

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

**FORM 10-K**

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2023

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD  
FROM TO

Commission File Number 001-41949

**Metagenomi, Inc.**

(Exact name of Registrant as specified in its Charter)

Delaware

(State or other jurisdiction of  
incorporation or organization)

5959 Horton Street, 7th Floor

Emeryville, California

(Address of principal executive offices)

81-3909017

(I.R.S. Employer  
Identification No.)

94608

(Zip Code)

Registrant's telephone number, including area code: (510) 871-4880

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value \$0.0001 per share	MGX	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES  NO

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES  NO

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES  NO

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES  NO

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

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.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES  NO

As of June 30, 2023, the last business day of the Registrant's most recently completed second quarter, there was no established public trading market for the Registrant's equity securities as the Registrant was not a public company and therefore cannot calculate the aggregate market value of its voting and non-voting equity held by non-affiliates as of such date. The Registrant's common stock began trading on the Nasdaq Global Select Market on February 9, 2024.

The number of shares of Registrant's Common Stock outstanding as of March 15, 2024 was 37,472,351.

DOCUMENTS INCORPORATED BY REFERENCE

None

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K 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 and which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. 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 Annual Report on Form 10-K 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 Investigational New Drug ("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
- 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," "will," "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 and are subject to change. 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. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties.

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 Annual Report on Form 10-K. If one or more of 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 Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K and have filed with the SEC as exhibits to this Annual Report on Form 10-K 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 Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. 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 Annual Report on Form 10-K.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for our programs and 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 Annual Report on Form 10-K, 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 Annual Report on Form 10-K.

#### **Trademarks and Service Marks**

This Annual Report on Form 10-K contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities’ trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

#### **Market, Industry and Other Data**

Unless otherwise indicated, information contained in this Annual Report on Form 10-K concerning our industry and the markets in which we operate, including our general expectations about our product candidates, market position, market opportunity, market size, competitive position and the incidence of certain medical conditions, is based on or derived from publicly available information released by industry analysts and third-party sources, independent market research, industry and general publications and surveys, governmental agencies, our internal research and our industry experience. Our estimates of the potential market opportunities for our product candidates include a number of key assumptions based on our industry knowledge and industry publications, the latter of which may be based on small sample sizes and fail to accurately reflect such information, and you are cautioned not to give undue weight to such estimates. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. Industry publications and third-party research often 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 and such information is inherently imprecise. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. In addition, projections, assumptions and estimates of our future performance and the future performance of the industry in which we operate is necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in Part I, Item 1A of this Annual Report on Form 10-K titled “Risk Factors” and elsewhere in this Annual Report on Form 10-K. These and other factors could cause results to differ materially from those expressed in the estimates made by independent third parties and by us.

## SUMMARY OF MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties that you should be aware of in evaluating our business. These risks include, but are not limited to, the following:

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We will need substantial additional funding in addition to the net proceeds we received from our initial public 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.
- 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 subject to additional development challenges and risks due to the novel nature of our genome editing technology.
- 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.
- 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.
- 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.
- 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 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.
- It is difficult and costly to protect our intellectual property and our proprietary technologies, and we may not be able to ensure their protection.
- The impacts of cyber attacks and data privacy breaches on our business.

The summary risk factors described above should be read together with the text of the full risk factors below in the section titled “Risk Factors” in Part I, Item 1.A. and the other information set forth in this Annual Report on Form 10-K, as well as in other documents that we file with the U.S. Securities and Exchange Commission (SEC). The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us, or that we currently deem to be immaterial, may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

## PART I

### Item 1. Business.

#### Overview

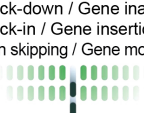
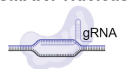


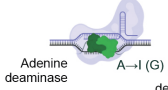
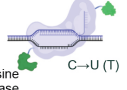

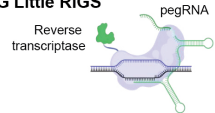

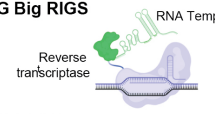
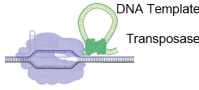
We are a precision genetic medicines company committed to developing curative therapeutics for patients using our proprietary, comprehensive metagenomics-derived genome editing toolbox. Genetic diseases are caused by a diverse set of mutations that have been largely inaccessible by genome engineering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

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 (knock-down).

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.

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

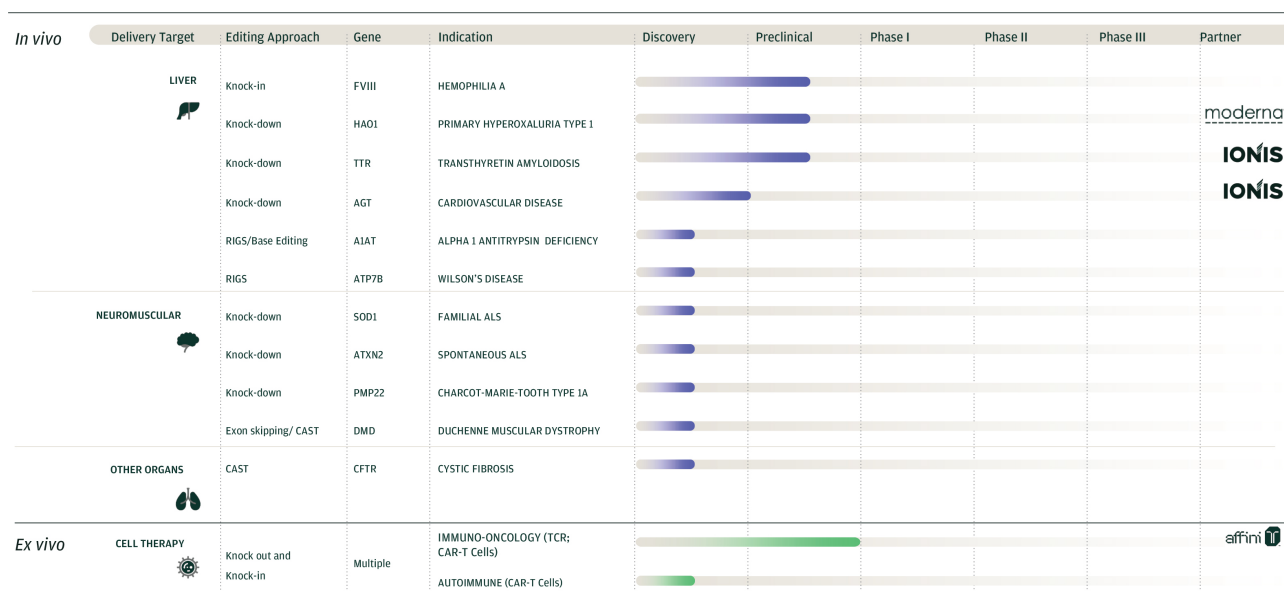
used to construct base editors that are small enough to fit within the packaging limitations of adeno-associated viruses (“AAV”). SpCas9, which is currently used in most base editing applications, is roughly three times the size of some of the smallest SMART nickases and cannot be efficiently packaged 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 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 mid-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 knock-down 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 knock-down 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 knock-down and halt further deposition of amyloid fibrils. Previous experience suggests a clinical correlation between the degree of TTR knock-down 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 knock-down 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% knock-down 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 knock-down 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 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, M.Sc, 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 Intellectual Property and Legal Operations, 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.
- Matthew L. Wein, J.D., VP of Corporate Legal and Compliance, and Corporate Secretary, has spent more than 20 years in legal leadership positions at biotechnology companies, including Mustang Bio and Amgen.
- 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.
- 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 knock-down 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.

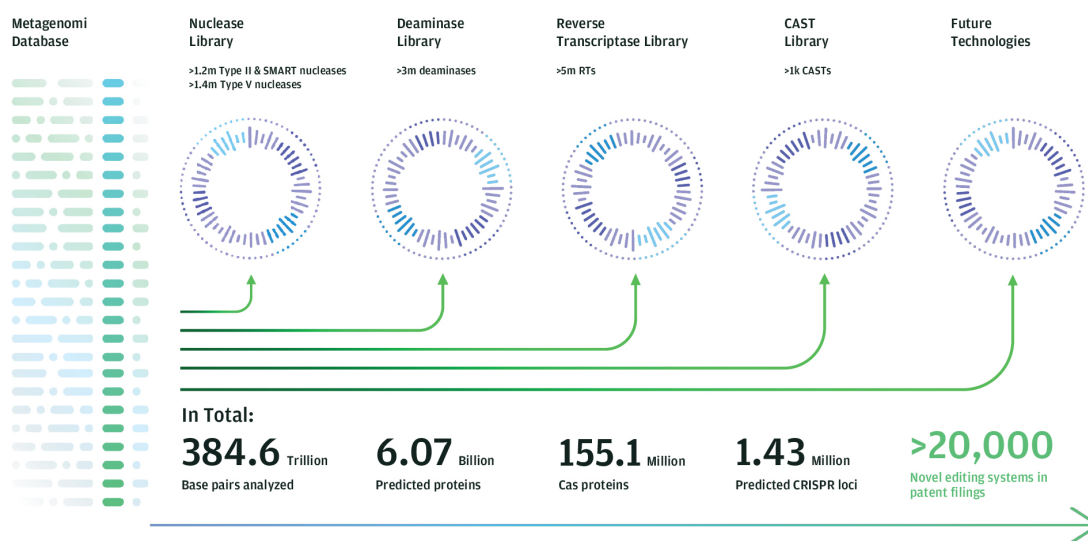
Through our metagenomics process, DNA is extracted from these environmental samples and sequenced in order to reconstruct the genomes of the resident microbes. The process of DNA extraction and sequencing results in the fragmentation of each individual microbial genome into small sections which are blended 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

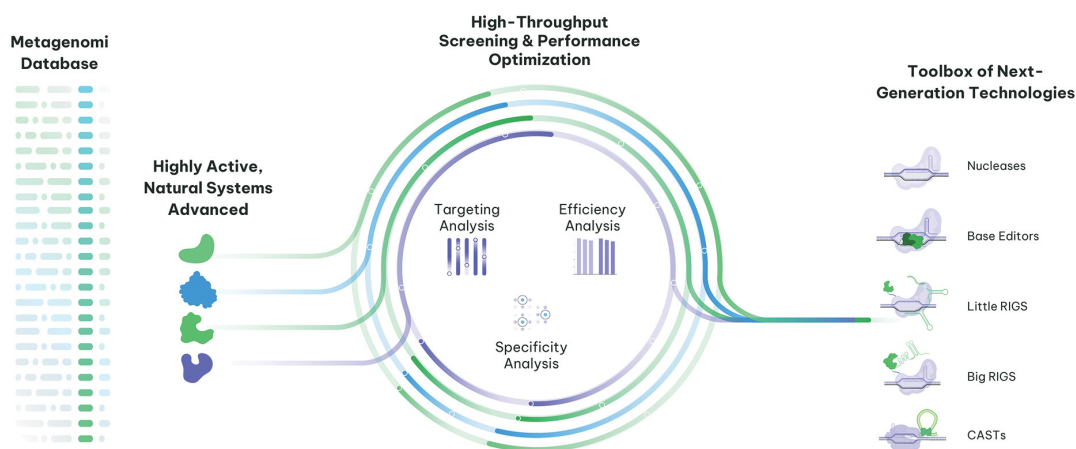
to build upon our metagenomic library, we expect to make additional discoveries of novel genome editing technology and expand our toolbox.

**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.



Modular Engineering Translates Metagenomic Discoveries into Genetic Medicines

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

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 knock-down, 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:



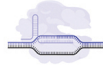
- 1) *Potential to create a full spectrum of genetic medicines* – Our broad suite of genome editing technologies include: programmable nucleases, base editors, RIGS and CASTs, that, together, can potentially effectuate any desired modification to the genome – gene knock-down, gene knock-in, and replacements. 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"> <li>• Efficient and precise genome editing systems</li> <li>• Diverse nucleases have extensive genome targeting capabilities</li> <li>• Compact and ultra-small systems will enable delivery via a single AAV</li> <li>• Function as programmable modules for base editing and RIGS</li> </ul>

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.

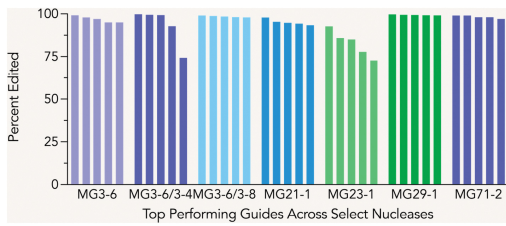
### ***Our best-characterized type II and type V nucleases are suitable for a wide variety of genome editing applications***

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.

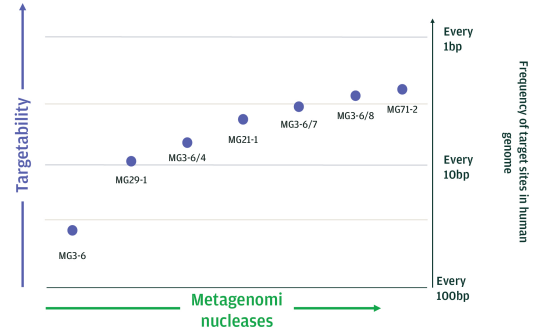
**Figure 6.** Our Expanding Nuclease Toolbox is Designed to Enable Extensive Targeting throughout the Human Genome.

**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.

**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.



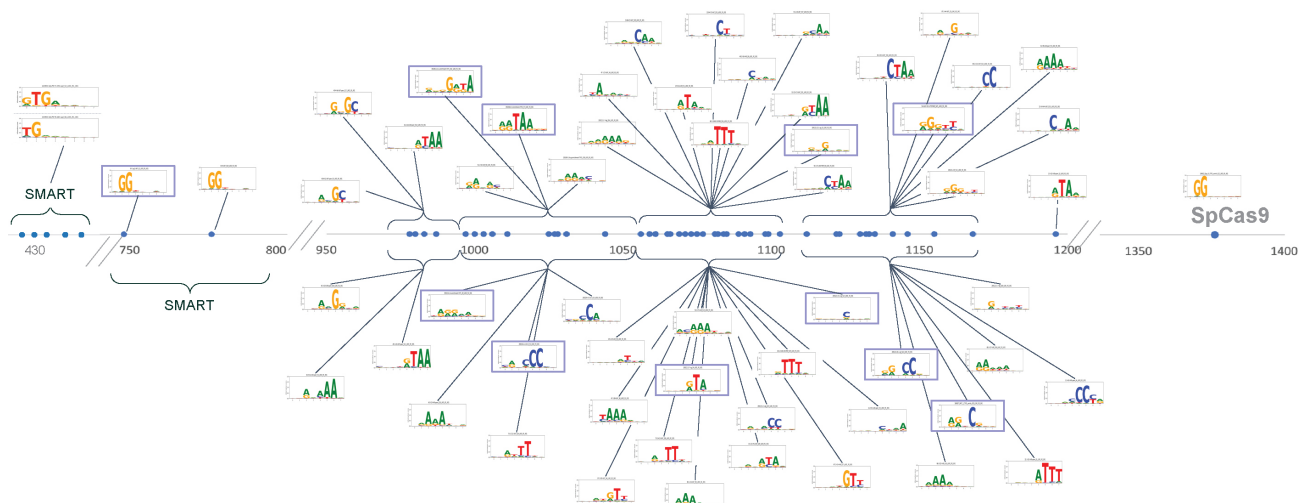
\* Graph depicts cumulative targetability.  
 \* Targeting density (targetability) is the average distance between nuclease target sites in the human genome.

Our 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 seven 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.

*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.



