectively.

Other assets consist of the following (in thousands):

	December 31, 2022	September 30, 2023
Operating lease deposit	\$ 237	\$ 238
Long-term prepaid services	213	175
Deferred finance issuance costs	—	4,405
Total other assets	\$ 450	\$ 4,818

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Accrued expenses and other current liabilities consist of the following (in thousands):

	December 31, 2022	September 30, 2023
Accrued personnel related expenses	\$ 4,819	\$ 4,908
Accrued legal and professional services	1,200	2,985
Accrued purchases of property and equipment	896	544
Accrued research and development expenses	1,684	1,954
Other accrued liabilities	191	408
Total accrued expenses and other current liabilities	<u>\$ 8,790</u>	<u>\$ 10,799</u>

7. Significant agreements

Moderna strategic collaboration and license agreement

Terms of the agreement

On October 29, 2021, the effective date, the Company entered into a Strategic Collaboration and License Agreement (the "Moderna Agreement") with ModernaTX, Inc. ("Moderna"). The parties will collaborate on the research and development of in-vivo genome editing therapies directed at certain targets and the commercialization of such genome editing therapies. The collaboration provides Moderna with exclusive access to the Company's technology platform during the research period in (1) the field of in vivo gene editing technology for a therapeutic, ameliorative or prophylactic application by way of knock-out through InDel formation or base editing or insertion of an exogenous DNA template (such field, "DT Field") and (2) the field of in vivo gene editing technology for a therapeutic, ameliorative or prophylactic application outside the use of (a) DNA donor templates and (b) no exogenous template at all but including (c) correction by base editing (such field, "RT Field"). The parties formed a joint steering committee, a joint research subcommittee and a joint patent subcommittee to oversee the collaboration activities.

Under the terms of the Moderna Agreement, the parties will collaborate on one or more programs in the RT Field (the "Moderna RT program") and two programs in the DT Field (the "Moderna DT program" and the "DT Co-Co program").

With respect to the Moderna RT and Moderna DT programs, the parties will collaborate on the research and development of product candidates under the approved research plans. The initial research term of the Moderna RT program is four years, which may be extended by Moderna for an additional three years upon written notice and a payment of extension fees. The initial research term of the Moderna DT program is four years. The Company granted to Moderna an option to obtain an exclusive license to develop, manufacture and commercialize up to ten Moderna RT program candidates and up to two Moderna DT program candidates at any time during the research term and prior to filing of an investigational new drug ("IND") application with the Food and Drug Administration ("FDA") or any similar application filed with a regulatory authority in a country other than the United States ("U.S."), subject to Moderna's payment of an option exercise fee of \$10.0 million per target.

With respect to the DT Co-Co program, the parties will work together on the co-development and commercialization of products and share costs and profits equally. The Company maintains commercialization rights in the U.S. (subject to Moderna's right to appoint up to 50% of the U.S. sales force for the DT Co-Co program), while Moderna maintains these rights in countries other than the U.S. The initial research term for

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the DT Co-Co program is four years, and each party has a right to opt-out of the DT Co-Co program at any time, at which point the other party has the right to solely continue the development and commercialization activities. If there is no development candidate nomination by the end of the initial research term, the DT Co-Co program will expire, unless the parties have mutually agreed to continue the program.

During the year ended December 31, 2021, the Company received a non-refundable upfront payment of \$40.0 million and a \$5.0 million payment for the first year of research costs. Concurrent with the Moderna Collaboration Agreement, Moderna also provided \$30.0 million in cash in the form of a convertible promissory note pursuant to a convertible promissory note agreement dated October 29, 2021 (the "Moderna Convertible Promissory Note Agreement"). The convertible promissory note was converted into shares of Series B redeemable convertible preferred units in January 2022 (see Note 9). Moderna will reimburse the Company up to \$5.0 million in annual research and development costs related to the Moderna DT and Moderna RT programs, or up to the agreed amount of expenses per the budget. As of September 30, 2023, the Company has received a total of \$49.6 million under the Moderna Agreement, not including cost-sharing payments under the DT Co-Co program.

For the Moderna RT and Moderna DT programs, the Company is eligible to receive (i) technology milestone fees related to the achievement of certain preclinical research objectives, of up to \$75.0 million, (ii) development and regulatory milestones of up to \$100.0 million per target, (iii) sales milestones of up to \$200.0 million per target and (iv) royalties ranging from a mid-single digit to a low-teens percentage of annual net sales of a licensed product. Any profits and losses from the co-development and commercialization of the DT Co-Co program are shared equally between the Company and Moderna. With respect to the DT Co-Co program for which the opt-out party has exercised its opt-out right, the continuing party will pay to the opt-out party, certain development, regulatory and sales milestone payments that will not exceed an aggregate \$239.0 million per DT Co-Co target, and opt-out royalties ranging from a high-single digit to a low-teens percentage of annual net sales of a licensed product.

The term of the Moderna Agreement will continue on a licensed product-by-licensed product and country-by-country basis, until the expiration of the applicable royalty term. The royalty term commences on the first commercial sale of a licensed product and terminates on the latest of: (a) the expiration or abandonment of the last valid claim of a patent within the licensed Moderna DT or RT technology; (b) 10 years after the first commercial sale of a licensed product; and (c) expiration of the regulatory exclusivity. Upon the expiration of the term of a licensed product in the Moderna DT or Moderna RT program, the licenses granted to Moderna will survive and become perpetual, fully paid and royalty-free. Each party may terminate the Moderna Agreement on a program-by-program basis upon written notice to the other party for an uncured material breach or insolvency. The Company may terminate the Moderna Agreement upon written notice to Moderna for a patent challenge. Additionally, Moderna may terminate the agreement at its convenience with respect to Moderna DT or Moderna RT programs for any reason upon at least: (a) 60 days' prior written notice if a first commercial sale has not occurred for the products in such program, or (b) 180 days' prior written notice if a first commercial sale of a product in such program has occurred.

Accounting analysis and revenue recognition

The Company concluded that the Moderna DT and Moderna RT programs are in the scope of ASC 606. The Company determined that the licenses granted to Moderna, and its participation in the joint steering committee are not capable of being distinct from the preclinical research and development services and therefore concluded that there are two performance obligations: (1) the Moderna RT program and (2) the Moderna DT

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program. The Company also concluded that the option to obtain an exclusive license and options to extend Moderna RT program term do not include significant incremental discounts, and as such, the options do not provide material rights.

The Company concluded the DT Co-Co program research activities are within the scope of ASC 808, as the Company and Moderna are both active participants in the research, development and commercialization activities, are exposed to significant risks and rewards that are dependent on the success of the DT Co-Co program activities and share costs and profits equally. The Company determined that the guidance in ASC 730, *Research and Development*, was appropriate to apply to the DT Co-Co program research activities by analogy, based on the nature of the cost sharing provisions of the agreement. The Company concluded that DT Co-Co program is one unit of accounting, as the co-exclusive license is not distinct from the research and development and the participation in joint steering committee activities. The Company recognizes payments to or from Moderna related to the DT Co-Co program cost sharing research activities as an increase to or reduction of research and development expenses, respectively.

The Company concluded that the Moderna Collaboration Agreement and the Moderna Convertible Promissory Note Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. The Company estimated the contract consideration to be \$90.0 million, which consisted of: 1) the non-refundable upfront collaboration payment of \$40.0 million received in 2021, 2) \$30.0 million in cash received in 2021 in exchange for the convertible promissory note and 3) the estimated cost reimbursements for Moderna DT and Moderna RT programs of \$20.0 million. The Company constrained future milestones, as it assessed that it is probable that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in future periods. During the year ended December 31, 2021, the Company recorded \$30.0 million of the contract consideration for the convertible promissory note based on the fair value and allocated the transaction price of \$60.0 million to each of the following programs on a relative standalone selling price basis: 1) \$49.5 million to the Moderna RT program, 2) \$5.5 million to the Moderna DT program and 3) \$5.0 million to the DT Co-Co program.

The variable consideration is reevaluated at each reporting period and as changes in circumstances occur. The Company recognizes revenue for each of the Moderna DT and Moderna RT programs as collaboration revenue based on the measure of progress using an estimated cost-based input method each reporting period. The Company also amortizes the allocation consideration for the DT Co-Co program of \$5.0 million as a credit to research and development expenses during the discovery and lead optimization phases for the DT Co-Co program.

The Company recognized collaboration revenue of \$10.7 million and \$14.2 million in the condensed consolidated statements of operations and comprehensive loss for the nine months ended September 30, 2022 and 2023, respectively. As of September 30, 2023, the Company recorded \$1.5 million in accounts receivable on the condensed consolidated balance sheet, related to services performed. As of December 31, 2022 and September 30, 2023, deferred revenue related to the Moderna Agreement was \$30.2 million and \$17.2 million, respectively. Collaboration revenue recognized during the nine months ended September 30, 2022 and 2023 included \$10.7 million and \$14.2 million that was included in deferred revenue as of December 31, 2021 and 2022, respectively. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligations was approximately \$27.8 million as of September 30, 2023, which the Company expects to recognize as revenue over the next two-to-three years.

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The Company recognized \$0.5 million and \$2.7 million in credits to research and development expenses related to cost sharing allocation and amortization of the collaboration advance, respectively, within research and development expenses in the condensed consolidated statement of operations and comprehensive loss during the nine months ended September 30, 2022. The Company recognized \$0.3 million and \$0.5 million in credits to research and development expenses related to cost sharing allocation and amortization of the collaboration advance during the nine months ended September 30, 2023, respectively. As of December 31, 2022, the collaboration advance balance was \$1.1 million, partially offset by the cost-sharing receivable balance of \$0.4 million, which was presented as a collaboration advance on the Company's condensed consolidated balance sheet. As of September 30, 2023, the collaboration advance balance was \$0.7 million, partially offset by the cost-sharing receivable balance of \$0.2 million, which was presented as a collaboration advance on the Company's condensed consolidated balance sheet.

Affini-T development, option and license agreement

Terms of the agreement

On June 14, 2022, the effective date, the Company entered into a Development, Option and License Agreement (the "Affini-T Agreement") with Affini-T. Pursuant to the Affini-T Agreement, the parties have agreed to identify, develop or optimize certain reagents using the Company's proprietary technology for Affini-T to use such reagents to develop and commercialize gene edited T-cell receptor ("TCR")-based therapeutic products exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with any engineered primary TCR alpha/beta T cells and non-exclusively in the field of treatment, prevention or diagnosis of any human cancer using products with certain other engineered immune cells worldwide. A joint steering committee was established by both parties to assign alliance managers and project leaders to oversee the collaboration activities.

Pursuant to the Affini-T Agreement, the Company granted Affini-T options to receive, on a pre-specified target-by-pre-specified target basis, for up to six pre-specified targets, either (i) an exclusive, royalty-bearing, sublicensable worldwide license under all of the Company's applicable intellectual property to research, develop, manufacture, use, commercialize and otherwise exploit any TCR-based therapy, preventative treatment, or diagnostic for humans that is directed to such pre-specified target, contains or comprises Primary TCR alpha/beta T Cells and is derived from ex vivo application of a Company reagent (the "Exclusive Option") or (ii) a non-exclusive, royalty-bearing, sublicensable worldwide license under all of the Company's applicable intellectual property to research, develop, manufacture, use, commercialize and otherwise exploit any TCR-based therapy, preventative treatment, or diagnostic for humans that is directed to such pre-specified target, contains or comprises TCR natural killer ("NK") cells derived from iPSC immune cells or TCR T cells derived from donor-derived or iPSC immune cells. Affini-T can exercise its options for either an exclusive license or a non-exclusive license, or both, for each pre-specified target by providing written notice prior to the earlier of (x) the end of the Affini-T Agreement term or (y) 90 days following the filing of an IND for a licensed product directed to a pre-specified target, subject to the payment of certain fees per each option exercised. After the option exercise, Affini-T has agreed to use commercially reasonable efforts to conduct all development and commercialization activities for a licensed product, and development and commercialization of all licensed products will be at Affini-T's sole cost and expense.

In connection with the Affini-T Agreement, the Company received upfront equity consideration of 719,920 shares of Affini-T's common stock with an estimated fair value of \$1.3 million in June 2022. The fair value of Affini-T's shares of common stock was estimated by management, considering the most recent third-party

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valuation. Affini-T has also agreed to reimburse the Company for expenses incurred while performing research activities under the research plans. As of September 30, 2023, the Company received a total of \$3.2 million from Affini-T related to reimbursable expenses. Additionally, the Company is eligible to receive (i) 933,650 shares of Affini-T's common stock upon the achievement of a regulatory milestone, which is the earlier of a submission of a drug master file to the FDA or an acceptance of an IND filing for a licensed product by the FDA, (ii) up to \$18.8 million in future developmental milestone payments depending on the completion of or the number of patients dosed in, the relevant human clinical trial, or the initiation of a pivotal trial, and \$40.6 million in future regulatory approval milestone payments, which include regulatory approvals in the U.S. and other markets for licensed products directed to a pre-specified target if options for both exclusive and non-exclusive licenses are exercised with respect to such target, (iii) up to \$250.0 million in sales-based milestones for aggregate sales of all licensed products directed to a given pre-specified target and (iv) royalties ranging from a low-single digit to high-single digit percentage of worldwide annual net sales of licensed products.

The initial term of the Affini-T Agreement is five years from the effective date. If Affini-T exercises an Exclusive Option with respect to any pre-specified target during the initial term, the initial term will be extended by an additional five years. Following the expiration of the extended term, if any, the agreement will continue on a target-by-target basis and expire with respect to such target upon the expiration of the royalty term for all licensed products directed to such target. The Affini-T Agreement may be terminated during the term by either party for an uncured material breach by, or bankruptcy of, the other party. Additionally, Affini-T may terminate the Affini-T Agreement for convenience, in its entirety, on a research plan-by-research plan basis, on a target-by-target basis or on a licensed product-by-licensed product basis, by providing prior written notice.

Accounting analysis and revenue recognition

The Company concluded that the Affini-T Agreement is in the scope of ASC 606 and that there is one performance obligation to perform research activities under the Affini-T Agreement. Exclusive and non-exclusive licenses are optional contingent purchases that do not include significant incremental discounts, and therefore do not provide a material right.

At the effective date, the transaction price consisted of the upfront equity consideration with an estimated fair value of \$1.3 million and estimated research reimbursement costs. Research reimbursement costs represent variable consideration, and the Company's management estimates what portion to include in total consideration at the end of each reporting period. Other payments under the Affini-T Agreement, including additional equity consideration and development and regulatory milestones, also represent variable consideration, and are constrained to the extent that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in future periods. As of December 31, 2022 and September 30, 2023, additional equity consideration and future development and regulatory milestone payments were excluded from the estimated total transaction price as they were considered constrained. The transaction price is reevaluated in each reporting period and as changes in circumstances occur. The Company recognizes revenue each reporting period based on the measure of progress using an estimated cost-based input method.