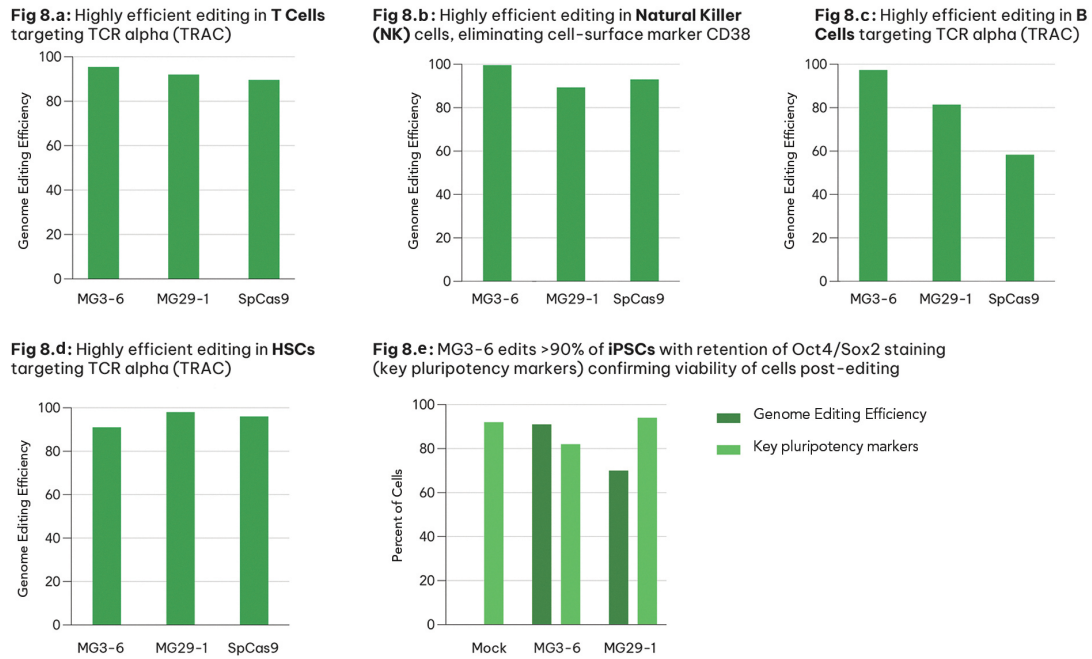
\* Graph depicts a selection of our nucleases, including their size in aa on the horizontal axis and their corresponding targeting motifs shown as sequence logos (PAM and TAM sequences), compared to SpCas9.

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.



\* Two example nucleases are shown, type II MG3-6 and type V MG29-1.

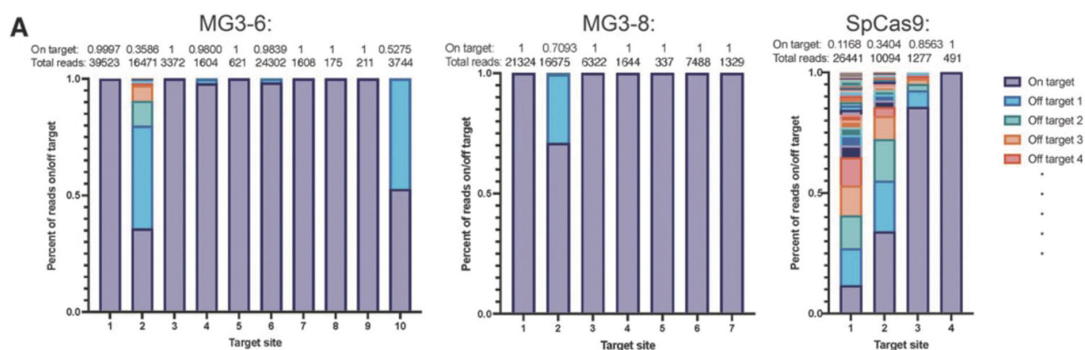
\* Editing efficiency was determined based on the frequency of InDels detected by NGS at genomic sites targeted by each nuclease.

*Our nucleases exhibit high specificity when benchmarked in multiple mammalian cell types*

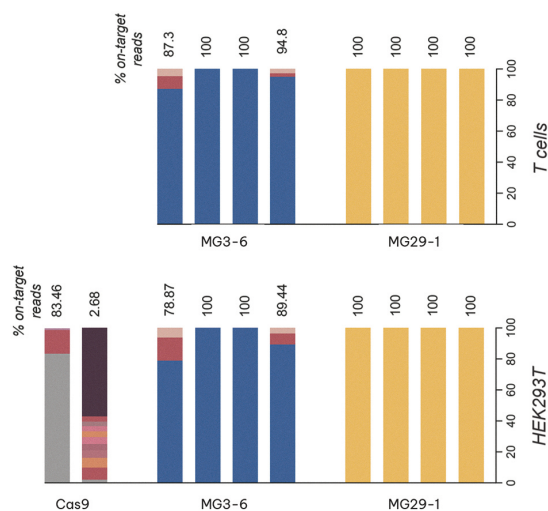
Our therapeutic development of genome editing systems require that they exhibit high activity and specificity across multiple cell-based models. We employ a broad set of specificity and off-target assessment methodologies, including *in silico*, biochemical, and cell-based approaches. Figure 9 shows 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.



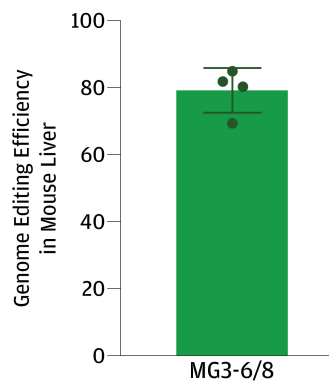
\* Figure 9a: Off-target analysis showed that our type II MG3-6 and MG3-8 nucleases have high specificity in multiple mammalian cell types as measured by the number of off-target sites and the fraction of on-target reads. The target sites are the same between the three nucleases, including SpCas9. Off-target 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.

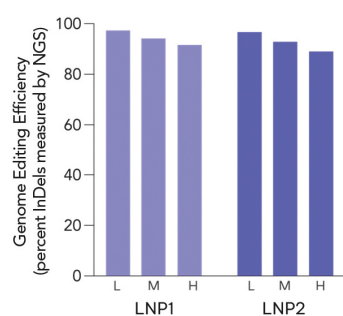
\* Mean of 79% genome editing efficiency as measured by the frequency of InDels detected by NGS at the targeted genomic site.

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).

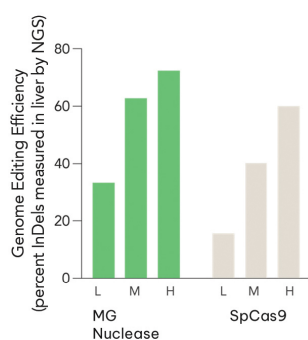
In cynomolgus monkeys, it is estimated that hepatocytes make up 60% of the cells in the liver. Therefore, 50% editing in the whole liver achieved with MG29-1 in NHP (Figure 11c, guide 2) translates to editing of approximately 80% of the hepatocyte genomes which are the therapeutically relevant target cell.

**Figure 11.** Our Type V MG29-1 Nuclease is a Highly Active Natural Enzyme for *In Vivo* Genome Editing.

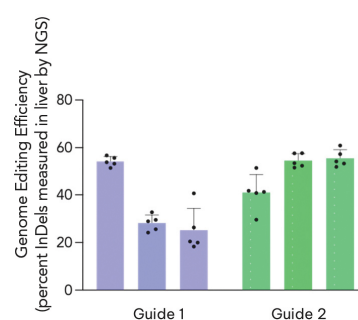
**Figure 11a.** MG29-1 achieved saturating levels of editing in primary mouse hepatocytes.



**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.



\* 50% whole liver editing = 80% hepatocytes editing.

- \* 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.

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

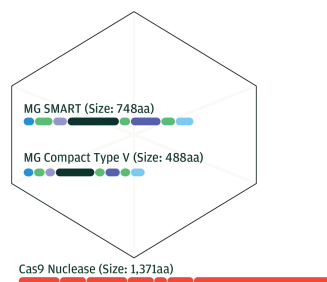


the liver. Because of their novel biochemistry and divergence from typical type II, we refer to some of these ultra-small nucleases as SMART. In addition, we identified several novel families of ultra-small type V nucleases. Unlike compact type V, and all other previously studied type V, SMART have a dual catalytic domain structure that enables engineering of nickase variants that can be used for base and prime editing.

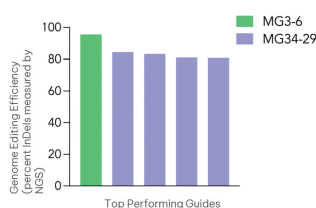
Figure 12 shows that genome editing efficiencies achieved for SMART and compact type V nucleases are comparable to other lead systems. These results show that our ultra-small nucleases are highly efficient genome editing systems that have the potential for extensive therapeutic applications, including 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.

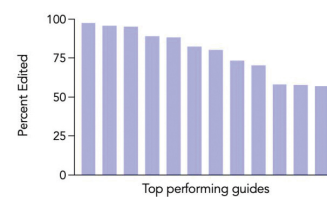


**Figure 12b.** SMART nuclease showed high editing efficiency in mammalian cells, prior to optimization.



\* InDels are measured by NGS.  
 \* Each bar represents a distinct guide.  
 \* MG3-6 used as internal control.

**Figure 12c.** Compact type V nuclease showed high editing efficiency in mammalian cells, prior to optimization.

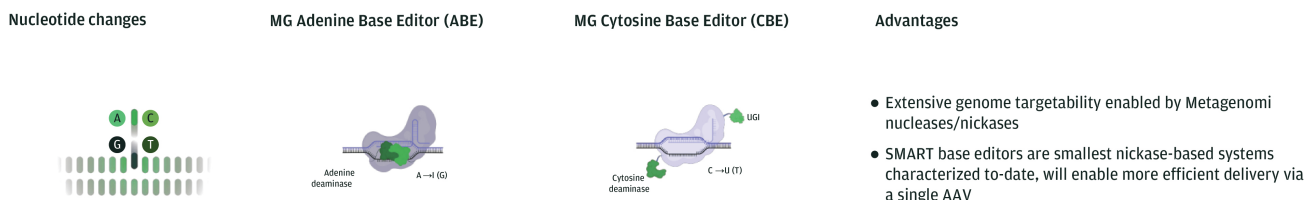


\* InDels are measured by NGS.  
 \* Each bar represents a distinct guide.

## 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 knock-down genes by introducing premature stop codons or interrupting gene splice sites.

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*

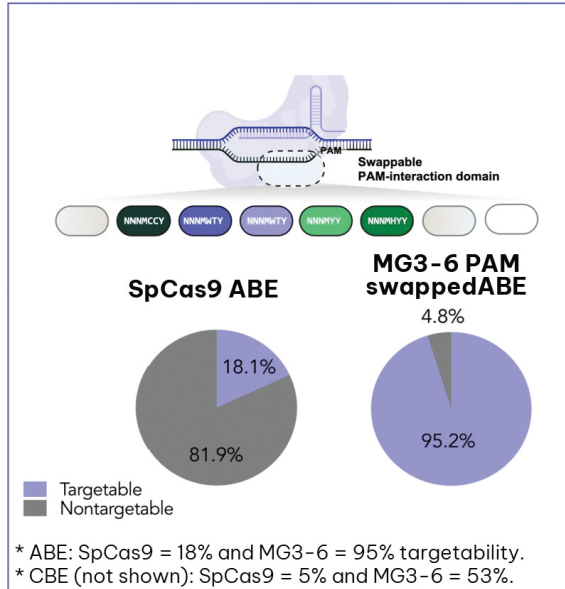
We are leveraging our toolbox of programmable nucleases and our metagenomics discovery platform to develop next generation base editing tools. Our programmable nucleases provide the ability to efficiently and precisely target locations in the genome required in order to potentially create a wide-variety 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.

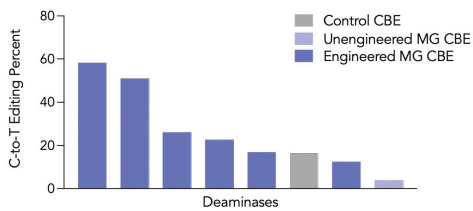
**Figure 14a.** PAM interacting domain engineering was used to develop a suite of chimeric MG3-6 base editors with extensive genome targetability.



\* ABE: SpCas9 = 18% and MG3-6 = 95% targetability.

\* CBE (not shown): SpCas9 = 5% and MG3-6 = 53%.

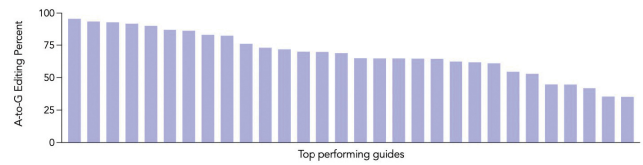
**Figure 14c.** CBE screening identified highly active deaminases for C-to-T editing, compared to published control.



\* Unoptimized CBE construct tested in HEK293T cells with plasmid delivery.

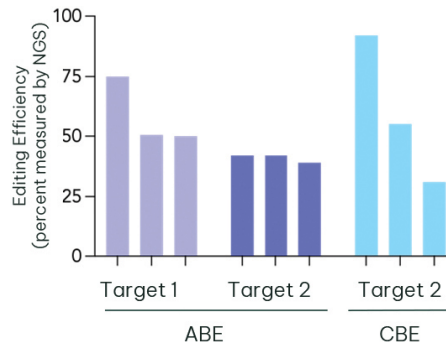
\* CBE control uses hyperactive CDA A0A2K5RDN7.

**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.

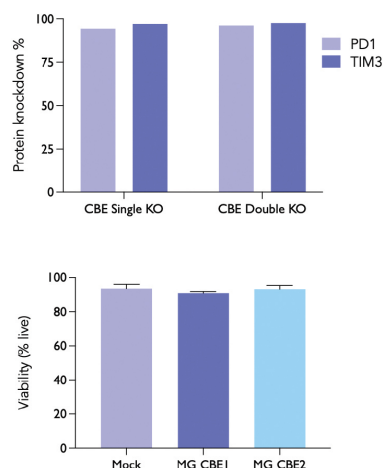
**Figure 14d.** MG3-6 PAM chimera ABE and CBE achieved efficient editing at splice-sites for enacting therapeutically-relevant knock-out of genes in human cells.



\* 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.

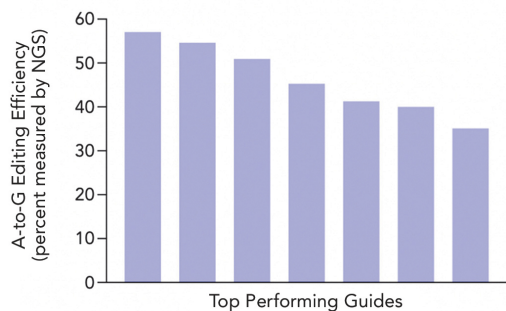
Our base editors are highly active and progressing towards *in vivo* therapeutic applications. Both of our ABE and CBE systems have been tested in mammalian cells in order to determine editing efficiency, where a large collection of guides spanning various genomic loci were tested for each system. Figure 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 knock-down, 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.

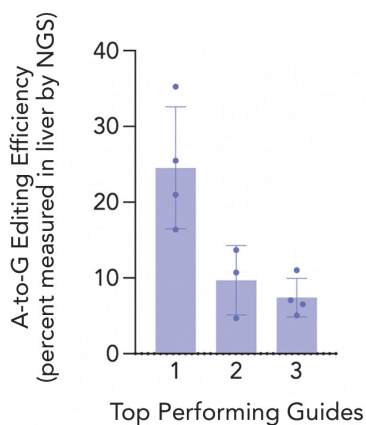
Our base editing platform has broad *in vivo* therapeutic potential

**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.

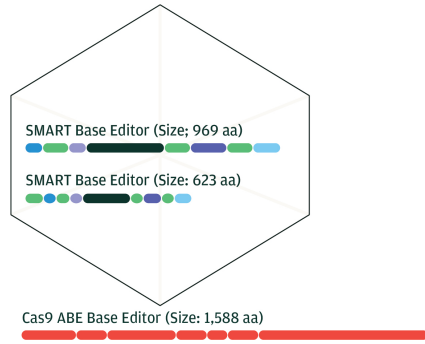


In order to demonstrate the utility of the MG3-6 ABE platform for *in vivo* base editing, a lead construct design was tested both in primary cells and in mice. Multiple guides were tested in each study, designed to target different genomic loci. Figure 15 shows the results of these evaluations of the 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.