The Company recognized \$0.9 million and \$3.7 million in collaboration revenue in the condensed consolidated statements of operations and comprehensive loss during the nine months ended September 30, 2022 and 2023, respectively. As of December 31, 2022, the Company recorded \$1.3 million in contract assets on the condensed consolidated balance sheet, related to services performed but not invoiced. There was no contract asset related to services performed as of September 30, 2023. As of September 30, 2023, the Company recorded \$2.4 million in accounts receivable on the condensed consolidated balance sheet, related to services performed. As of

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December 31, 2022 and September 30, 2023, deferred revenue related to the Affini-T Agreement was zero and \$0.6 million, respectively. In June 2023, the joint steering committee approved the budget for estimated research reimbursement costs for the Affini-T Agreement, which resulted in a \$2.4 million reduction to variable consideration. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligation was approximately \$2.1 million as of September 30, 2023, which the Company expects to recognize as revenue over the next four-to-five years.

Ionis collaboration and license agreement

Terms of the agreement

On November 10, 2022, the effective date, the Company entered into a Collaboration and License Agreement (the "Ionis Agreement") with Ionis Pharmaceuticals, Inc. ("Ionis") to collaborate on drug discovery and exploratory research activities to advance new medicines using gene editing strategies, with the goal of discovering novel medicines. Pursuant to the terms of the Ionis Agreement, the Company granted Ionis and its affiliates a worldwide exclusive, royalty-bearing license, with the right to grant sublicenses, to use all licensed systems and licensed products in the field of in vivo gene editing for all therapeutic, prophylactic, palliative, and analgesic uses in humans. In connection with the Ionis Agreement, the Company also has the right to exercise an exclusive option to co-develop and co-commercialize certain products under a drug discovery program. A joint steering committee was established by both parties to coordinate, oversee and monitor the research and drug discovery activities under the Ionis Agreement.

The parties will collaborate to discover therapeutic products under a drug discovery program and develop a drug discovery plan for each target, selected by Ionis. The target selection is divided into two waves: up to four targets in Wave 1 and up to four targets in Wave 2. For each drug discovery program, once the parties identify a development candidate that is suitable for further development, Ionis will be responsible for the development and commercialization of products resulting from such program. Per the terms of the Ionis Agreement, at any time prior to the designation of a development candidate for a drug discovery program and for any reason, Ionis may replace the collaboration target, provided such target has not previously been substituted out. Ionis may substitute (i) up to two Wave 1 targets and (ii) up to two Wave 2 targets.

The drug discovery activities for a program commence on the selection of a target and expire upon the earlier of (a) completion of all drug discovery activities for such program, (b) the fifth anniversary of the effective date and (c) selection of a development candidate for such drug discovery program. If one or more Wave 2 targets become collaboration targets as a result of the parties achieving enabled delivery and less than two years are remaining in the drug discovery term, then the term will be extended to the earlier of (i) the time that the Company completes all of its activities under the applicable drug discovery plan and (ii) the seventh anniversary of the effective date, subject to the Company's consent.

The parties will also conduct an exploratory research program, and will jointly optimize gRNA and select delivery technologies and other activities. The exploratory research activities commence on the effective date and expire upon the earlier of (a) completion of all exploratory research activities established in the exploratory research plan, and (b) the fifth anniversary of the effective date.

The Company has the exclusive option to co-develop and co-commercialize the licensed products under a drug discovery program (the "Co-Co Option") with Ionis. The Co-Co Option may be exercised for (a) the initial Wave 1 target ("Target 1"), (b) no more than one of the other three discovery programs for the Wave 1 targets, and (c) no more than two drug discovery programs for the Wave 2 targets that become collaboration targets. If the

Notes to the Unaudited Condensed Consolidated Financial Statements

Company exercises the Co-Co Option for a particular drug discovery program, that drug discovery program will automatically be deemed a "Co-Co Program", all corresponding licensed products be deemed "Co-Co Products," the Company will be obligated to pay Ionis an option exercise fee, and the parties will enter into a separate co-development and co-commercialization agreement. The Co-Co Option exercise fee will equal 50% of Ionis' internal costs and out-of-pocket costs incurred in the conduct of the drug discovery activities prior to the exercise of the Co-Co Option and be reduced by 50% of the Company's corresponding costs incurred. Future development and commercialization costs will be shared equally. The Company may elect to reduce its cost-share percentage anywhere between 50% and 25% on a go-forward basis, provided the Company will continue to bear 50% of the costs of any clinical trials ongoing at the time of the election through the completion of the clinical trials.

The Company will manufacture all licensed systems and certain components of the applicable licensed products that are needed by Ionis for use in its development activities and all of the Company's manufactured components needed by Ionis for use in its commercialization activities. The Company will provide the manufactured components at a price that represents the cost of goods plus 15%.

Pursuant to the terms of the Ionis Agreement, the Company has also been granted an option to obtain a non-exclusive, royalty-bearing license, with the right to grant sublicenses, for certain Ionis' background technology to use in up to eight therapeutic products discovered by the Company in the field of in vivo gene editing and directed to a Collaboration Target (each such product, a "Metagenomi Product" and each such option an "Ionis IP Option"), but subject to encumbrance checks with respect to particular targets. A Collaboration Target is a target that is selected by Ionis, and, with respect to the Company is not the subject of discussions with a third party, is not the subject of a contractual grant of rights to a third party nor the subject to an internal research and development program. If the Company exercises its Ionis IP Option, the Company will pay to Ionis up to several million dollars per Metagenomi Product upon achievement of certain clinical and regulatory milestones. The Company is also obligated to pay Ionis royalties in an amount equal to a low single-digit royalty on the net sales of the applicable Metagenomi Product on product-by-product and country-by-country basis.

In November 2022, the Company received an \$80.0 million upfront payment from Ionis for the Wave 1 drug discovery research collaboration and selected Target 1. Ionis selected its second target ("Target 2") in Wave 1 in December 2022 and its third target ("Target 3") in Wave 1 in November 2023. In November 2023, the Company agreed to extend the period during which the Company expects Ionis will select its fourth target ("Target 4") in Wave 1 by an additional three months from the 12-month anniversary of the effective date, as permitted under the arrangement. Ionis has an option to select up to four Wave 2 targets at any time during the drug discovery term, if (a) an IND for any licensed product directed to a Wave 1 target is filed with the applicable regulatory authority or (b) the parties achieve enabled delivery for a non-liver target under the exploratory research activities, by providing written notice and by paying a Wave 2 target selection fee of \$15.0 million or \$30.0 million, depending on and per the selected target.

Ionis is obligated to reimburse the Company for all internal costs and out-of-pocket costs incurred in the performance of the exploratory research activities, up to an aggregate of \$10.0 million, which is payable in quarterly installments of \$0.5 million during the exploratory research term. As of September 30, 2023, the Company received a total of \$1.5 million related to the reimbursable expenses. The Company is also eligible to receive (a) up to \$29.0 million in future development milestone payments for each licensed product; (b) up to \$60.0 million in future regulatory milestone payments for each licensed product; (c) up to \$250.0 million in

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sales-based milestones for each licensed product, and (d) royalties on annual net sales of licensed products from a mid-single-digit to low-teens percentage, subject to customary reductions.

The term of the Ionis Agreement will continue (i) with respect to the drug discovery programs, until the expiration of all applicable royalty terms for a licensed product, (ii) with respect to the Co-Co Programs, until the parties cease all exploitation for the Co-Co Products that are the subject to such Co-Co Program, and (iii) with respect to the Metagenomi Products, until the expiration of the royalty term for a Metagenomi Product. The royalty term ends on the latest of the following two dates: (i) the expiration of (A) the last claim of any issued and unexpired patent, or (B) a claim within a patent application that has not been pending for more than seven years from the earliest date to which the claim or applicable patent application is entitled to claim priority and which claim has not been revoked, cancelled, withdrawn, held invalid, or abandoned, or (ii) 12 years following the first commercial sale of a licensed product.