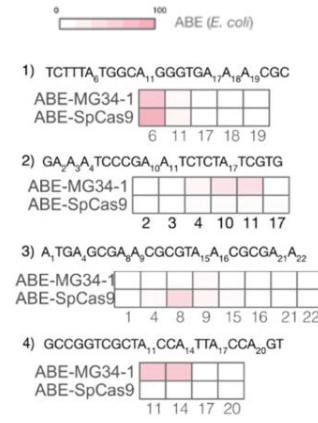
Our SMART have been engineered to create ultra-small base editors, expanding the potential deliverability of base editing technology

**Figure 16.** SMART Can be Engineered into Ultra-Small Base Editors with Naturally High Editing Efficiency and AAV Compatibility.

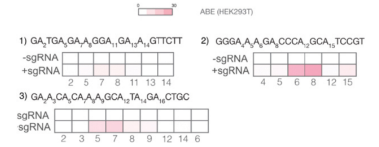
**Figure 16a.** Ultra-small SMART base editors are a fraction of the size of a typical Cas9 system, enabling AAV delivery.



**Figure 16b.** SMART ABE exhibited a similar editing profile *in vitro* compared to SpCas9.



**Figure 16c.** SMART ABE were active in mammalian cells.



\* 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.

\* 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.

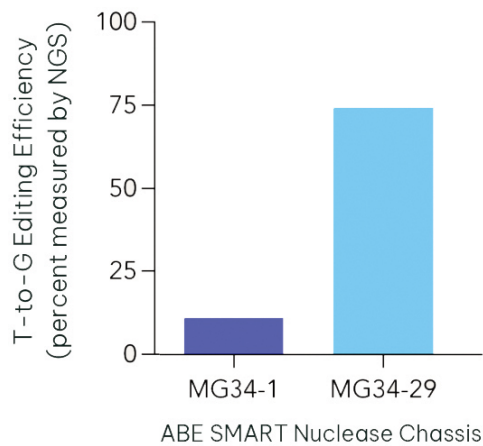
\* Heatmap values represent the mean of three independent experiments.

\* The target sequence for each locus is shown above the heatmap.

\* Heatmaps represent the percentage of NGS reads supporting an edit at each position.

Source: Goltsman et al 2022 Nature Communications

**Figure 16d.** SMART ABE optimization improved editing efficiency in human cells.



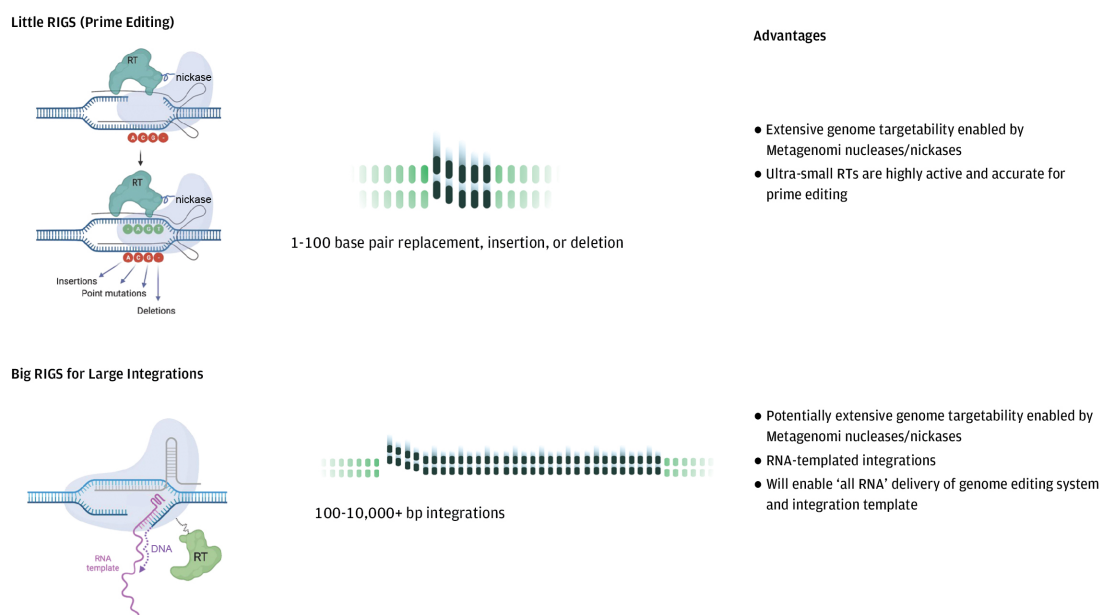
\* Top guide shown for each SMART ABE system.

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.



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 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.

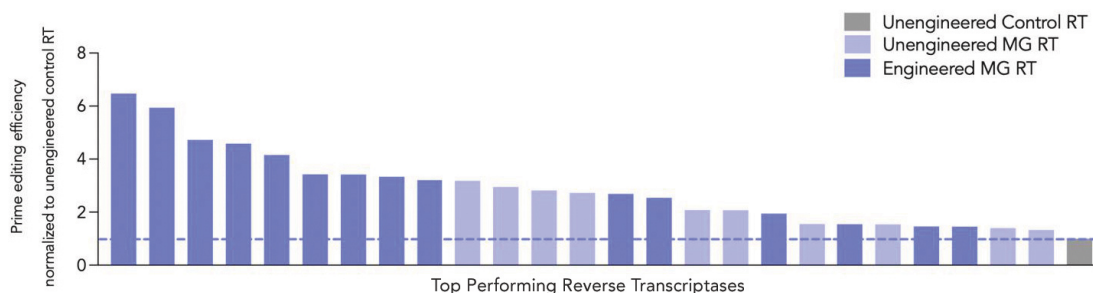
### Our Approach

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.

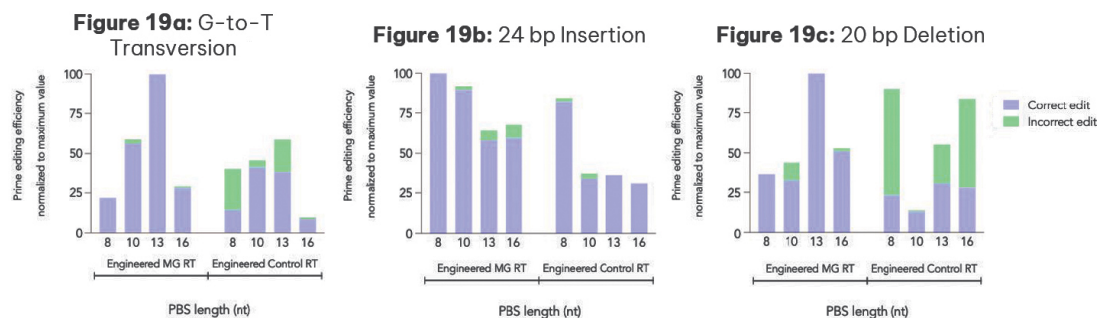


\* Unengineered prime editing control RT is from Moloney murine leukemia virus (“MMLV”).  
 \* RTs were cloned into a plasmid backbone that was co-transfected with chemically synthesized pegRNAs designed to edit the genome of human HEK293T cells.  
 \* Genomic DNA was isolated 72 hours post transfection 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.



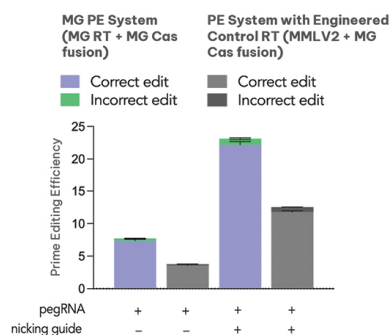
\* The engineered prime editing benchmark RT is the MMLV variant used in PE2 prime editing systems.

\* 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.

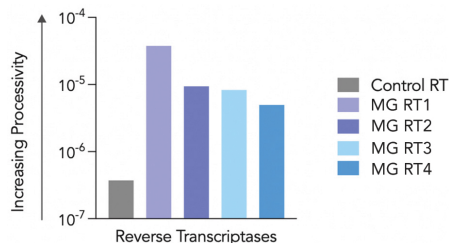
\* Co-transfection with chemically synthesized guides designed to program the Cas to create a nick in the vicinity of the edit were included to bias DNA repair towards the edited strand.

\* 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.

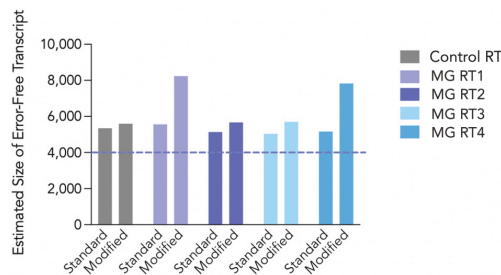


\* Prime editing benchmark RT is MMLV.

\* 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.

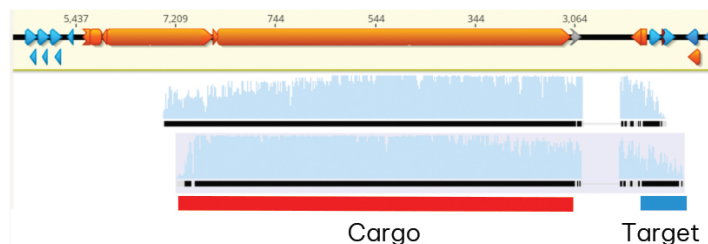
**Figure 20b.** Our RTs were more accurate than industry-standard RT.



\* 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.

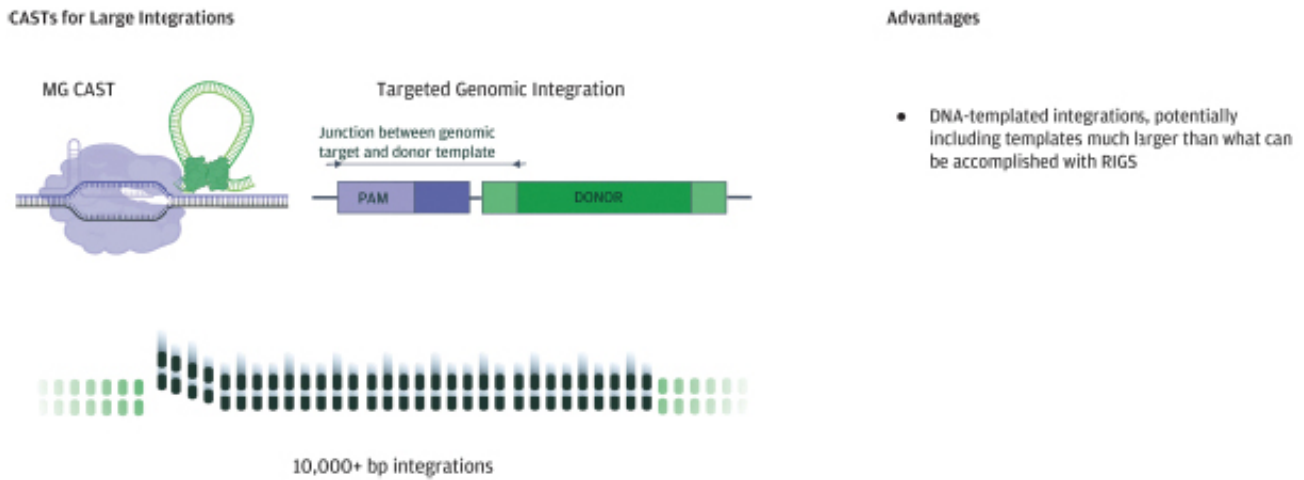
\* Integration was targeted to an engineered landing pad located in the genome of HEK293T cells.

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.



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.

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.

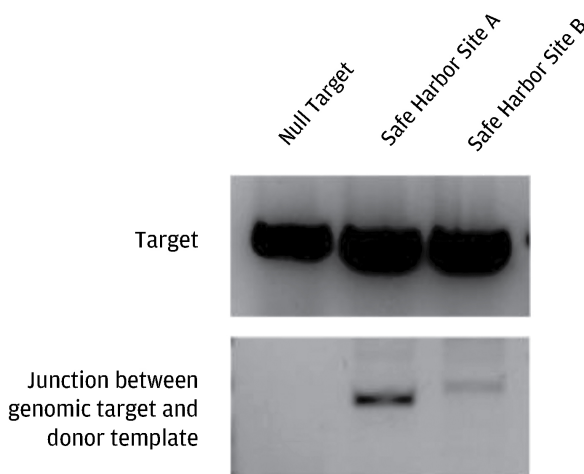
We are also developing systems based on recombinases and other mobile elements that can be used in combination with programmable nucleases, including catalytically dead variants, as well as with Little RIGS in order to affect large, targeted genomic integrations under circumstances where CASTs are not 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.

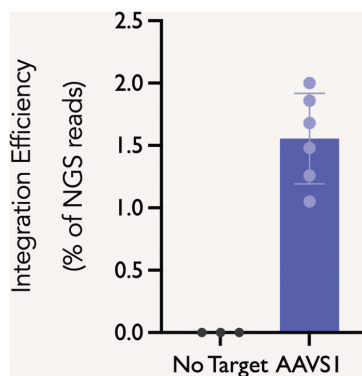


\* PCR of junction between template and target confirms integration at target loci in HEK293T cells.

\* 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.

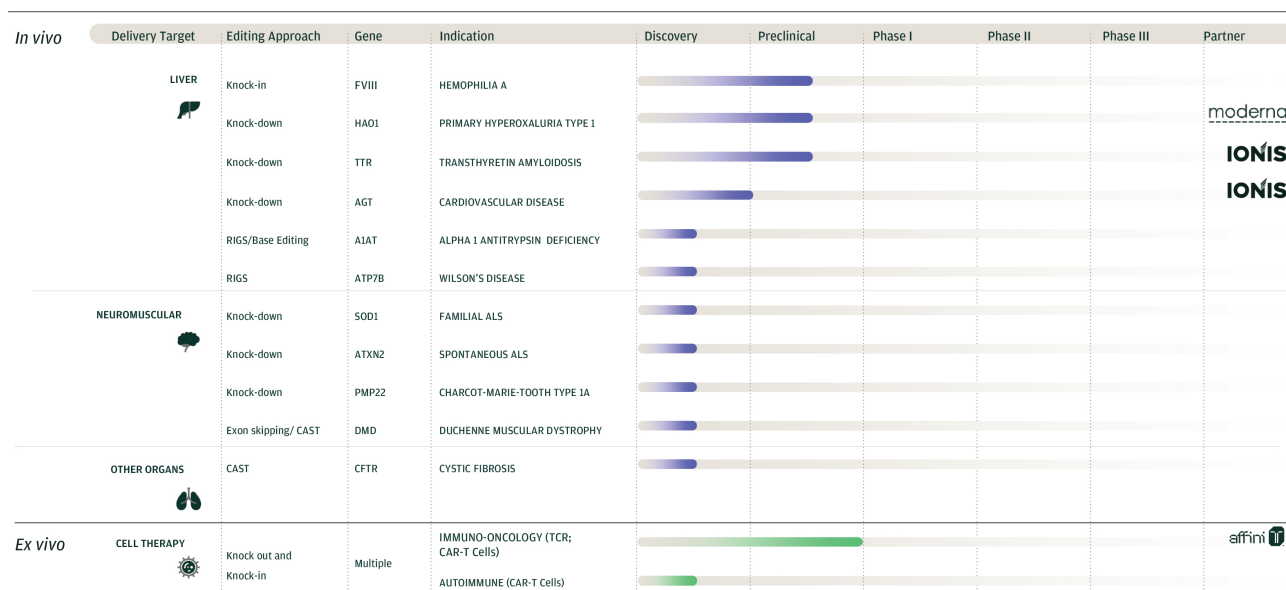
### *Future Novel Editing System Discoveries*

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.

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 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. 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*

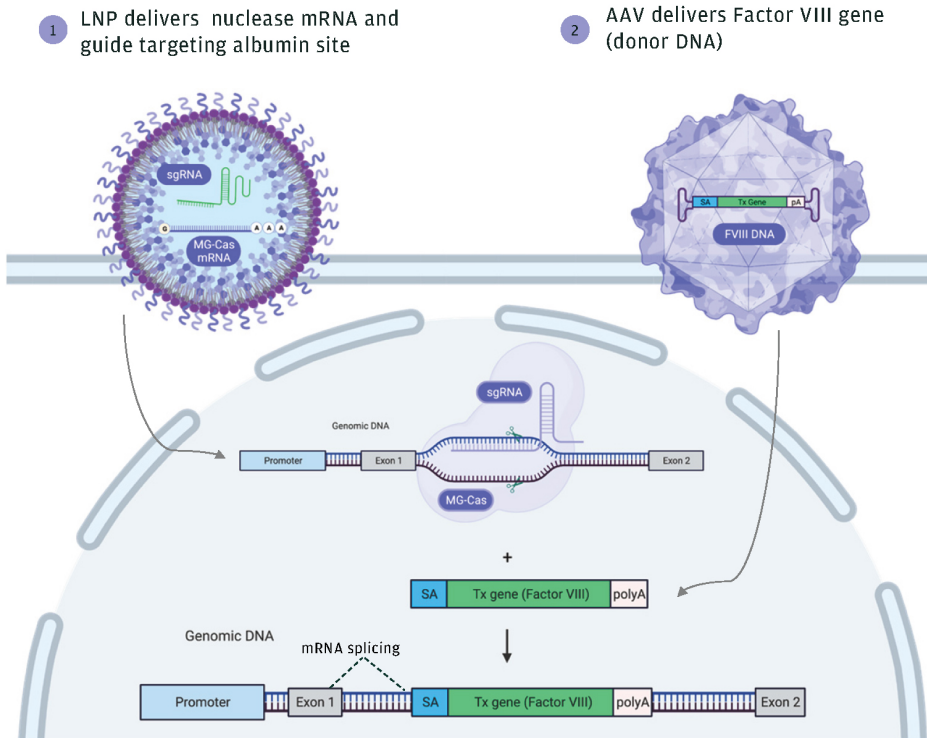
Experience with early hemophilia A gene therapy approaches suggest that morbidity and mortality from the disease can be markedly reduced by achieving only moderate amounts of stable FVIII expression. For instance, achieving stable FVIII activity above 5-10% of normal activity level has the potential 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.

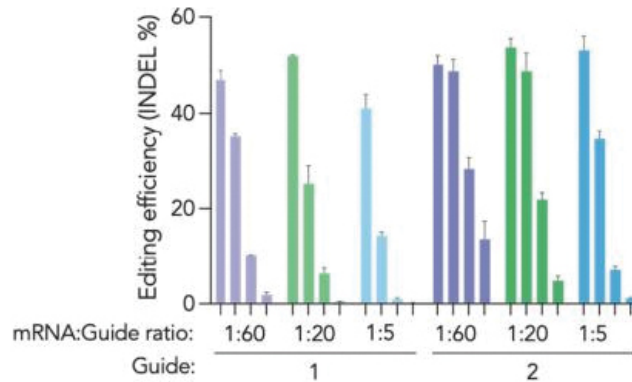
As shown in Figure 24, our hemophilia A genome editing program has two components: a LNP component that is designed to deliver mRNA along with a gRNA to the liver to produce a highly efficient and specific nuclease to create a precise cut at the albumin safe harbor gene locus; and an AAV vector that 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.

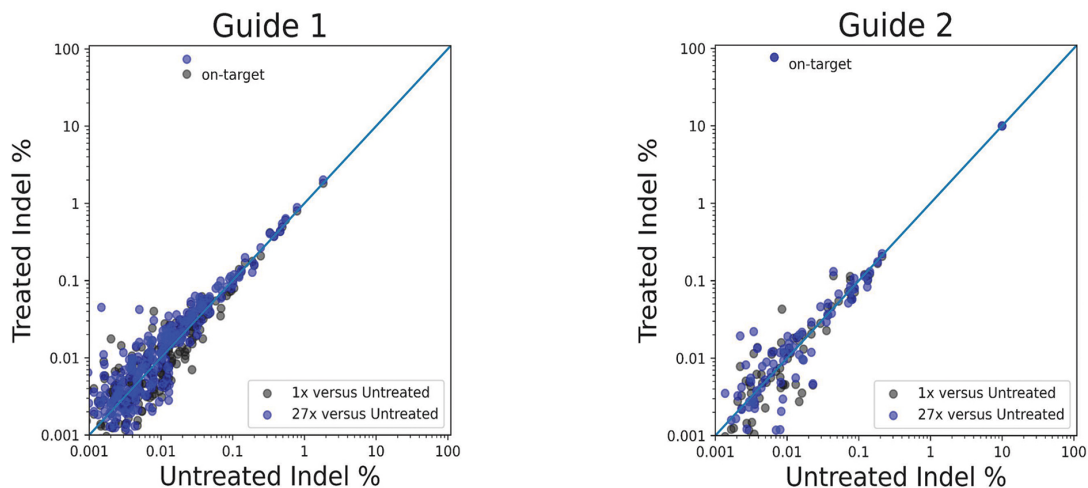


Genome editing nucleases can edit at sites other than the intended target site, an activity that is dependent on the specific nuclease and guide. Editing at non-target sites (called off-target editing) is undesirable due to the potential to cause damage to the host cell DNA (sometimes called “genotoxicity”). In accordance with recent FDA guidelines and insights from the FDA workshop (Assessing Genetic Heterogeneity in the Context of Genome Editing Off-Targets in Gene Therapy Products, December 2022) we have applied a combination of 3 methods; in cell oligo integration in PHH, a biochemical assay, and in silico prediction using the variant aware software CRISPRme referencing gnomad v4 variants to identify potential off-target sites for our two lead guides. We generated two panels to query these potential off-target sites. In Panel 1 we combined cell based and biochemical based discovery to query potential off-target sites. Panel 2 combined Panel 1 and variant aware in silico methods. There were a total of 372 potential off-target sites for guide 1 and 113 potential off-target sites for guide 2 in Panel 1. 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 from Panel 1 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 an 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 nominated in Panel 1 for either guide 1 or guide 2. No signal was detected above the limit of detection after correcting for InDel frequencies in unedited control samples.

In summary, no editing was detectable at any of the potential off-target sites in Panel 1 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 variant aware in silico prediction using CRISPRme software referencing genomic variants from gnomAD v4 (Panel 2) that evaluates the impact of naturally occurring sequence variation within the human population on potential off-target activity. Additional tests have been conducted using the same methodology but with different PHH donors and these reached 2X target dose with similar on-target editing. Higher doses demonstrated cellular toxicity and reduced on-target editing in the new donors. Further studies using expanded methodologies to identify potential risks of off-target editing and expand our experience with supersaturating doses are ongoing.

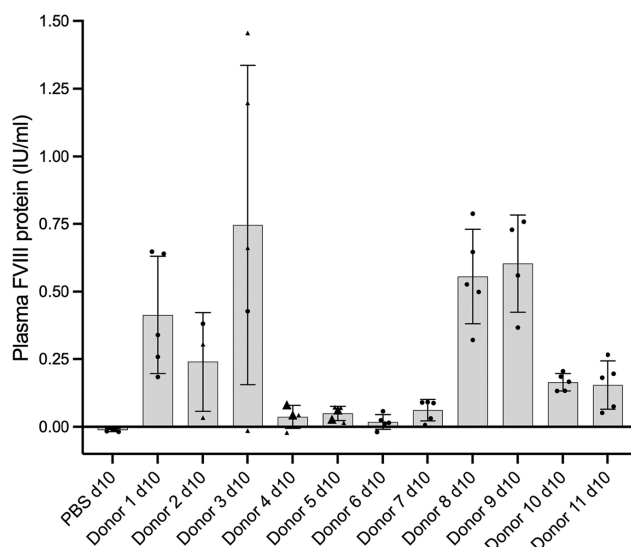
**Figure 26.** Measurement of editing at potential off-target sites from Panel 1 for the two lead guides for Hemophilia A in PHH using amplicon sequencing.



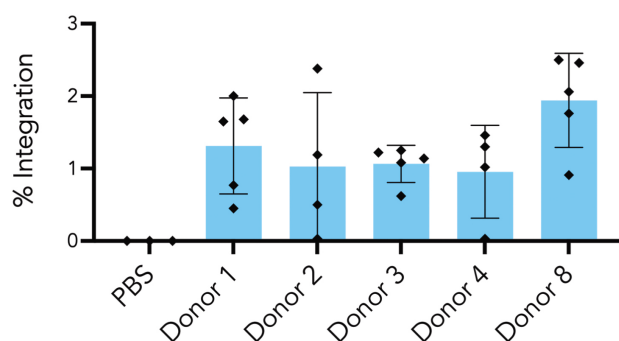
\* 372 and 113 sites were nominated and evaluated for guide 1 and guide 2, respectively at both a 1x and a 27x saturating dose. For each potential off-target site as well as the on-target site, the InDel frequency was plotted for 1x compared to untreated (black points) and for 27x compared to untreated (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.



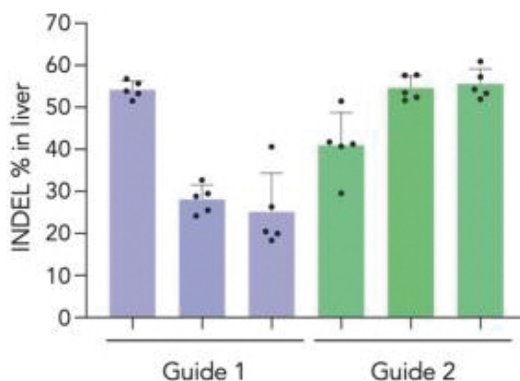
**Figure 28.** Integration of FVIII in Mice after genome editing.



\* 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.

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.

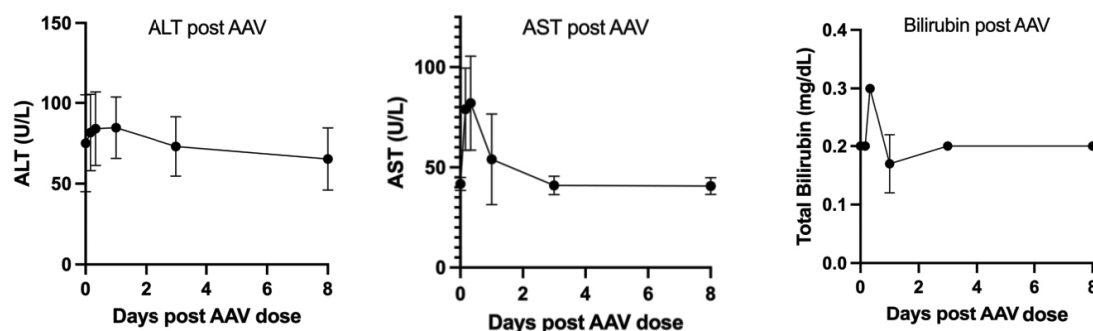
**Table 1.** cFVIII donor integration frequency, FVIII mRNA level and Mean FVIII activity level in NHPs.

Animal ID	Editing in the liver (InDel %) <sup>1</sup>	FVIII gene integration frequency (copies per 100 genomes) <sup>2</sup>	FVIII mRNA (% of endogenous control mRNA) <sup>3</sup>	Mean FVIII activity % of normal (d14 to d126) <sup>4</sup>
1001	45 %	2.9	177	75 +/- 9
1002	50 %	0.7	79	13 +/- 4
1003	55 %	1.4	131	29 +/- 5

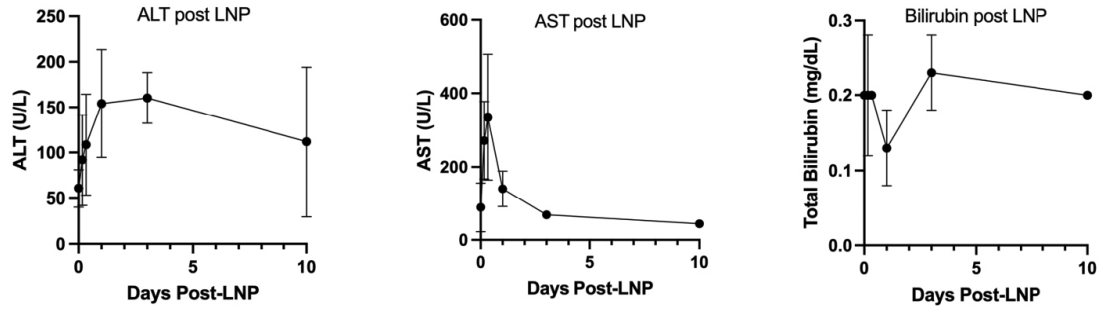
Table footnotes: (1) InDels at the on-target site in albumin intron 1 were measured by NGS in a liver biopsy taken at day 7 post LNP dosing. (2) The FVIII donor gene integration frequency in the forward orientation was quantified by droplet digital PCR analysis of the liver biopsy at day 7 post LNP and 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 aminotransferase (“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.

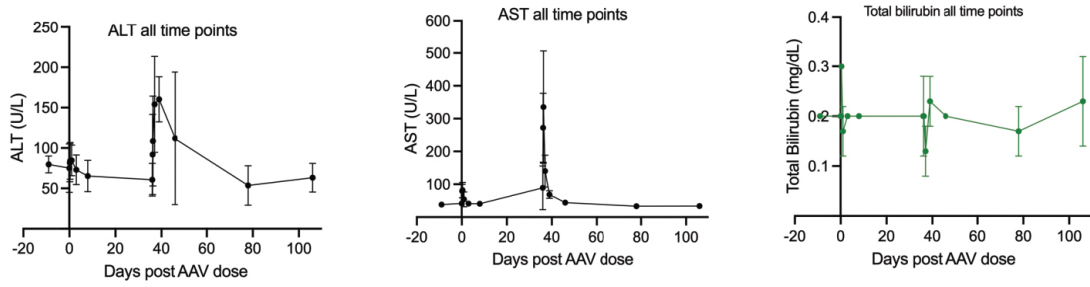
**Figure 30a.** ALT, AST, and total bilirubin levels in the blood of NHP up to day 8 after AAV dosing in the integration study.



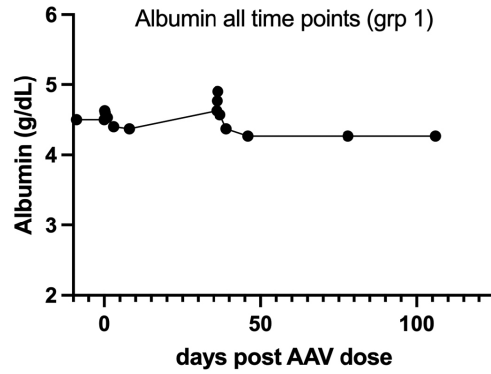
**Figure 30b.** ALT and AST levels in the blood of NHP up to day 10 after LNP dosing in the integration study.