The Ionis Agreement may be terminated during the term by either party for an uncured material breach or bankruptcy by the other party. Additionally, Ionis may terminate the Ionis Agreement for convenience and without penalty, in its entirety or on a licensed product-by-licensed product basis, by providing 90 days' written notice.

Accounting analysis and revenue recognition

The Company concluded that the Ionis Agreement is in the scope of ASC 606 at the effective date and until the Company exercises its Co-Co Option for any drug discovery program, which was determined to not be probable at the effective date and as of December 31, 2022 and September 30, 2023. The Company also concluded that exclusive licenses and participation in a joint steering committee are not distinct from discovery research services and should thus be combined into one performance obligation (the "discovery program"). The Company also concluded that exploratory research services are a separate and distinct performance obligation (the "exploratory program"). As the Ionis options for Wave 2 targets are optional purchases and do not have significant incremental discounts, as such, the options do not provide material rights.

The Company allocated the total estimated transaction price of \$90.0 million, which consisted of an \$80.0 million upfront payment received in November 2022 and a \$10.0 million reimbursement for research costs, into two performance obligations, and was determined based on their estimated standalone selling prices. The Company concluded that future development and commercial supply agreements are at market terms, as the terms were consistent with industry standards as of the effective date. The Company constrains future milestone payments under the arrangement to the extent that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in future periods. The Company constrained all development and regulatory milestone payments at the effective date and as of December 31, 2022 and September 30, 2023. The Company is recognizing revenue of \$80.0 million related to the discovery program and of \$10.0 million related to exploratory program over the research terms using an estimated cost-based input method as a measure of progress for each obligation.

The Company recognized \$14.4 million in collaboration revenue in the condensed consolidated statements of operations and comprehensive loss during the nine months ended September 30, 2023, which was included in deferred revenue as of December 31, 2022. As of December 31, 2022 and September 30, 2023, deferred revenue related to the Ionis Agreement was \$79.9 million and \$67.0 million, respectively. The value of the transaction price allocated to the remaining performance obligations was approximately \$75.5 million as of September 30, 2023, which the Company expects to recognize as revenue over the next four-to-five years.

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8. Commitments and contingencies

Operating leases

In January 2021, the Company entered into a ten-year operating lease for laboratory and office space in Emeryville, California. The lease commencement date was in February 2021. In conjunction with signing this lease, the Company secured a letter of credit for \$3.3 million, which is recorded as noncurrent restricted cash in the condensed consolidated balance sheets. As of December 31, 2022 and September 30, 2023, the balance of this letter of credit was \$3.3 million and \$2.5 million, respectively. The lease agreement includes a renewal provision allowing the Company to extend this lease for an additional five years, which the Company is not reasonably certain to exercise. In addition to base rent, the Company pays variable costs related to its share of operating expenses and taxes, which are recognized as incurred.

In September 2021, the Company entered into a 9.25-year operating lease for office space in Emeryville, California, with a lease commencement date in November 2021. In conjunction with signing the lease, the Company secured a letter of credit for \$0.8 million, which is recorded as noncurrent restricted cash in the condensed consolidated balance sheets as of December 31, 2022 and September 30, 2023. In addition to base rent, the Company pays variable costs related to its share of operating expenses and taxes, which are recognized as incurred.

In November 2022, the Company entered into an 8.25-year sublease for office, research and laboratory space in Emeryville, California, with a lease commencement date in January 2023. In conjunction with signing the lease, the Company secured a letter of credit for \$2.0 million, which is recorded as noncurrent restricted cash in the condensed consolidated balance sheet as of December 31, 2022 and September 30, 2023. Monthly base rent under the lease is approximately \$0.5 million and is subject to annual escalation. During the initial 18 months from the lease commencement date, 50% of the monthly base rent is abated. In addition to base rent, the Company pays variable costs related to its share of operating expenses and taxes, which are recognized as incurred.

Operating lease costs for the nine months ended September 30, 2022 and 2023 totaled \$4.1 million and \$8.5 million, respectively, including \$0.4 million and \$2.1 million of variable lease cost, respectively.

Supplemental information related to the Company's operating leases is as follows (in thousands):

	Nine months ended September 30,	
	2022	2023
Cash paid for amounts included in the measurement of lease liabilities	\$ 1,663	\$ 5,006
Weighted average remaining lease term (in years)	8.3	7.4
Weighted-average discount rate	10.1%	11.3%

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The following table summarizes a maturity analysis of the Company's operating lease liabilities showing the aggregate lease payments as of September 30, 2023 (in thousands):

2023 (remaining)	\$ 1,617
2024	8,345
2025	9,361
2026	9,673
2027	9,995
Thereafter	33,283
Total future lease payments	72,274
Less imputed interest	(24,067)
Total lease liability balance	48,207
Less: current operating lease liabilities	(2,269)
Non-current operating lease liabilities	\$ 45,938

Legal contingencies

From time to time, the Company may become involved in legal proceedings arising from the ordinary course of business. The Company records a liability for such matters when it is probable that future losses will be incurred and that such losses can be reasonably estimated. Significant judgment by the Company is required to determine both probability and the estimated amount. Management is currently not aware of any legal matters that could have a material adverse effect on the Company's financial position, results of operations or cash flows.

Guarantees and indemnifications

In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. Its exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To the extent permitted under Delaware law, the Company has agreed to indemnify its directors and officers for certain events or occurrences while the director or officer is, or was serving, at a request in such capacity. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2022 and September 30, 2023, the Company did not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded related liabilities.

9. Redeemable convertible preferred units

On January 21, 2022, the Company closed the Series B financing and issued 12,446,876 shares of the Series B redeemable convertible preferred units for gross cash proceeds of \$145.0 million. The Company incurred \$0.7 million in issuance costs. Concurrently with the closing of the Series B financing, the outstanding Moderna convertible promissory note and accrued interest of \$30.4 million was converted into 2,607,387 Series B Preferred Units, at a conversion price equal to the price per unit paid by the Series B investors.

On December 20, 2022, the Company entered into Series B-1 redeemable convertible preferred unit purchase agreement to sell up to 7,108,480 Series B redeemable convertible preferred units at the purchase price of \$14.06770. In December 2022, the Company sold and issued 6,773,726 shares of the Series B-1 redeemable

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convertible preferred units for gross cash proceeds of \$95.3 million in the initial closing. The Company incurred \$0.4 million issuance costs. Additional shares may be sold within 90 days of the initial closing.

In January 2023, the Company sold an additional 334,754 Series B-1 redeemable convertible preferred units in accordance with the Series B-1 purchase agreement and received gross cash proceeds of \$4.7 million. The Company incurred \$0.1 million in issuance costs.

As of December 31, 2022, the Company operated under the Amended and Restated Limited Liability Company Agreement dated December 20, 2022 (the "LLC Agreement"). As of September 30, 2023, the Company operated under the LLC Agreement, as amended on July 31, 2023 (see Note 11 for details around the amendment). The LLC Agreement provides for eight classes of units: common units, Series A-1 redeemable convertible preferred units (Series A-1), Series A-2 redeemable convertible preferred units (Series A-2), Series A-3 redeemable convertible preferred units (Series A-3), Series A-4 redeemable convertible preferred units (Series A-4), Series A-5 redeemable convertible preferred units (Series A-5), Series B redeemable convertible preferred units (Series B) and Series B-1 redeemable convertible preferred units (Series B-1).