**Figure 30c.** ALT, AST and total bilirubin levels in the blood of NHP throughout the study to the data cut-off date.

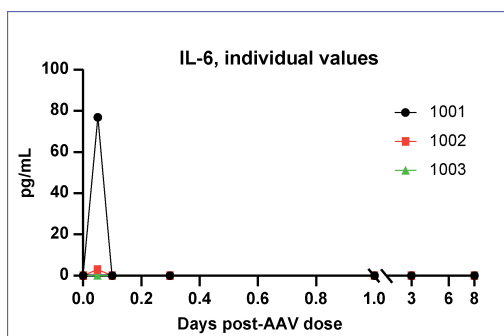


**Figure 30.** Albumin levels in the blood of the 3 NHP after AAV and LNP dosing in the integration study.

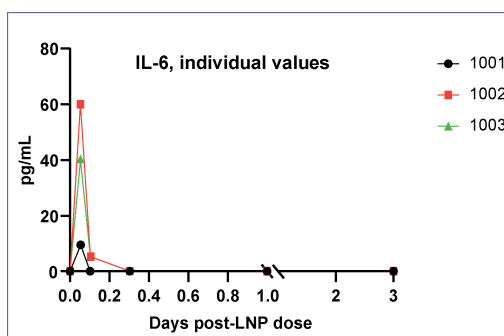


**Figure 31.** Levels of the cytokine IL-6 in the blood of the 3 NHP in the integration study post AAV dosing and post LNP dosing.

**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 mid-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 knock-down 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 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.

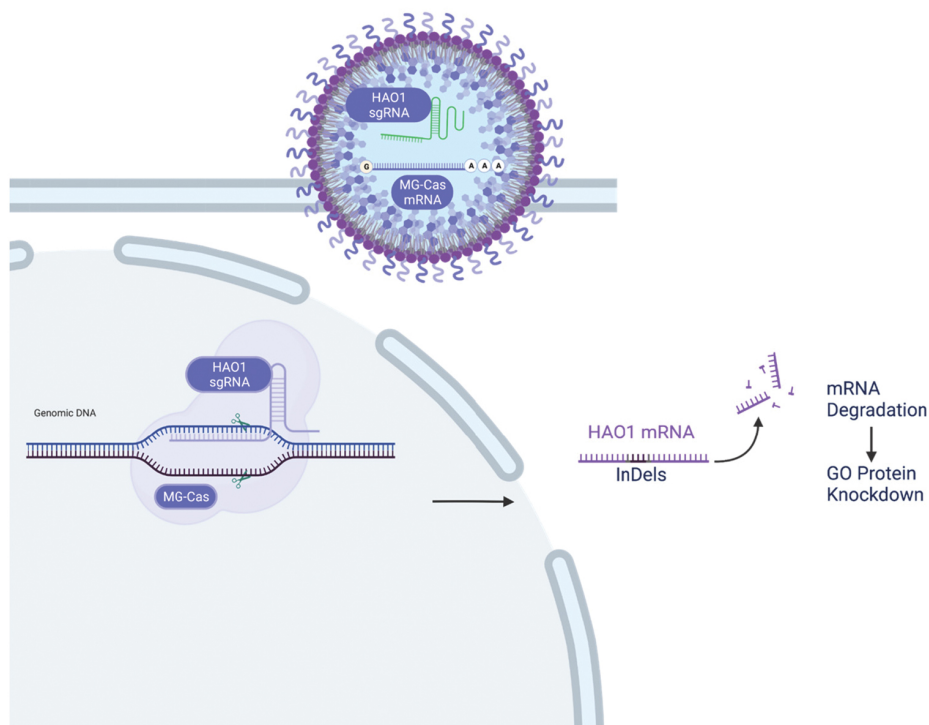
More recently, the standard of care has been updated to include treatment with lumasiran, a siRNA therapeutic approved in adults and children with PH1 that acts to reduce the levels of urinary oxalate. Using a therapeutic approach known as substrate reduction therapy, lumasiran targets mRNA from a separate 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.



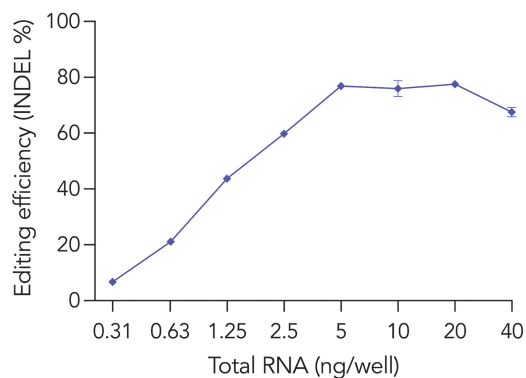
**Figure 32.** Genome Editing Strategy for Targeting HAO1.



The safety of this durable knock-down 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.



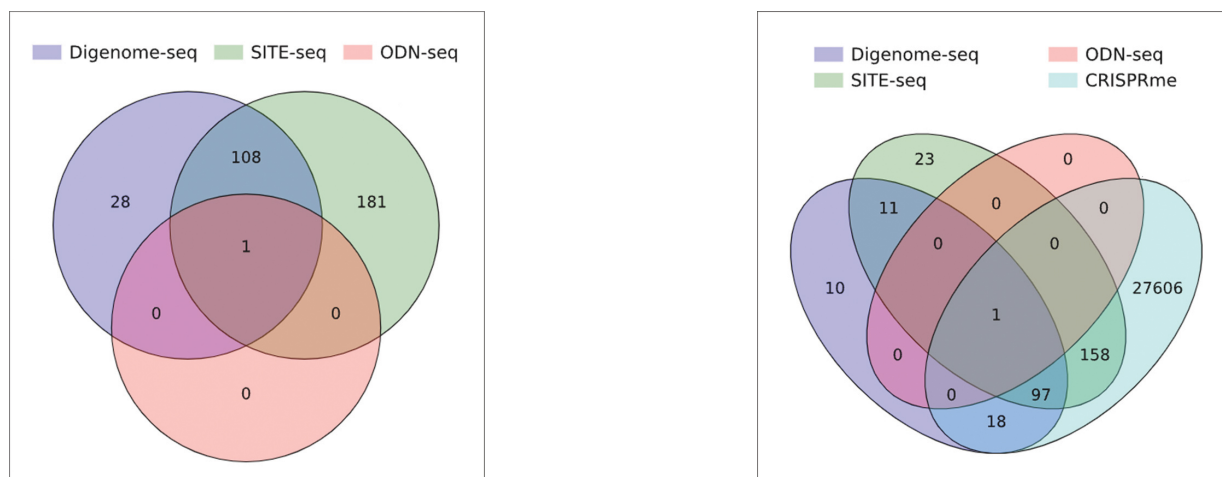
The off-target profile of the lead human guide targeting HAO1 is being evaluated in accordance with FDA guidelines published in March 2022. Potential off-target sites were identified using a combination of *in silico* prediction, biochemical discovery assays, and a cell-based discovery assay. To predict potential off-target sites *in silico* we used the variant aware CRISPRme software using a permissive PAM for MG29-1 (YYN) and permitting up to 5 changes (4MM + 1 bulge) from the HAO1 reference protospacer to identify potential off-target sites referencing both the GRCh38 human genome reference and the Genome Aggregation Database gnomAD v4 (Minor Allele Frequency of  $\geq 1\%$  in subpopulations).

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 empirical discovery 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 of potential off-target sites identified through cell-based and biochemical discovery methods for the lead HA01 targeting guide (n=318) (left panel). Venn diagram demonstrating the overlap of the potential off-target sites identified through cell-based and biochemical discovery methods with in silico predicted off-target sites (right panel).

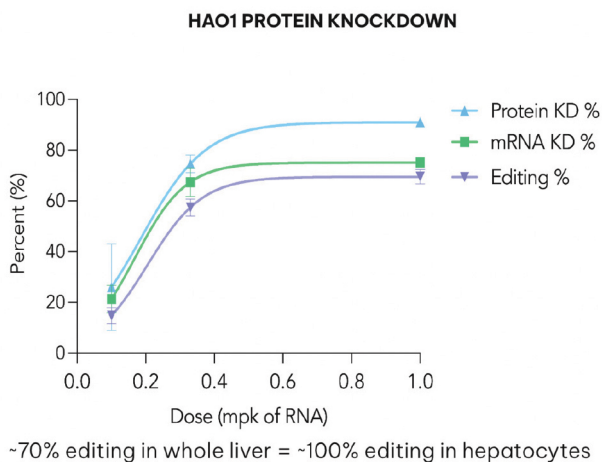


These 318 potential off-target sites were tested in primary human hepatocytes that had been edited by MG29-1 and the lead *HAO1* targeting gRNA using LNP delivery.

Off-target editing at all 317 amplifiable 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 (one centromere-proximal site identified in one SITE-seq replicate and by CRISPRme could not be amplified by standard PCR methods) 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 Knock-down and Protein Knock-down 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.

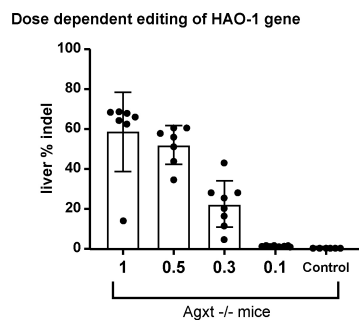


Additionally, along with our partner Moderna, we have achieved preclinical proof-of-concept in an AGXT knock-out mouse which is an accepted disease model of PH1 (Figure 36). AGXT knock-out mice have elevated oxalate in the urine (measured with a mass spec assay) of about 500 mg per gram of creatinine 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.

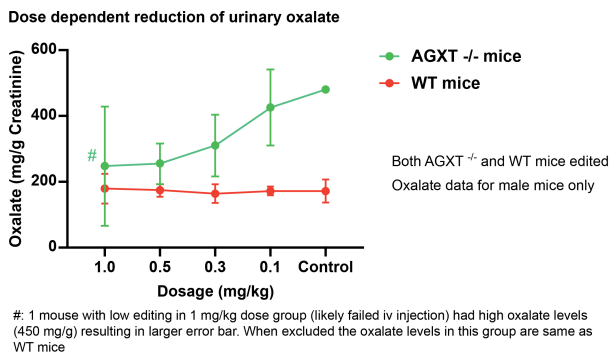
**Figure 36.** Preclinical Proof of Concept in PH1 Disease Model (AGXT <sup>-/-</sup> mice).

**Figure 36a.** Dose dependent editing of the HAO1 gene in AGXT <sup>-/-</sup> mice.



Source: Moderna

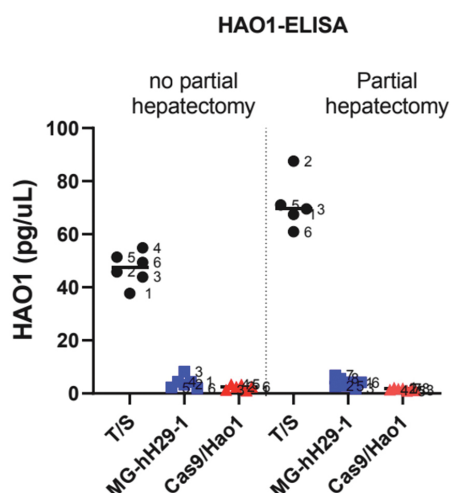
**Figure 36b.** Dose-dependent reduction in urinary oxalate reaching normalization at highest dose.



Source: Moderna

The durability of this approach was demonstrated by continued knock-down 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 knock-down in edited mice that did not undergo hepatectomy. This result demonstrates that the knock-down of HAO1 expression was not compromised by extensive liver growth and that the fitness of edited hepatocytes was not impacted by editing.

**Figure 37.** Knock-down 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 knock-down 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.

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.

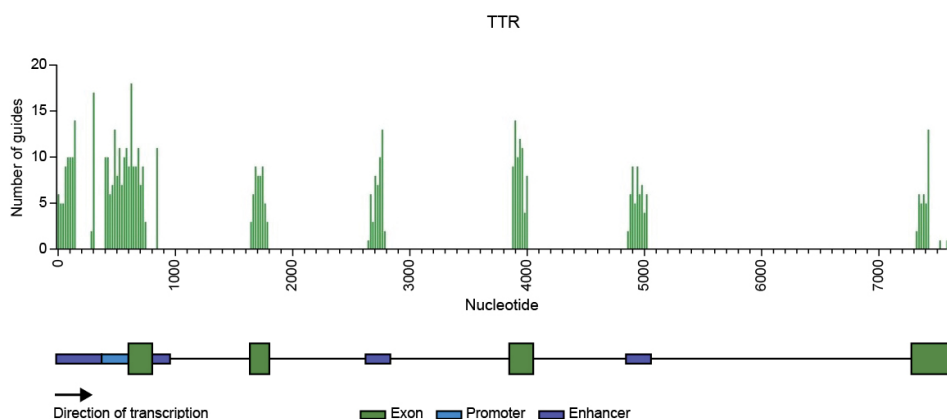
#### Our Approach/Next Steps

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 knock-down approach is provided by antisense and siRNA clinical experience and further suggests the potential longer-term safety and tolerability of this approach.

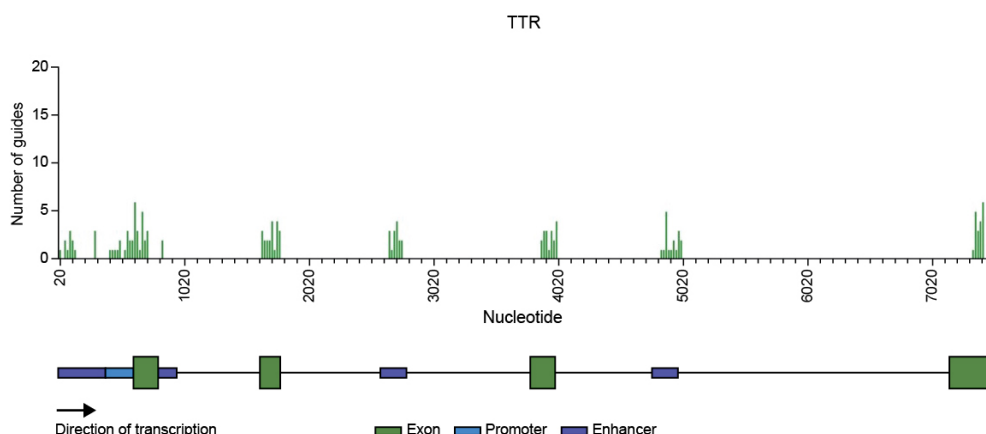
Using our novel nucleases, we aim to provide efficient TTR knock-down and halt further deposition of amyloid fibrils. Previous experience suggests a clinical correlation between the degree of TTR knock-down and potential for benefit in familial forms of the disease, which are expected to translate similarly 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 knock-down 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.



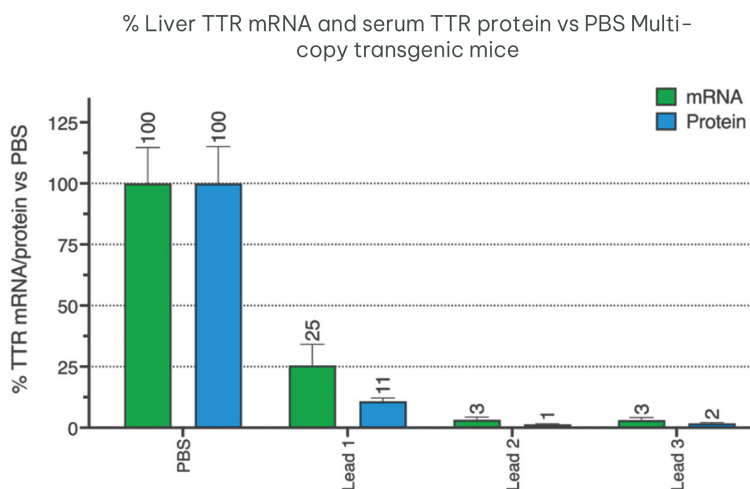
**Figure 38b.** Density of SpCas9 gRNA targeting the coding and regulatory regions of the TTR gene.



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 knock-down 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 knock-down 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 knock-down 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<sub>RX</sub>) 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.