The redeemable convertible preferred units as of December 31, 2022, consisted of the following (in thousands, except unit data):

	Units authorized	Units issued and outstanding	Aggregate liquidation preference	Net carrying value
Series A-1	7,501,002	7,501,002	\$ 24,247	\$ 24,067
Series A-2	774,473	774,473	500	581
Series A-3	1,513,860	1,513,860	1,773	1,892
Series A-4	8,280,360	8,280,360	40,149	40,007
Series A-5	1,580,937	1,580,937	10,000	9,948
Series B	15,054,263	15,054,263	175,375	174,678
Series B-1	7,108,480	6,773,726	95,291	94,930
	<u>41,813,375</u>	<u>41,478,621</u>	<u>\$ 347,335</u>	<u>\$ 346,103</u>

The redeemable convertible preferred units as of September 30, 2023, consisted of the following (in thousands, except unit data):

	Units authorized	Units issued and outstanding	Aggregate liquidation preference	Net carrying value
Series A-1	7,501,002	7,501,002	\$ 24,247	\$ 24,067
Series A-2	774,473	774,473	500	581
Series A-3	1,513,860	1,513,860	1,773	1,892
Series A-4	8,280,360	8,280,360	40,149	40,007
Series A-5	1,580,937	1,580,937	10,000	9,948
Series B	15,054,263	15,054,263	175,375	174,678
Series B-1	7,108,480	7,108,480	100,000	99,585
	<u>41,813,375</u>	<u>41,813,375</u>	<u>\$ 352,044</u>	<u>\$ 350,758</u>

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The holders of the redeemable convertible preferred units have various rights and preference as follows:

Voting rights

Each redeemable convertible preferred unit is entitled to one vote for each common unit into which such redeemable convertible preferred unit is then convertible. The redeemable convertible preferred unitholders and the common unitholders vote together on all matters as a single class, except as otherwise provided by law or the provisions of the LLC Agreement.

The Board of Managers consists of up to seven individuals. As long as at least 618,716 Series A-1 redeemable convertible preferred units, Series A-2 redeemable convertible preferred units and/or Series A-3 redeemable convertible preferred units remain outstanding, the members holding a majority of the outstanding Series A-1 redeemable convertible preferred units, Series A-2 redeemable convertible preferred units and Series A-3 redeemable convertible preferred units, voting together as a single class on an as-converted basis, are entitled to elect one manager. As long as at least 1,654,555 Series A-4 redeemable convertible preferred units remain outstanding, the members holding a majority of the Series A-4 redeemable convertible preferred units, voting as a single class, are entitled to elect one manager. As long as at least 316,187 Series A-5 redeemable convertible preferred units remain outstanding, the members holding a majority of the Series A-5 redeemable convertible preferred units, voting as a single class, are entitled to elect one manager. As long as at least 3,010,852 Series B redeemable convertible preferred units remain outstanding, the members holding a majority of the Series B redeemable convertible preferred units, voting as a single class, are entitled to elect one manager. The members holding a majority of the common units, voting as a single class are entitled to elect one manager. The members holding a majority of the units then outstanding, voting together as a single class on an as-converted to common units basis are entitled to elect any remaining managers. As of each December 31, 2022 and September 30, 2023 the Company's Board of Managers consisted of six individuals.

Conversion

Each redeemable convertible preferred unit is convertible into common units at the option of a holder at the then applicable conversion price, which is equal the original purchase price, subject to adjustments for recapitalization and others. The original purchase price is equal to \$3.2325 per Series A-1 Preferred Unit, \$0.6456 per Series A-2 Preferred Unit, \$1.1713 per Series A-3 Preferred Unit, \$4.84875 per Series A-4 Preferred Unit, \$6.32536 per Series A-5 Preferred Unit, \$11.64951 per Series B Preferred Unit, and \$14.06770 per Series B-1 Preferred Unit. As of December 31, 2022 and September 30, 2023, the redeemable convertible preferred units were convertible into common units at a one-for-one conversion ratio.

Each redeemable convertible preferred unit is automatically convertible into common units (or shares of common stock, if the Company is converted into a corporation), based on the then-effective applicable conversion rate (A) at any time upon the affirmative vote or written consent of (i) the members holding a majority of the redeemable convertible preferred units then outstanding, (ii) the members holding a majority of the Series B redeemable convertible preferred units then outstanding, and (iii) the members holding a majority of the Series B-1 redeemable convertible preferred units then outstanding, or (B) immediately upon the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common units (or other common securities) with the gross cash proceeds to the Company, before underwriting discounts, commissions and offering expenses, are at least \$100.0 million, or (C) the closing of a merger, acquisition or other business combination involving the Company and a publicly traded special purpose acquisition company ("SPAC") or its subsidiary or affiliate in which the

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surviving public company has available immediately cash of at least \$100.0 million in the aggregate greater than the cash on the Company's condensed consolidated balance sheets as of immediately prior to such merger, acquisition or other business combination (including proceeds of a private investment in public equity transaction that is substantially contemporaneous with or conditioned on such merger, acquisition or other business combination, and any redemptions from the SPAC's trust account).

Anti-dilution and other protective provisions

The holders of the redeemable convertible preferred units have proportional anti-dilution protection right for unit splits, unit dividends and similar recapitalizations, subject to certain exclusions, anti-dilution price protection for additional sales of securities by the Company for consideration per unit less than the applicable conversion price per unit of any series of the redeemable convertible preferred units, on a broad-based weighted average basis.

The holders of the redeemable convertible preferred units have certain protective rights. The Company shall not, either directly or by amendment, merger, consolidation or otherwise, without the prior written approval of members holding a majority of the redeemable convertible preferred units then outstanding to alter or change the rights, preferences or privileges of the redeemable convertible preferred units; consummate a liquidation or a deemed liquidation event; change the Company's LLC Agreement; authorize or create any new class or series of units or other equity security; increase or decrease the authorized number of the common units or the redeemable convertible preferred units or any series; redeem, acquire or repurchase any, or make any distribution on, any common units or redeemable convertible preferred units; change the compensation or equity awards granted to executive officers of the Company, unless such transaction is approved by the Board of Managers; increase or decrease the authorized number of managers constituting the Board of Managers and amend other rights or enter into certain transactions.

Liquidation preference

In the event of a liquidation, a deemed liquidation event (including a consolidation, merger or reorganization or a sale, lease, transfer, exclusive irrevocable license or other disposition of all or substantially all of the assets of the Company), dissolution or winding-up of the Company, the funds are distributed first to the members holding the redeemable convertible preferred units in proportion to and to the extent of their unreturned original purchase price per redeemable convertible preferred unit, until each member holding the redeemable convertible preferred units has received cumulative distributions in an amount equal to the unreturned original purchase price for each of such member's redeemable convertible preferred unit. Second, to the members holding common units and the redeemable convertible preferred units pro rata based on the number of units held by each such holder, assuming for this purpose that all the redeemable convertible preferred units have been converted into common units as of the date of such operating distribution or distribution of net proceeds or assets available for distribution, whether in cash or in other property. Third, the amounts that would otherwise be distributed to any redeemable convertible preferred unit holder pursuant to the liquidation preference on as-converted to common units basis will be reduced by an amount equal to the remaining preferred participation threshold amount for such redeemable convertible preferred unit. The preferred participation threshold amount for a redeemable convertible preferred unit is equal to the original purchase price, reduced by distributions paid.

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Distributions preference

Distributions, when determined by the Board of Managers, are payable to the members holding the redeemable convertible preferred units, pro rata in proportion to the liquidation preference amounts in respect of the redeemable convertible preferred units held by such members; thereafter, to the members in proportion to the number of shares held by such members, on as converted basis. No distributions were declared or made from inception and during the nine months ended September 30, 2022 and 2023.

Redemption

The redeemable convertible preferred units are not redeemable except in the event of certain effected deemed liquidation events, that are not in the Company's control.

10. Common units

As of December 31, 2022 and September 30, 2023, the Company was authorized to issue 66,000,000 common units. Each common unit is entitled to cast one vote. The holders of common units are also entitled to receive distributions whenever funds are legally available and when declared by the Company's Board of Managers, subject to prior rights of the holders of the redeemable convertible preferred units. No distributions have been declared from inception to date.