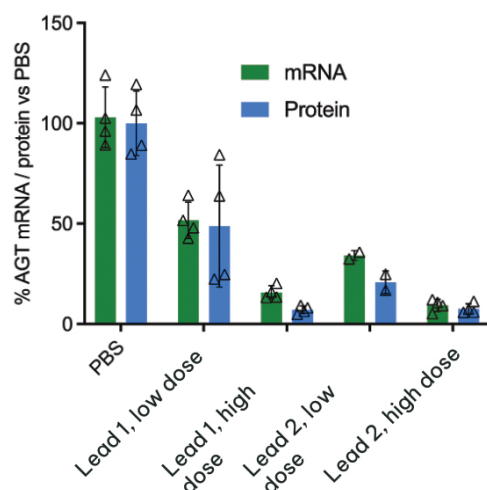
Along with our partner Ionis Pharmaceuticals we are currently in advanced stages of nuclease and guide screening and expect to move into NHP studies in late 2024 or early 2025. We believe one of the strengths of our technology platform is being able to access a larger proportion of the human genome by 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 knock-down 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 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 AAG (PiZ). Converting the PiZ sequence (AAG) 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 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.

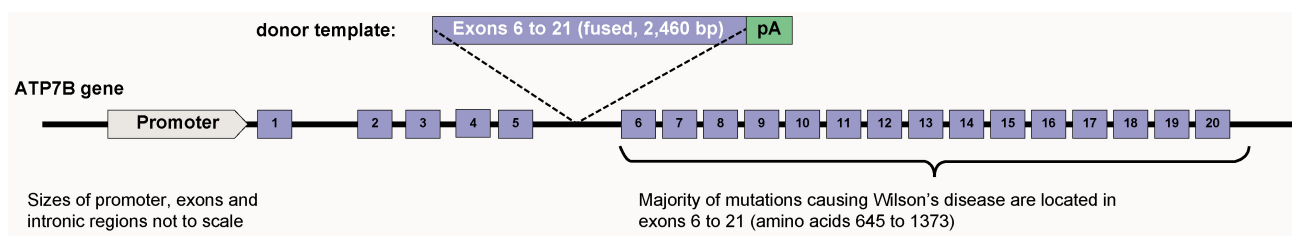
### *Our Approach/Next Steps*

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).

Our approach would be 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, knock-down 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 potentially 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 knock-down 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 knock-down. 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 (etiqlrsen), 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.

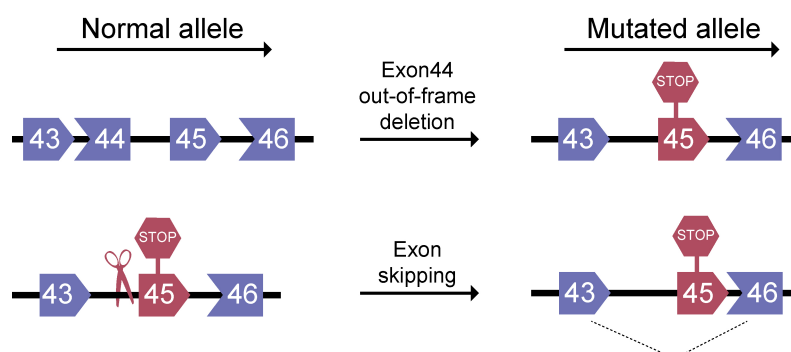
### *Our Approach/Next Steps*

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*

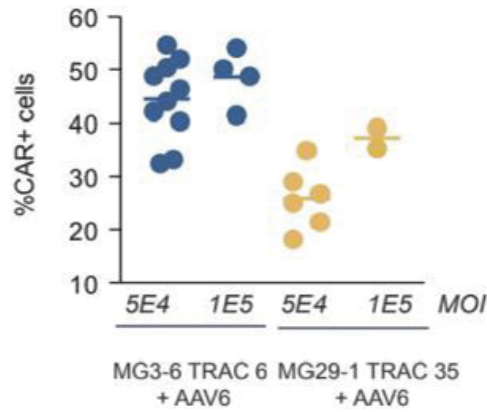
Identifying and optimizing novel nucleases from our metagenomics platform has involved a series of stringent efficiency, activity, and specificity testing in a variety of immune cell types which yields a comprehensive dataset that demonstrates our genome editing capabilities for cell therapy applications. 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.



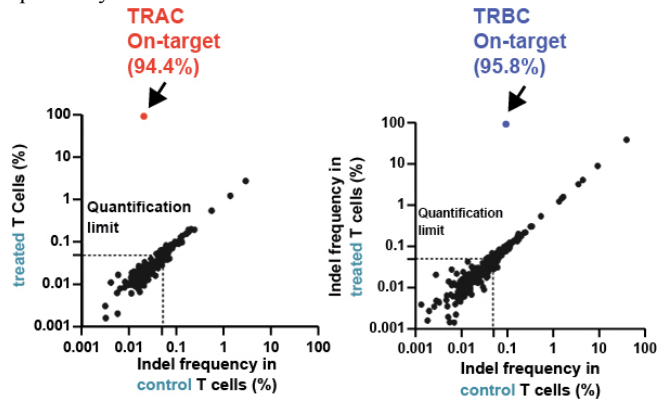
\* Nucleases were delivered as RNP and CAR donor template by AAV.

\* 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.

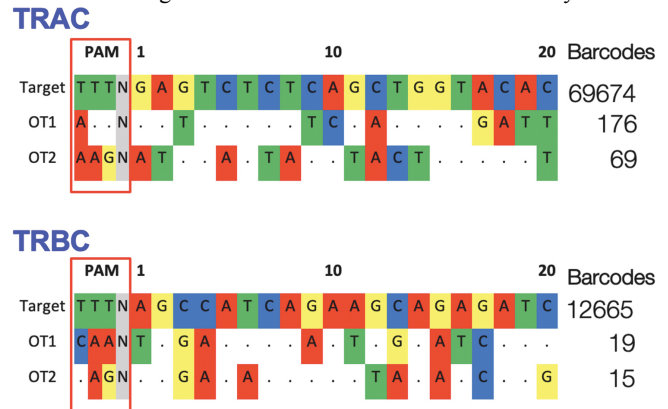
Our MG29-1 nuclease is a highly active and specific nuclease being used for *ex vivo* T cell engineering in collaboration with Affini-T Therapeutics. Affini-T Therapeutics is developing a cell therapy based on engineering the TCR of T cells to recognize mutant KRAS for the treatment of patients with 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.

**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.

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.

### **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”). The use of RIGS with mRNA and base editing correction with mRNA is within the RT Field exclusive to Moderna within the Term. 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 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 December 31, 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 December 31, 2023, we received a total of \$4.3 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’ 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 to 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, its third target (“Target 3”) in Wave 1 in November 2023, and its fourth target (“Target 4”) in Wave 1 in February 2024. 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 December 31, 2023, we received a total of \$2.0 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 December 31, 2023, we own three issued U.S. patents, 21 pending U.S. non-provisional patent applications, 38 pending U.S. provisional patent applications, nine issued foreign patents in Great Britain, Hong Kong, Mexico and Australia, 129 pending foreign patent applications, including in Australia, Canada, China, Europe, Great Britain, Hong Kong, India, Japan, Korea, Mexico and Brazil, and 23 Patent Cooperation Treaty (“PCT”) patent applications.

The patent portfolios for our genome editing systems as of December 31, 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, six 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 South Korea, 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 one PCT

patent application 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.

Our type V CRISPR systems are protected by one issued U.S. patent and four pending U.S. non-provisional patent applications with composition of matter claims covering genome editing systems using Type V nucleases 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, 19 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 one 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 seven 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 three 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 two 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 21 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 and one pending U.S. 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 eleven 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, and one 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 one pending U.S. non-provisional patent applications with composition of matter claims covering genome editing systems using small nucleases, and two pending U.S. provisional patent applications 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 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 December 31, 2023, we own the trademark registrations for Metagenomi in the United States and we have trademark applications for Metagenomi SMART 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 or 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;
- 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](http://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.

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.

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.

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 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 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 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 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.

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 December 31, 2023, we had 236 full-time employees, of which 80 have M.D. or Ph.D. degrees. Within our workforce, 199 employees are engaged in research and development and 37 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.

#### *Information Available on the Internet*

Our Internet website address is <https://metagenomi.co>. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K. We have included our website address in this in this Annual Report on Form 10-K solely as an inactive textual reference. We will make available, free of charge, through our website, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We will make these reports available through the “Investors” section of our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or SEC. We will also make available, free of charge on our website, the reports filed with the

SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. You can review our electronically filed reports and other information that we file with the SEC on the SEC's website at <http://www.sec.gov>.

Investors and others should note that we announce material information to our investors using one or more of the following: SEC filings, press releases, public conference calls and webcasts and our corporate website, including without limitation the "Investors-News & Events" sections of our website. We use these channels, as well as social media channels such as LinkedIn and X (formerly Twitter), to communicate with the public about our company, our business, our approved drugs and drug candidates and other matters. It is possible that the information we post on our corporate website or other social media could be deemed to be material information. Therefore, we encourage investors, the media, and others interested in our company to review the information we post on the "Investors-News & Events" section of our corporate website and on our social media channels. The contents of our corporate website and social media channels are not, however, a part of this Annual Report on Form 10-K.

### **Facilities**

Our corporate headquarters is located in Emeryville, California, where we sublease and occupy approximately 75,662 square feet of combined office, research and laboratory space at 5959 Horton Street, 7th Floor, Emeryville, California 94608. The current term of our sublease expires in March 2031. The company also leases approximately 23,155 square feet of office space at 1485 Park Avenue, Emeryville, California 94608 and approximately 23,851 square feet of laboratory and office space at 1545 Park Avenue, Emeryville, California 94608.

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.

### **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. On January 24, 2024, we completed a series of transactions, which we refer to collectively as the Reorganization. As a result of the Reorganization, Metagenomi Technologies, LLC merged 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 received shares of common stock of Metagenomi, Inc., (ii) all of the outstanding preferred unitholders of Metagenomi Technologies, LLC received shares of preferred stock of Metagenomi, Inc. and (iii) certain holders of profits interest units in Metagenomi Technologies, LLC received 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 the IPO, all outstanding shares of preferred stock of Metagenomi, Inc. were converted into shares of common stock.

Metagenomi, Inc. is the registrant for purposes of Annual Report on form 10-K. Our consolidated financial statements for reporting periods prior to the Reorganization were reported from Metagenomi Technologies, LLC.

Our principal executive offices are located at 5959 Horton Street, 7th Floor, 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.

## Item 1A. 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 Annual Report on Form 10-K, including our consolidated financial statements and related notes appearing at the end of this Annual Report on Form 10-K, 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 \$68.3 million and \$43.6 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of \$144.9 million. We have financed our operations primarily through issuing redeemable convertible preferred units and convertible promissory notes, entering into collaboration agreements, and through the IPO proceeds. 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.

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;
- 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 received from our initial public offering (the "IPO"). 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, we expect to continue incurring 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 December 31, 2023, our cash, cash equivalents and available-for-sale marketable securities were \$271.2 million. We expect that the net proceeds from the IPO, approximately \$81.1 million, 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 2027, and provide cash runway to support 2 INDs and 2 additional Development Candidate nominations. 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;
- 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.

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, 2023, we had U.S. federal net operating loss carryforwards of less than \$0.1 million (which are not subject to expiration) and state net operating loss carryforwards of \$17.5 million (which begin to expire in various amounts in 2037), and \$4.7 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. As of December 31, 2023, the Company has completed an IRC Section 382 analysis from inception through the year ended December 31, 2023. 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. In addition, we may experience ownership changes in the future, 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;
- 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 relatively 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 any 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 relatively novel, the regulatory requirements that will govern any novel genome editing product candidates we develop may continue to evolve. Only one genome editing therapy, CASGEVY, has received marketing authorization from the FDA and EMA to date and, within the broader genetic therapy field, a limited number of gene therapy products have received marketing authorization from the FDA and the EMA. 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 January 2024, the FDA published a final 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 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 Collectis 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;
- 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.

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 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 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;
- 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;
- 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 fulfill 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 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.

We have adopted 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 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;
- 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
- 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 Annual Report on Form 10-K 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 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 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;
- 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;

- 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 December 31, 2023, we had 236 full-time employees, of which 80 have M.D. or Ph.D. degrees. Within our workforce, 199 employees are engaged in research and development and 37 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 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 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 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.

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.

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.

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 our Common Stock, and Operating as a Public Company***

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

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;
- 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. 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 incurred, and continue to incur, increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.***

As a public company, and particularly after we are no longer an “emerging growth company,” we have incurred, and continue to 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 be sustained 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.***

Although our common stock is listed on the Nasdaq Global Select Market, an active or liquid market in our common stock may not be sustained. If a market for our common 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. 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 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.

3,404,585 shares of our common stock were outstanding as of December 31, 2023, after giving effect of the Reorganization and reverse stock split of Metagenomi, Inc. in connection with our IPO. Shares of unvested restricted common stock 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.

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 a “smaller reporting company,” and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting 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 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 is different than the information that is available with respect to other public companies.

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 are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than \$700 million and our annual revenue is less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

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 have substantial influence over us, which could limit your ability to affect the outcome of key transactions, including a change of control.***

Our directors and executive officers and their affiliates beneficially own a significant amount 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 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 in accordance with generally accepted accounting principles. We have begun 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 Annual Report on Form 10-K for the year ending December 31, 2024.

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.***

We are 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 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, 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 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 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 and amended and restated bylaws 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;
- 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 deferring 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.

Following SVB’s failure, we have diversified our cash deposit holdings between multiple financial institutions, 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. 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.

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.

#### **Item 1B. Unresolved Staff Comments.**

None

#### **Item 1C. Cybersecurity.**

##### **Cybersecurity Risk Management and Strategy**

We have implemented a cybersecurity program in accordance with our risk profile and business size that is informed by recognized industry standards, including elements of the National Institute of Standards and Technology Cybersecurity Framework. We leverage the cybersecurity services of third-party vendors, including virtual chief information security officer services, to support our cybersecurity risk management program.

Our cybersecurity risk management program is comprised of a number of components, including but not limited to a risk assessment incorporating elements of industry standard frameworks, penetration testing, endpoint detection and response, and system monitoring. We have an employee training program that includes annual cybersecurity awareness training that is reinforced by approximately monthly phishing campaigns. We also maintain an incident response plan and related processes to help guide our response to cybersecurity incidents.

As part of our cybersecurity risk management program, we take a risk-based approach to the evaluation of third-party vendors, and apply mitigations and processes based on our evaluation of the sensitivity of the data accessed by the vendor and the maturity of the vendor's programs. Our current vendor evaluation procedures include, as appropriate, a review of certain vendors' security standards.

We have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition. However, like other companies in our industry, we and our third-party vendors have experienced threats relating to our and our third-party vendors' information systems. For more information, please see "Item 1A, Risk Factors."

##### **Governance Related to Cybersecurity Risks**

Our Head of Information Technology ("Head of IT") is responsible for the strategic leadership and direction of the Company's information technology organization. Our current Head of IT has over thirty years of experience leading information technology teams

in the life sciences industry. The Head of IT reviews threat intelligence, and receives updates from the Company's third-party providers, to help identify risks from cybersecurity threats.

The Head of IT reports to the Chief Financial Officer (CFO) , and attends regular meetings with the CFO to discuss updates relating to the Company's cybersecurity program. The Head of IT also provides cybersecurity updates on a quarterly basis to the Company's executive team.

The Board of Directors has delegated oversight of cybersecurity risk management to the Audit Committee. The Audit Committee reviews the Company's major cybersecurity risk exposures and the steps that the Company's management has taken to monitor and control such exposures. Specifically, the Audit Committee reviews reports on data management, security initiatives, and significant existing and emerging cybersecurity risks, including material cybersecurity incidents, the impact on the Company and its stakeholders of any significant cybersecurity incident, and any disclosure obligations arising from any such incidents.

## **Item 2. Properties.**

Our corporate headquarters is located in Emeryville, California, where we sublease and occupy approximately 75,662 square feet of combined office, research and laboratory space at 5959 Horton Street, 7th Floor, Emeryville, California 94608. The current term of our sublease expires in March 2031. The company also leases approximately 23,155 square feet of office space at 1485 Park Avenue, Emeryville, California 94608 and approximately 23,851 square feet of laboratory and office space at 1545 Park Avenue, Emeryville, California 94608.

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.

## **Item 3. Legal Proceedings.**

From time to time, we may be a party to litigation or subject to claims incident to the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, we currently believe that the final outcome of these ordinary course matters will not have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which would have a material adverse effect on our results of operations, financial condition or cash flows, nor are we aware of any governmental proceedings involving potential monetary sanctions of \$300,000 or more.

## **Item 4. Mine Safety Disclosures.**

Not applicable.

## PART II

### Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

#### Market Information

Our common stock began trading on the Nasdaq Global Select Market under the symbol "MGX" on February 9, 2024. Prior to this date, there was no public trading market for our common stock.

#### Holders

As of March 15, 2024, we had approximately 282 holders of record of our common stock. The approximate number of holders is based upon the actual number of holders registered in our records at such date and excludes holders in "street name" or persons, partnerships, associations, corporations, or other entities identified in security positions listings maintained by depository trust companies.

#### Dividend Policy

We have not declared or paid cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends to holders of common stock in the foreseeable future. Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our board of directors, subject to applicable laws, and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant. In addition, our ability to pay cash dividends on our capital stock in the future may be limited by the terms of any future debt or preferred securities we issue or any credit facilities we enter into.

#### Securities authorized for issuance under equity compensation plans

Information about securities authorized for issuance under our equity compensation plans is incorporated herein by reference to Part III, Item 12 of this Annual Report on Form 10-K.

#### Use of Proceeds from our IPO

On February 13, 2024, we closed the IPO, pursuant to which we issued and sold 6,250,000 shares of common stock at an initial public offering price of \$15.00 per share.

The offer and sale of all of the shares of our common stock in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333- 276413 ), which was declared effective by the SEC on February 8, 2024. J.P. Morgan, Jefferies, TD Cowen, Wells Fargo Securities, and BMO Capital Markets acted as joint book-running managers and Chardan acted as lead manager for the IPO.

We received aggregate gross proceeds from the IPO of \$93.8 million, or aggregate net proceeds of \$81.1 million after deducting underwriting discounts and commissions and other offering costs. None of the underwriting discounts and commissions or offering expenses were incurred or paid, directly or indirectly, to (i) our directors or officers or their associates, (ii) persons owning 10% or more of our common stock or (iii) any of our affiliates.

There has been no material change in our planned use of the net proceeds from the IPO as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on February 12, 2024.

#### Recent Sales of Unregistered Securities

##### *Preferred Units*

During the year ended December 31, 2023, we sold an aggregate of 191,624 Series B-1 redeemable convertible preferred units, at a purchase price of \$24.5750 per unit, for an aggregate amount of \$4.7 million. The Company incurred \$0.1 million in issuance costs.

No underwriters were involved in the foregoing sale of securities. The sale 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.

#### *Profits Interests*

During the year ended December 31, 2023, we granted an aggregate of 1,298,081 profits interests, with a weighted average grant date fair value of \$11.75, to employees, directors and consultants pursuant to the 2019 Plan. No common units were 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.

#### **Purchases of Equity Securities by the Issuer and Affiliated Purchasers**

None.

#### **Item 6. [Reserved]**

## Item 7. 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 consolidated financial statements and the related notes included in Part II, Item 8 of this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K 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 Annual Report on Form 10-K. 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 \$68.3 million and \$43.6 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of \$144.9 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;
- 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 December 31, 2023, we had cash, cash equivalents and available-for-sale marketable securities of \$271.2 million. In February 2024, Metagenomi Inc., completed its initial public offering of its common stock (the “IPO”) and raised approximately \$81.1 million in net proceeds. We believe that our existing cash, cash equivalents and available-for-sale marketable securities together with the IPO proceeds will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next 12 months from the date of this Annual Report on Form 10-K. 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.”

### **Reorganization**

We previously operated as a Delaware limited liability company under the name Metagenomi Technologies, LLC. On January 24, 2024, we completed a series of transactions pursuant to which Metagenomi Technologies, LLC merged 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 received shares of common stock of Metagenomi, Inc., (ii) all of the outstanding redeemable convertible preferred unitholders of Metagenomi Technologies, LLC received shares of redeemable convertible preferred stock of Metagenomi, Inc. with the same rights and privileges and (iii) certain holders of profits interests in Metagenomi Technologies, LLC received shares of common stock or unvested restricted common stock in Metagenomi, Inc. as determined by the applicable provisions of the Amended and Restated Limited Liability Company Agreement in effect immediately prior to the Reorganization. In connection with the Reorganization, by operation of law, Metagenomi, Inc. acquired all assets of the Metagenomi Technologies, LLC, and assumed all of its liabilities and obligations. The Reorganization generally did not result in a taxable event to Metagenomi, Inc. for U.S. income tax purposes.

### **Initial Public Offering**

On February 8, 2024, Metagenomi, Inc.’s Form S-1 Registration Statement for its IPO was declared effective, and on February 13, 2024, its IPO was completed. Metagenomi, Inc. issued 6,250,000 shares of common stock at a price to the public of \$15.00 per share and received gross proceeds of \$93.8 million. Net proceeds were approximately \$81.1 million, after deducting underwriting discounts and commissions and other offering costs totaling approximately \$12.7 million. Our common stock began trading on the Nasdaq Global Select Market on February 9, 2024, under the symbol “MGX”.

On January 26, 2024, following the Reorganization, Metagenomi, Inc. effected a reverse stock split of the shares of common stock at a ratio of 1-for-1.74692. Immediately prior to the IPO closing, each share of Metagenomi, Inc.’s redeemable convertible preferred stock then outstanding converted into a number of shares of common stock based on the formula set forth in Metagenomi Inc.’s amended and restated certificate of incorporation in effect immediately prior to the closing of the IPO and giving effect to the reverse stock split.

### **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 Annual Report on Form 10-K.

## 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”). The use of RIGS with mRNA and base editing correction with mRNA is within the RT Field exclusive to Moderna within the Term. 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 pursuant to a convertible promissory note agreement dated October 29, 2021. 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 December 31, 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. 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 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 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 \$18.1 million and \$14.5 million in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we recorded \$0.5 million in accounts receivable on the consolidated balance sheet, related to services performed. As of December 31, 2023 and 2022, deferred revenue related to the Moderna Agreement was \$18.7 million and \$30.2 million, respectively. Collaboration revenue recognized during the years ended December 31, 2023 and 2022 included \$18.1 million and \$14.5 million that was included in deferred revenue as of December 31, 2022 and 2021, respectively. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligations was approximately \$23.7 million as of December 31, 2023, which we expect to recognize as revenue over the next two-to-three years.

We recognized \$0.3 million and \$0.4 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, 2023. 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 during the year ended December 31, 2022, respectively. As of December 31, 2023, the collaboration advance balance was \$0.7 million and the cost-sharing payable balance was \$0.1 million, which were presented as a collaboration advance on our 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 our 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, 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 December 31, 2023, we received a total of \$4.3 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.

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, 2023 and 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. We recognize revenue each reporting period based on the measure of progress using an estimated cost-based input method.

We recognized collaboration revenue of \$4.7 million and \$2.6 million in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2023 and 2022, 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. As of December 31, 2023, we recorded \$2.0 million in accounts receivable on the consolidated balance sheet, related to

services performed. There was no contract asset related to services performed as of December 31, 2023. 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. As of December 31, 2023 and 2022, deferred revenue related to the Affini-T Agreement was \$0.2 million and zero, respectively. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligation was approximately \$1.7 million as of December 31, 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 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.

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, its third target (“Target 3”) in Wave 1 in November 2023, and its fourth target (“Target 4”) in February 2024. 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 December 31, 2023, we received a total of \$2.0 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, 2023 and 2022. 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 of cumulative revenue in future periods. We constrained all development and regulatory milestone payments at the effective date and as of December 31, 2023 and 2022. 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 collaboration revenue of \$21.9 million and \$0.1 million in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023 and 2022, deferred revenue related to the Ionis Agreement was \$60.0 million and \$79.9 million, respectively. Collaboration revenue recognized during the year ended December 31, 2023 included \$21.9 million that was included in deferred revenue as of December 31, 2022. The value of the transaction price allocated to the remaining performance obligations was approximately \$68.0 million as of December 31, 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.”

## **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 \$44.8 million and \$17.2 million for the years ended December 31, 2023 and 2022, respectively.

For additional information about our revenue recognition policy related to our collaboration agreements, refer to Note 2 in our consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

### ***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.

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 and 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 was 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.

Metagenomi, Inc., is a corporation for tax purposes and is subject to income taxes. Prior to the Reorganization, Metagenomi, Inc. was a wholly owned subsidiary of Metagenomi Technologies LLC. We recognized income tax expense for the year ended December 31, 2023 and 2022 for domestic, federal and state income taxes. After the Reorganization, Metagenomi, Inc. continues as the surviving corporation.

As of December 31, 2023, we had net operating loss carryforwards of less than \$0.1 million and \$17.5 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, 2023, we had state research and development credit carryforwards of \$4.7 million, which do not expire. As of December 31, 2023, we had \$0 million federal research and development credit carryforwards.

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 Years Ended December 31, 2023 and 2022***

The following table summarizes our results of operations for the years ended December 31, 2023 and 2022 (in thousands):

	Years ended December 31,		Change
	2023	2022	\$
Collaboration revenue	\$ 44,756	\$ 17,200	\$ 27,556
Operating expenses:			
Research and development	94,403	43,139	51,264
General and administrative	28,845	18,701	10,144
Total operating expenses	123,248	61,840	61,408
Loss from operations	(78,492)	(44,640)	(33,852)
Other income (expense):			
Interest expense	—	(98)	98
Interest income	15,468	3,419	12,049
Change in fair value of long-term investments	2,870	94	2,776
Other income, net	(74)	201	(275)
Total other income, net	18,264	3,616	14,648
Net loss before provision for income taxes	(60,228)	(41,024)	(19,204)
Provision for income taxes	(8,027)	(2,569)	(5,458)
Net loss	\$ (68,255)	\$ (43,593)	\$ (24,662)

#### ***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 \$27.6 million, from \$17.2 million for the year ended December 31, 2022 to \$44.8 million for the year ended December 31, 2023. The increase in collaboration revenue for the year ended December 31, 2023, was primarily driven by a \$21.8 million increase in revenue related to the Ionis Agreement, a \$3.6 million increase in revenue related to the Moderna Agreement and a \$2.2 million increase in revenue related to the Affini-T

Agreement as we performed more services and collaboration activities progressed.

The collaboration revenue for the years ended December 31, 2023 and 2022 included the following (in thousands):

	Years ended December 31,		Change
	2023	2022	\$
Ionis	\$ 21,915	\$ 112	\$ 21,803
Moderna	18,119	14,518	3,601
Affini-T	4,722	2,570	2,152
Total collaboration revenue	\$ 44,756	\$ 17,200	\$ 27,556

### **Research and Development Expenses**

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

	Years ended December 31,		Change
	2023	2022	\$
Personnel-related costs	\$ 39,848	\$ 22,436	\$ 17,412
Laboratory materials and supplies	20,014	10,518	9,496
Facilities and overhead costs	20,927	7,325	13,602
Other research and development expenses and consulting costs	13,614	2,860	10,754
Total research and development expense	\$ 94,403	\$ 43,139	\$ 51,264

Research and development expenses increased by \$51.3 million, from \$43.1 million for the year ended December 31, 2022 to \$94.4 million for the year ended December 31, 2023.

Personnel-related costs, including employee payroll and related expenses, increased by \$17.4 million, including a \$2.6 million increase in unit-based compensation expense, as a result of increased headcount in our research and development organization. Unit-based compensation expense was \$3.3 million and \$0.8 million for the years ended December 31, 2023 and 2022, respectively. Laboratory materials and supplies increased by \$9.5 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 \$13.6 million including a \$7.8 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 \$2.4 million increase in depreciation and amortization expense as we continue investing in our lab and manufacturing capabilities. Other research and development and consulting costs increased by \$10.8 million due to external research and development costs of \$8.8 million and consulting services of \$2.0 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 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, 2023 and 2022, the total cost true-ups reduced our research and development expenses by \$0.3 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, 2023 and 2022, \$0.4 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 \$10.1 million, from \$18.7 million for the year ended December 31, 2022 to \$28.8 million for the year ended December 31, 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 \$6.3 million, including a \$2.6 million increase in unit-based compensation expense, as a result of increase in our administrative personnel. Unit-based compensation expense was \$3.6 million and \$0.9 million for the years ended December 31, 2023 and 2022, respectively. Expenses related to professional consulting services increased by \$3.3 million due to increased spending on consulting and outside services to support our business operations. Other general and

administrative expenses, including insurance, information technology, office supplies, subscriptions and licenses, and other miscellaneous expenses, increased by \$0.5 million.

### ***Total Other Income, Net***

Total other income, net, increased by \$14.6 million, from \$3.6 million net income for the year ended December 31, 2022 to \$18.3 million for the year ended December 31, 2023.

Interest income, which includes interest income and amortization of premiums and discounts on our investment in available-for sale marketable securities, increased by \$12.0 million from \$3.4 million for the year ended December 31, 2022 to \$15.5 million for the year ended December 31, 2023, due to higher average balances in cash and cash equivalents and available for sale marketable securities and higher interest rates during the year ended December 31, 2023.

The change in fair value of long-term investments increased by \$2.8 million, from \$0.1 million for the year ended December 31, 2022 to \$2.9 million for the year ended December 31, 2023, as our investment in Affini-T was re-measured at fair value. For more details on our investment in the Affini-T, refer to Note 5 in our consolidated financial statements included elsewhere in Part II, Item 8 of this Annual Report on Form 10-K.

### ***Provision for Income Taxes***

Provision for income taxes increased by \$5.5 million, from \$2.6 million for the year ended December 31, 2022 to \$8.0 million for the year ended December 31, 2023.

Income tax expense for the year ended December 31, 2023 was mainly due to our taxable income related to an upfront payment received under the Ionis Agreement and capitalization of research and development expenses under the 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.

Income tax expense for the year ended December 31, 2022 was mainly due to 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 Section 174.

## **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 \$351.7 million in aggregate gross proceeds. Additionally, through December 31, 2023, we received approximately \$120.0 million upfront cash payments from collaboration and licensing agreements. As of December 31, 2023, we had \$271.2 million in cash, cash equivalents and available-for-sale marketable securities. In February 2024, upon the closing of the IPO, we received net proceeds of approximately \$81.1 million, after deducting underwriting discounts and commissions and other offering costs.

### ***Future Funding Requirements***

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance our portfolio of products toward the clinical trials. In addition, 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;
- 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 December 31, 2023, we had \$271.2 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 together with the IPO proceeds 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 our IPO, will be sufficient to fund our projected operating expenses and capital expenditure requirements into 2027. 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 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,	
	2023	2022
Net cash used in (provided by) operating activities	\$ (91,409)	\$ 29,724
Net cash provided by (used in) investing activities	45,734	(122,200)
Net cash provided by financing activities	1,012	239,594
Net (decrease) increase in cash, cash equivalents and restricted cash	\$ (44,663)	\$ 147,118

### **Cash Flows from Operating Activities**

Net cash used in operating activities for the year ended December 31, 2023 was \$91.4 million. This was primarily due to our net loss of \$68.3 million, decreased by non-cash charges of \$3.3 million and increased by a net reduction of \$26.4 million in our net operating assets and liabilities. The net non-cash charges consisted of \$6.9 million unit-based compensation expense, \$4.2 million non-cash



lease expense and \$4.2 million depreciation and amortization expense, all partially offset by \$8.5 million credit related to amortization of the discounts on available-for-sale marketable securities, \$2.9 million increase in fair value of our investments in Affini-T and \$0.7 million 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 \$30.3 million decrease in deferred revenue and collaboration advances as we recognized revenue under our collaboration agreements, a \$2.5 million increase in accounts receivable related to the Affini-T Agreement and the Moderna Agreement, a \$1.2 million decrease in operating lease liabilities due to recurring payments under the existing lease agreements, a \$1.1 million increase in prepaid expenses and other assets, and a \$0.1 million decrease in account payable due to the timing of payments to our vendors, all partially offset by a \$4.0 million increase in other non-current liabilities, a \$1.7 million increase in income tax payable due to additional tax expense, a \$1.6 million increase in accrued expenses and other current liabilities and a \$1.3 million decrease in contract assets related to the Affini-T Agreement.