As of December 31, 2022 and September 30, 2023, the Company reserved common units for future issuance as follows:

	December 31, 2022	September 30, 2023
Outstanding redeemable convertible preferred units	41,478,621	41,813,375
Outstanding profits interests	7,516,073	9,556,687
Units available for grants under 2019 Equity Incentive Plan	7,088,092	5,047,478
Total common units reserved for future issuance	56,082,786	56,417,540

Founders and investors common units

In June 2017, Metagenomi Inc. issued 4,687,500 shares of its common stock at a purchase price of \$0.0001 per share to its founders and investors for services, which was an estimated fair value determined by the Board of Managers at the issuance date. Pursuant to the terms of the stock purchase agreements, 25% of the shares vested on the first anniversary of the vesting start date and monthly over the next 36 months. Vesting of shares is accelerated upon a change of control event (including an acquisition of the Company by another entity by means of any transaction or series of related transactions, or a sale of all or substantially all of the assets of the Company). The Company has a right to repurchase unvested shares upon termination of services provided by the founders to the Company at the price lower of i) the purchase price or ii) the fair value at the date of repurchase. In November 2018, in connection with the reorganization, common stock issued by Metagenomi Inc. was exchanged for common units of Metagenomi with the same terms. The estimated fair value of common unit at the modification date was determined to be \$0.02 per unit, based on the Company's recent common unit valuation, and the modification expense was immaterial.

In March 2019, the Company issued 1,260,000 common units to an investor for services with a purchase price of \$0.02 per unit, which was based on the recent Company's common stock valuation. As long as the investor

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continues to provide services, 25% of the shares vested immediately and the remainder vested monthly over the next 36 months. Vesting of shares is accelerated upon a change of control event. The Company has a right to repurchase unvested shares upon termination of services provided by the founders to the Company at the price lower of i) the purchase price or ii) the fair value at the date of repurchase.

The Company accounts for issued common units as unit-based compensation to founders and investors as service providers and recognizes unit-based compensation expense of \$0.1 million over the vesting period. The Company had 78,750 common units vested during the nine months ended September 30, 2022, having a fair value of less than \$0.1 million. There were no common units unvested as of December 31, 2022 and September 30, 2023.

11. Profits interests plan

The Company grants profits interests under the 2019 Equity Incentive Plan, adopted on March 13, 2019 (the "2019 Plan"). The Company may grant profits interests with a threshold amount, which may be zero, established by the Board of Managers on the date of issuance. Accordingly, such profits interests do not give a holder a share of the proceeds if the Company's assets were sold at fair market value and the proceeds of such disposition were distributed in complete liquidation of the Company immediately after the date of grant but give a holder a right to share in the appreciation in the value of a common unit from the date of receipt to the future, as specifically provided in the LLC Agreement. The 2019 Plan allows for grants of profits interests to the Company's officers, employees, directors and consultants. Profits interests generally vest monthly over four years, with or without one- year cliff vesting in the first year. In the event of a profits interest holder's termination, the unvested portion of such profits interest is automatically forfeited and cancelled without any additional consideration. Additionally, the Company has the right to repurchase the vested portion of such profits interest at its fair market value, which is based on the fair market value of a common unit (as determined by the Board of Managers), less the applicable profits interest threshold amount, at any time during the 12-month period after termination of a profits interest holder's service to the Company.

The Company's LLC Agreement was amended on July 31, 2023 to provide for "catch-up" distributions for profits interests once the applicable catch-up threshold amount for such profits interests was met (the "Amendment to the LLC Agreement").

The LLC Agreement provides each profits interest with a distribution threshold amount, which is determined on the date of issuance and represents the amount that would be distributed if, immediately after issuance, the Company sold all of its assets at fair market value and distributed the net proceeds in liquidation. A profits interest does not participate in Company distributions until an amount equal to its distribution threshold amount has been distributed to other members of the Company with units that either have a lower threshold amount or no threshold amount.

In accordance with the Amendment to the LLC Agreement, once the applicable distribution threshold amount has been met for a particular profits interest, such profits interest will participate in Company distributions on a pro rata basis until the catch-up threshold amount has been met. Once the catch-up threshold amount has been met, subsequent "catch-up" distributions will be made solely to holders of profits interests until such holders have received an amount equal to the amount such holders would have received had the distribution threshold not existed. Once the profits interest holders have received distributions in an amount equal to what they would have received had the distribution threshold not existed, all subsequent distributions are made on a pro rata basis with common unitholders.

Notes to the Unaudited Condensed Consolidated Financial Statements

As a result of the amendment, the Board approved an \$11.84 catch-up threshold amount, which was based on the estimated fair value of the Company's common unit as of July 31, 2023.

Refer below for discussion around the accounting treatment and financial statement impact of the catch-up.

The number of common units reserved for issuance under the 2019 Plan was 14,604,165 as of September 30, 2023.

The table below presents a summary of activities and a reconciliation of common units authorized and remaining for grant under the 2019 Plan during the nine months ended September 30, 2023:

	Units available for grants	Profits interests	Weighted- average threshold amount	Aggregate intrinsic value (in thousands)
Outstanding as of January 1, 2023	7,088,092	7,516,073	\$ 1.17	\$ 34,398
Profits interests granted	(2,267,813)	2,267,813	\$ 7.60	
Forfeited and expired	227,199	(227,199)	\$ 3.62	
Outstanding as of September 30, 2023	5,047,478	9,556,687	\$ 2.64	\$ 92,502
Vested and expected to vest	5,047,478	9,556,687	\$ 2.64	\$ 92,502

The aggregate intrinsic value is calculated as the positive difference between the threshold amount of the profits interests and the fair value of the Company's common unit as of September 30, 2023.

During the nine months ended September 30, 2022 and 2023, the Company granted 2,244,356 and 2,267,813 profits interests with a weighted average grant date fair value of \$1.89 and \$6.73, respectively. The total fair value of the profits interests vested during the nine months ended September 30, 2022 and 2023 was \$0.4 million and \$2.2 million, respectively.

Unit-based compensation expense

The grant date fair value of common units issued prior to July 31, 2023 utilized in the Black-Scholes model is determined by the Company's Board of Managers with the assistance of management. The grant date fair value of common units is determined using valuation methodologies which utilizes certain assumptions including probability weighting of expected exit events, volatility, time to liquidation, a risk-free interest rate and an assumption for a discount for lack of marketability.

After giving the effect to the Amendment to the LLC Agreement, the grant date fair value of profits interests issued after July 31, 2023 and profits interests at the modification date was estimated using the valuation model based on the Probability Weighted Expected Return Method ("PWERM"). The estimated equity fair value was allocated via the distribution waterfall in accordance with the Amendment to the LLC Agreement to all outstanding redeemable convertible preferred units, common units and profits interests.

Notes to the Unaudited Condensed Consolidated Financial Statements

The value of profits interests calculated using the Black-Scholes model and the option-pricing model within the PWERM model was based on the following assumptions for the nine months ended September 30, 2022 and 2023:

	Nine months ended September 30, 2022	From January 1 to July 30, 2023	From July 31 to September 30, 2023
Expected volatility	79.57% — 82.60%	78.57% — 86.33%	85.00%
Expected dividend yield	0%	0%	0%
Expected term (in years)	3.52 — 4.00	2.00 — 4.12	1.75
Risk-free interest rate	2.65% — 3.05%	3.50% — 4.47%	5.00%
Threshold range	3.20	5.75 — 7.40	11.84

Expected volatility—The Company is a private company and lacks company-specific historical and implied volatility information. Therefore, the Company estimates its expected unit's volatility based on the historical volatility of a publicly traded set of peer companies and expect to continue to do so until the Company has adequate historical data regarding the volatility of the Company's traded unit or stock price.

Expected term—The expected term of profits interests has been determined based on the expected time to liquidity and expected vesting term.

Risk-free interest rate—The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award.

Dividends—Expected dividend yield is zero because the Company does not pay cash dividends on common units and does not expect to pay any cash dividends in the foreseeable future.

The PWERM is the hybrid method, where the equity value in one or more scenarios is calculated using an option pricing model. The PWERM is a scenario based methodology that estimates the fair value of common unit based upon an analysis of future values for the company, assuming various outcomes. The common unit value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of members' units. The future value of the common unit under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common unit. A discount for lack of marketability of the common unit is then applied to arrive at an indication of value for the common unit.

In determining the fair value of the common units, the methodologies used to estimate the enterprise value were performed using methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

Notes to the Unaudited Condensed Consolidated Financial Statements

The following table presents the classification of unit-based compensation expense for the nine months ended September 30, 2022 and 2023 (in thousands):

	Nine months ended September 30,	
	2022	2023
Research and development expenses	\$ 495	\$ 2,166
General and administrative expenses	896	2,287
Total unit-based compensation expense	\$ 1,391	\$ 4,453

The above unit-based compensation expense related to the following unit-based awards for the nine months ended September 30, 2022 and 2023 (in thousands):

	Nine months ended September 30,	
	2022	2023
Profits Interests	\$ 1,389	\$ 4,453
Common Units	2	—
Total unit-based compensation expense	\$ 1,391	\$ 4,453

As part of the catch-up and Amendment to the LLC Agreement, the Company modified the terms and conditions of the profits interest, which resulted in a change in the fair value of the awards. The change was treated as a modification under ASC 718, *Stock Compensation*, in which the fair value of the profits interests were remeasured at the modification date and compared to the fair value of the modified award immediately prior to the modification, with the difference resulting in incremental compensation expense. The Company estimated total modification expense of \$10.3 million. The company recognized \$1.1 million of this expense related to vested profits interests as of the modification date and the remaining \$9.2 million is expected to be recognized over the next 3.3 years as profits interests continue to vest.

There was \$5.3 million and \$19.3 million in unrecognized unit-based compensation expense related to the profits interests as of September 30, 2022 and 2023, respectively, that is expected to be recognized over a weighted-average period of 3.2 and 2.9 years, respectively. There was no unrecognized unit-based compensation expense related to the common units as of December 31, 2022 and September 30, 2023, as all common units were fully vested.

12. Related party transactions

In connection with Series B financing, the Company reimbursed certain investors for finance issuance costs that they incurred totaling \$0.3 million during the nine months ended September 30, 2022.

In connection with Series B-1 financing, the Company reimbursed certain investors for finance issuance costs that they incurred totaling \$0.1 million during the year ended December 31, 2022. As of December 31, 2022, \$0.1 million of Series B-1 financing costs reimbursable to investors is recorded in accrued expenses and other current liabilities in the condensed consolidated balance sheets. The reimbursable Series B-1 financing costs were fully paid during the nine months ended September 30, 2023.

Notes to the Unaudited Condensed Consolidated Financial Statements

13. Income taxes

Metagenomi is treated as a partnership for tax purposes, and thus, is not subject to income taxes. It is the responsibility of the LLC members to report their proportionate share of any taxable income or loss generated by Metagenomi to the appropriate taxing authorities and pay the associated taxes, if any. With respect to the Company's subsidiary, Metagenomi Inc. is a corporation for tax purposes and is subject to income taxes which have been included in the condensed consolidated financial statements. All pre-tax losses have been incurred in the United States.

The Company provides for income taxes in interim periods based on the estimated annual effective tax rate for the year, adjusting for discrete items in the quarter in which they arise. The income tax provision for the nine months ended September 30, 2022 and 2023 was related to the timing differences of the recognition of upfront payments received under the Company's collaboration agreements for tax and financial reporting purposes and capitalization of its research and development expenses under the newly enacted Internal Revenue Code Section 174 ("Section 174"), which became effective on January 1, 2022. The effective tax rate differs from the U.S. statutory rate primarily due to the full valuation allowances on the Company's net deferred tax assets as it is more likely than not that all of the deferred tax assets will not be realized.

For the nine months ended September 30, 2022 and 2023, the Company recorded a provision for income taxes of \$1.7 million and \$5.3 million by applying its estimated annual effective tax rate to its year-to-date measure of ordinary income, respectively. The increase in the provision for income taxes during the nine months ended September 30, 2023 is primarily due to the increase in forecasted research and development spend, which results in corresponding increases to Section 174 capitalization, and taxable income related to the Ionis upfront payment which is partially offset by an increase in forecasted research and development credit.

14. Net loss per unit

Basic and diluted net loss per unit attributable to common unitholders is calculated as follows (in thousands except share and per share amounts):

	Nine months ended September 30,	
	2022	2023
Numerator:		
Net loss attributable to common members	\$ (28,966)	\$ (48,961)
Denominator:		
Weighted-average common units outstanding	5,947,500	5,947,500
Less: Weighted-average unvested common units subject to repurchase	(11,827)	—
Weighted-average units used to compute basic and diluted net loss per share	5,935,673	5,947,500
Net loss per unit attributable to common unitholders—basic and diluted:	\$ (4.88)	\$ (8.23)

Notes to the Unaudited Condensed Consolidated Financial Statements

The following outstanding potentially dilutive securities have been excluded from the calculation of diluted net loss per unit, as their effect is anti-dilutive:

	Nine months ended September 30,	
	2022	2023
Redeemable convertible preferred units	34,704,895	41,813,375
Profits interests	7,085,437	9,556,687
Total	41,790,332	51,370,062

15. Subsequent events

The Company has reviewed and evaluated subsequent events and concluded there were no subsequent events through December 8, 2023, the date that the condensed consolidated financial statements were available to be issued, except for the selection of Target 3 in Wave 1 and the extension of the Target 4 selection period under the Ionis Agreement in November 2023 as discussed in Note 7.

Shares



Common Stock

Prospectus

J.P. Morgan

Jefferies

TD Cowen

Wells Fargo Securities

BMO Capital Markets

Chardan

, 2024

Through and including , 2024 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Part II

Information Not Required in Prospectus

Item 13. Other Expenses of Issuance and Distribution

The following table sets forth the costs and expenses, other than underwriting discounts and commissions, to be paid by us in connection with the sale of the shares of common stock being registered hereby. All amounts shown are estimates except for the SEC registration fee, the FINRA filing fee and the Nasdaq Global Market initial listing fee.

SEC registration fee	\$	14,760
FINRA filing fee		15,500
Nasdaq listing fee		*
Printing and engraving expenses		*
Legal fees and expenses		*
Accounting fees and expenses		*
Transfer agent and registrar fees and expenses		*
Miscellaneous		*

* To be provided by amendment.

Item 14. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law (the "DGCL") authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys' fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys' fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

We have adopted provisions in our amended and restated certificate of incorporation and amended and restated bylaws to be in effect upon the effectiveness of this registration statement that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

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These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our amended and restated bylaws to be in effect upon the effectiveness of this registration statement provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and
- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements provide that we will indemnify each of our directors, certain of our executive officers and, at times, their affiliates to the fullest extent permitted by Delaware law. We will advance expenses, including attorneys' fees (but excluding judgments, fines and settlement amounts), to each indemnified director or executive officer in connection with any proceeding in which indemnification is available and we will indemnify our directors and officers for any action or proceeding arising out of that person's services as a director or officer brought on behalf of us or in furtherance of our rights. Additionally, certain of our directors or officers may have certain rights to indemnification, advancement of expenses or insurance provided by their affiliates or other third parties, which indemnification relates to and might apply to the same proceedings arising out of such director's or officer's services as a director referenced herein. Nonetheless, we have agreed in the indemnification agreements that our obligations to those same directors or officers are primary and any obligation of such affiliates or other third parties to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We also maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act.

The underwriting agreement filed as Exhibit 1.1 to this registration statement provides for indemnification of us and our directors and officers by the underwriters against certain liabilities under the Securities Act and the Exchange Act.

Item 15. Recent Sales of Unregistered Securities

In the three years preceding the filing of this registration statement, we have issued the following securities that were not registered under the Securities Act:

(a) Preferred Units

From 2020 to 2021, we sold an aggregate of 9,861,297 Series A preferred units in multiple closings, consisting of (i) 8,280,360 Series A-4 preferred units sold at a purchase price of \$4.84875 per unit for an aggregate amount of \$40.1 million and (ii) 1,580,937 Series A-5 preferred units sold at a purchase price of \$6.32536 per unit for an aggregate amount of \$10.0 million, for total aggregate proceeds of \$50.1 million.

In 2022 and 2023, we sold an aggregate of 22,162,743 Series B preferred units in multiple closings, consisting of (i) 15,054,263 Series B preferred units, which includes (a) 12,446,876 Series B preferred units sold at a purchase price of \$11.64951 per unit and (b) 2,607,387 Series B preferred units which converted pursuant to a promissory note with a principal amount of \$30.0 million and accrued interest of \$0.4 million between the Company and ModernaTX, Inc., for an aggregate amount of \$175.4 million and (ii) 7,108,480 Series B-1 preferred units sold at a purchase price of \$14.06770 per unit for an aggregate amount of \$100.0 million, for total aggregate proceeds of \$275.4 million.

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No underwriters were involved in the foregoing sales of securities. The sales of securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering. All of the purchasers in these transactions represented to us in connection with their purchase that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

(b) Profits Interests

Since January 1, 2020, we have granted an aggregate of 9,903,897 profits interests, with profits interests threshold amounts ranging from \$0.08 to \$11.84 per unit, to employees, directors and consultants pursuant to the 2019 Plan. No common units have been issued pursuant to the 2019 Plan.

The issuances of the securities under the 2019 Plan described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans. The profits interests are deemed to be restricted securities for purposes of the Securities Act.

The issuance of securities described above to employees and consultants outside of the 2019 Plan were deemed exempt from registration pursuant to Section 4(a)(2) of the Securities Act as transactions by an issuer not involving a public offering.

Item 16. Exhibits and Financial Statement Schedules

(a) Exhibits.

Exhibit number	Exhibit table
1.1*	Form of Underwriting Agreement
3.1*	Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect
3.2*	Form of Amended and Restated Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering)
3.3*	Amended and Restated Bylaws, as currently in effect
3.4*	Form of Amended and Restated By-laws (to be effective upon the closing of this offering)
4.1*	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated December 20, 2022
4.2*	Form of Common Stock Certificate
5.1*	Opinion of Goodwin Procter LLP
10.1#*	2019 Equity Incentive Plan, as amended, and forms of award agreements thereunder
10.2#*	2024 Stock Option and Incentive Plan and forms of award agreements thereunder
10.3#*	2024 Employee Stock Purchase Plan
10.4#*	Form of Officer Indemnification Agreement
10.5#*	Form of Director Indemnification Agreement
10.6†**	Strategic Collaboration and License Agreement by and between the Registrant and ModernaTX, Inc., dated October 29, 2021
10.7†**	Collaboration and License Agreement by and between the Registrant and Ionis Pharmaceuticals, Inc., dated November 10, 2022
10.8†**	Development, Option and License Agreement by and between the Registrant and Affini-T Therapeutics, Inc., dated June 14, 2022
10.9**	Lease Agreement between EPL Halleck Investors LLC and Metagenomi, Inc., dated January 22, 2021
10.10**	Sublease Agreement between Zymergen Inc. and Metagenomi, Inc., dated November 11, 2022
10.11**	Lease Agreement between Park Avenue Building LLC and Metagenomi, Inc., dated September 29, 2021
10.12#**	Employment Agreement between the Registrant and Brian C. Thomas, dated as of March 20, 2023
10.13#**	Offer of Employment between the Registrant and Jian Irish, dated as of January 19, 2021
10.14#**	Offer of Employment between the Registrant and Sarah Noonberg, dated as of January 30, 2023
10.15#**	Form of Confidentiality and Invention Assignment Agreement
10.16#*	Form of Executive Employment Agreement
10.17#**	Manager Offer Letter between the Registrant and Willard Dere, dated as of August 19, 2021
16.1**	Letter from KPMG LLP to the Securities and Exchange Commission dated August 3, 2023
21.1*	Subsidiaries of the Registrant
23.1**	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
23.2*	Consent of Goodwin Procter LLP (included in Exhibit 5.1)

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Exhibit number	Exhibit table
24.1**	Power of Attorney (included on signature page)
107	Filing Fees Exhibit

* To be filed by amendment.

** Previously filed

Indicates a management contract or any compensatory plan, contract or arrangement

† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the SEC because the Registrant has determined that information is not material and would be competitively harmful if publicly disclosed.

- (b) Financial Statement Schedules.

None.

Item 17. Undertakings

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the Underwriting Agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

- (i) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (ii) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Signatures

Pursuant to the requirements of the Securities Act, Metagenomi Technologies, LLC has duly caused this Amendment No. 1 to the registration statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Emeryville, California, on the 8th day of January, 2024.

Metagenomi Technologies, LLC

By: /s/ Brian C. Thomas
Brian C. Thomas, Ph.D.
Chief Executive Officer

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Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities indicated on the 8th day of January, 2024.

Signature	Title
<u>/s/ Brian C. Thomas</u> Brian C. Thomas, Ph.D.	Chief Executive Officer (Principal Executive Officer)
<u>/s/ Pamela Wapnick</u> Pamela Wapnick, MBA	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)
<u>*</u> Juergen Eckhardt, M.D., MBA	Director
<u>*</u> Sebastián Bernales, Ph.D.	Director
<u>*</u> Risa Stack, Ph.D.	Director
<u>*</u> Willard Dere, M.D.	Director
<u>*</u> Santhosh Palani, Ph.D.	Director
<u>* By: /s/ Brian C. Thomas</u> Brian C. Thomas, Ph.D. Attorney-in-Fact	

Calculation of Filing Fee Tables

Form S-1
(Form Type)Metagenomi Technologies, LLC
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Proposed Maximum Aggregate Offering Price(1)	Fee Rate	Amount of Registration Fee
Newly Registered Securities							
Fees to be Paid	Equity	Common Stock, \$0.0001 par value per share(2)	Rule 457(o)		\$100,000,000	\$0.00014760	\$ 14,760.00
Fees Previously Paid							
Carry Forward Securities							
Carry Forward Securities							
		Total Offering Amounts			\$100,000,000	\$0.00014760	\$ 14,760.00
		Total Fees Previously Paid					14,760.00
		Total Fees Offsets					\$ —
		Net Fee Due					\$ 0.00

- (1) Estimated solely for the purpose of computing the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended.
- (2) Metagenomi Technologies, LLC, the registrant whose name appears on the cover of the registration statement on Form S-1 of which this exhibit forms a part, is a Delaware limited liability company. Prior to the effectiveness of the registration statement, Metagenomi Technologies, LLC will complete a series of transactions pursuant to which Metagenomi Technologies, LLC will merge with and into its wholly-owned subsidiary, Metagenomi, Inc., a Delaware corporation, with Metagenomi, Inc. continuing as the surviving corporation.