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 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 provided by investing activities for the year ended December 31, 2023 was \$45.7 million, which consisted of \$263.6 million in proceeds from maturities of available-for-sale marketable securities, partially offset by \$208.1 million of purchases of available-for-sale marketable securities and \$9.8 million of purchases of property and equipment.

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 year ended December 31, 2023 was \$1.0 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 \$3.3 million of payments of IPO costs.

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, 2023, we leased our office and laboratory space under three lease agreements and had one vivarium lease agreement. Remaining lease obligations under our non-cancellable leases were \$71.0 million as of December 31, 2023, including \$8.6 million payable through December 31, 2024 and \$62.4 million for the remainder of the leases' terms, and had a weighted-average remaining lease term of 7.1 years.

Refer to Note 8 in our consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

#### **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 Part II, Item 8 of this Annual Report on Form 10-K.

#### **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 consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K, 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 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 \$6.9 million and \$2.0 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, there was \$15.5 million of total unrecognized unit-based compensation expense, which we expect to recognize over a remaining weighted-average period of 3.0 years. In connection with the Reorganization, all outstanding unvested profits interests were exchanged for unvested restricted common stock. We expect to continue to grant equity awards in the future under the 2024 Stock Option and Incentive Plan and 2024 Employee Stock Purchase Plan, and to the extent that we do, stock-based compensation expense recognized in future periods will likely increase.

#### ***Determination of Fair Value of Common Units***

As there has been no public market for our common units prior to the IPO, 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 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.

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.

Since a public trading market for our common stock has been established in connection with the completion of our IPO, the fair value of our common stock will be determined based on the quoted market price of our common stock.

### ***Income Taxes***

Prior to the Reorganization, we were taxed under the provisions of Subchapter K—Partners and Partnerships of the Internal Revenue Code. Under those provisions, we did not pay federal or state corporate income taxes on our taxable income. Instead, each member included 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 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.

#### **Item 7A. Quantitative and Qualitative Disclosures About Market Risk.**

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

#### **Item 8. Financial Statements and Supplementary Data.**

The information required by this item is presented at the end of this Annual Report on Form 10-K beginning on page F-1. An index of those financial statements is found in Part IV, Item 15, Exhibits, Financial Statement Schedules, of this Annual Report on Form 10-K.

#### **Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.**

[None]

#### **Item 9A. Controls and Procedures.**

##### ***Management's Evaluation of Disclosure Controls and Procedures***

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Our disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. As required by Rule 13a-15(b) or Rule 15d-15(b) promulgated by the SEC under the Exchange Act, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on the foregoing, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this Annual Report on Form 10-K at the reasonable assurance level.

##### ***Management's Report on Internal Control Over Financial Reporting***

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the Securities and Exchange Commission for newly public companies. Additionally, our independent registered public accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act.

### ***Changes in Internal Controls***

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

### **Item 9B. Other Information.**

(a) The Company's landlord for its office spaces located at 5959 Horton Street, Emeryville, California (the "Premises"), Zymergen Inc. ("Zymergen"), previously filed a voluntary petition for relief under Chapter 11 of the United States Code.

In connection with this filing for relief under Chapter 11 of the United States Code, on October 3, 2023, Zymergen, its master landlord, Dynavax Technologies Corporation ("Dynavax"), and the Company entered into that certain Termination and Release Agreement dated February 22, 2024 (the "Termination Agreement"), pursuant to which the Company's sublease agreement with Zymergen would terminate effective as of the date the conditions precedent set forth in the Termination Agreement had been satisfied. The Termination Agreement was subject to the approval of the United States Bankruptcy Court for the District of Delaware, which was obtained on February 22, 2024.

On March 7, 2024, Dynavax, as sublandlord, entered into a sublease (the "New Sublease") with the Company, as subtenant, for the Premises, attached hereto as Exhibit 10.9. The New Sublease was subject to the consent by Dynavax's master landlord, Emery Station West, LLC ("Emery"), which consent was received on March 7, 2024.

Under the terms of the New Sublease, which commenced on March 7, 2024, and the terms of which are substantially similar to the Company's prior lease with Zymergen, Metagenomi will sublease the Premises from Dynavax, at the initial rental rate of \$493,354 per month (the "Base Rate"), which Base Rate is subject to fifty percent (50%) abatement through June 30, 2024, as well as scheduled annual increases, all as set forth in the New Sublease. Metagenomi is also responsible for certain operating expenses and taxes throughout the term of the New Sublease. The New Sublease will continue until March 31, 2031, concurrent with the term of Dynavax's master lease with Emery, unless sooner terminated pursuant to the terms of the New Sublease.

The New Sublease had no effect on the Company's financial obligations.

(b) None.

### **Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.**

None.

## PART III

### Item 10. Directors, Executive Officers and Corporate Governance.

#### Board of Directors

Our board of directors consists of five members. In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes with staggered three-year terms. 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 directors are divided among the three classes as follows:

- Our Class I directors are Willard Dere and Sebastián Bernales;
- Our Class II director is Juergen Eckhardt; and
- Our Class III directors are Brian C. Thomas and Jian Irish.

There have been no material changes to the procedures by which security holders may recommend nominees to the Company's board of directors. The following table sets forth information regarding our directors as of March 15, 2024:

Name	Age	Position(s)
<i>Executive Officers</i>		
Brian C. Thomas, Ph.D.	55	Chief Executive Officer and Director
Jian Irish, Ph.D., MBA	60	President and Chief Operating Officer and Director
<i>Non-Employee Directors</i>		
Juergen Eckhardt, M.D., MBA	57	Director
Sebastián Bernales, Ph.D.	48	Director
Willard Dere, M.D.	70	Director

*Brian C. Thomas, Ph.D.*, is our founder and has served as our Chief Executive Officer since September 2016 and as our Chairman of the Board since February 2024. 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.

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. Our board of directors believes that Dr. Irish is qualified to serve as a director because of her considerable academic and research expertise, as well as her expansive knowledge about our Company as our President and Chief Operating Officer.

*Juergen Eckhardt, M.D., MBA*, served as our Chairman of the Board of Directors from September 2020 to February 2024. 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, Khloris 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.

*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.

## Executive Officers

The following table sets forth information regarding our executive officers as of March 15, 2024:

Name	Age	Position(s)
<i>Executive Officers</i>		
Brian C. Thomas, Ph.D.	55	Chief Executive Officer and Director
Jian Irish, Ph.D., MBA	60	President and Chief Operating Officer and Director
Pamela Wapnick, MBA	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.	62	Chief Scientific Officer
Simren Delaney, Ph.D., LL.M	38	Vice President of Intellectual Property and Legal Operations
Matthew L. Wein, J.D.	53	Vice President of Corporate Legal and Compliance, and Corporate Secretary

*Brian C. Thomas, Ph.D.*, Biographical information regarding Dr. Thomas is set forth above under “Board of Directors”.

*Jian Irish, Ph.D., MBA*, Biographical information regarding Dr. Irish is set forth above under “Board of Directors”.

*Pamela Wapnick, MBA*, 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 Collectis 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 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.*, is our Vice President of Intellectual Property and Legal Operations and previously served as our Vice President of Legal from February 2020 to January 2024 and 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.

*Matthew L. Wein, J.D.*, has served as our Vice President of Corporate Legal and Compliance, and Corporate Secretary since February 2024. Most recently, Mr. Wein served as General Counsel and Corporate Secretary of Mustang Bio, Inc. (Nasdaq: MBIO) from September 2021 to December 2023. Prior to Mustang, Mr. Wein held various roles as Senior Director in global strategy and alliance management for Sanofi between June 2016 and August 2021; and as Senior Counsel at Amgen Inc. (Nasdaq: AMGN) from September 2002 to May 2016. Mr. Wein was an associate attorney at Arter & Haden LLP from August 1999 to August 2002. Mr. Wein received his B.A. from Wesleyan University and his J.D. from University of Southern California Law School. Mr. Wein is admitted to practice law in California and Massachusetts.

#### **Other Key Personnel**

The following table sets forth information regarding our other key personnel as of March 15, 2024:

<b>Name</b>	<b>Age</b>	<b>Position(s)</b>
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

*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.

*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 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.

#### ***Family Relationships***

There are no family relationships between or among any of our executive officers or directors.

#### ***Legal Proceedings with Directors or Executive Officers***

There are no legal proceedings related to any of our directors or executive officers that require disclosure pursuant to Items 103 or 401(f) of Regulation S-K.

#### ***Code of Business Conduct and Ethics***

Our board of directors has adopted a Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics applies 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 on our website, at <https://www.Metagenomi.co>. The full text of our Code of Business Conduct and Ethics and our Code of Ethics is posted on our website at <https://www.Metagenomi.co>. The inclusion of our website address in this Annual Report on Form 10-K does not include or incorporate by reference the information on our website into this Annual Report on Form 10-K, and you should not consider that information a part of this Annual Report on Form 10-K.

#### ***Director Nominations***

No material changes have been made to the procedures by which security holders may recommend nominees to our board of directors from those that were described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on February 12, 2024.

#### ***Audit Committee***

We have a separately designated standing Audit Committee established in accordance with Section 3(a)(58)(A) of the Exchange Act. Our Audit Committee is currently comprised of Juergen Eckhardt, Willard Dere and Sebastián Bernal and is chaired by Juergen Eckhardt. Our board of directors has determined that each member of the Audit Committee is “independent” and “financially literate” under the rules of The Nasdaq Stock Market LLC, or Nasdaq, and the SEC and that Mr. Eckhardt is an “audit committee financial expert” under the rules of the SEC. Both our independent registered public accounting firm and internal financial personnel regularly meet privately with our Audit Committee and have unrestricted access to the Audit Committee. The information under the heading “Board Independence” in Item 13 below is incorporated herein by reference.

### **Item 11. Executive Compensation.**

#### ***EXECUTIVE COMPENSATION***

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 fiscal year ended December 31, 2023 is detailed in the 2023 Summary Compensation Table and accompanying footnotes and narrative that follows.

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.

### 2023 Summary Compensation Table

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 transitioned 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.

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	20,000	6,966,519	288,600	34,069	7,825,855
	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	15,000	1,783,211	231,449	18,368	2,513,028
	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	15,000	1,447,782	169,963	18,300	2,039,276

- The amounts reported in this column reflect one time special bonuses paid to Dr. Thomas, Dr. Irish and Dr. Noonberg for performance during the applicable fiscal year.
- 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 consolidated financial statements as of December 31, 2023 and for the year ended December 31, 2023 and 2022. These awards are described in more detail under "Narrative Disclosure to Summary Compensation Table – Equity-Based Compensation" below.
- 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. For more information on these bonuses, see description of the annual performance bonuses under the section titled "Narrative Disclosure to Summary Compensation Table – Annual Cash Bonuses" below.
- 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.

#### 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 %

With respect to the fiscal year ended December 31, 2023, our compensation committee approved a payout of cash bonuses in an amount of 111% of target for Dr. Thomas, 110% for Dr. Irish and 110% for Dr. Noonberg.

#### 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 were 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	Stock Awards(1)	
			Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$)(2)
Brian C. Thomas, Ph.D.(3) <i>Chief Executive Officer</i>	11/2/21	11/1/21	32,761	491,415
	5/26/22	1/21/22	125,919	1,888,785
	6/26/23	1/20/23	64,864	972,960
Jian Irish, Ph.D., MBA(4) <i>President and Chief Operating Officer</i>	1/26/21	1/5/21	71,745	1,076,175
	11/2/21	11/1/21	114,659	1,719,885
	5/26/22	1/21/22	32,231	483,465
	6/26/23	1/20/23	16,603	249,045
Sarah Noonberg, M.D., Ph.D <i>Chief Medical Officer</i>	3/24/23	1/30/23	42,611	639,165

(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 is based on the initial public offering price of \$15.00 per share.

(3) Awards held by Dr. Thomas are subject to certain acceleration provisions, as summarized below under “Employment Arrangements for Named Executive Officers.”

(4) Awards held by Dr. Irish are subject to certain acceleration provisions, as summarized below under “Employment Arrangements 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 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. The base salary for Dr. Thomas was adjusted effective as of March 1, 2023 from \$500,000 to \$520,000 and to \$650,000 effective March 1, 2024. Dr. Thomas is eligible to receive an annual bonus with an annual target amount of 50% of his annual base salary in 2023. Dr. Thomas’ annual target amount was increased to 60% of his base salary on March 1, 2024. 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. The base salary for Dr. Irish was adjusted effective March 1, 2023 from \$450,000 to \$468,000 and to \$550,000 effective March 1, 2024. Dr. Irish is eligible to receive an annual bonus with an annual target amount of 45% of her annual salary in 2023. Dr. Irish’s annual target amount was increased to 50% of her base salary on March 1, 2024. 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.

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 offer letter provides for a base salary of \$420,000 which was increased to \$475,000 effective March 1, 2024. Dr. Noonberg is eligible to receive an annual bonus with an annual target amount of 40% of her base salary. The target amount for 2023 was 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 her 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.

#### *2024 Stock Option and Incentive Plan*

The 2024 Plan replaced 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.

#### *2024 Employee Stock Purchase Plan*

The 2024 Employee Stock Purchase Plan (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.

#### *Senior Executive Cash Incentive Bonus Plan*

Our Senior Executive Cash Incentive 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.

#### *Executive Severance and Change in Control Policy*

Our board of directors adopted an Executive Severance and Change in Control Policy (the “Severance Policy”) in which our named executive officers, and certain other executives, participate. The benefits provided in the Severance Policy replaces any severance for which our executive officers may be eligible under their existing severance and change in control agreements; provided that, in the event an executive is party to an agreement or other arrangement that provides greater benefits than set forth in the Severance Policy, such executive will be entitled to receive the payments and benefits under such other agreement or arrangement and will not be eligible to receive any payments or benefits under the Severance Policy.

The Severance Policy provides that upon a termination due to death, “disability”, as defined in the Severance Policy, or “retirement” (as defined in the Severance Policy), an eligible executive will be entitled to receive, subject in the case of a termination due to retirement to the execution and delivery of an effective and irrevocable release of claims in favor of the Company and continued compliance with all applicable restrictive covenants, (i) a lump sum amount equal to the eligible executive’s annual target bonus in effect immediately prior to such termination, pro-rated for the number of days of service provided by the participant during the year of the termination, and (ii) for all outstanding and unvested equity awards of the company that are subject to time-based vesting held by the participant, full accelerated vesting of such awards; provided, that the performance conditions applicable to any outstanding and unvested equity awards subject to performance-based vesting will be deemed satisfied in accordance with the terms of the applicable award agreement.

The Severance Policy provides that upon a termination by us without “cause,” as defined in the Severance Policy, or a resignation by the executive for “good reason,” as defined in the Severance Policy, in each case outside of the change in control period (i.e., the period of one year after a “sale event,” as defined in the Severance Policy), an eligible executive will be entitled to receive, subject to the execution and delivery of an effective and irrevocable release of claims in favor of the company and continued compliance with all applicable restrictive covenants, (i) base salary continuation for 12 months for our Chief Executive Officer, 9 months for Tier 2 officers (which is determined by the plan administrator and includes the named executive officers other than the Chief Executive Officer) and 6 months for Tier 3 officers (which is determined by the Policy administrator but generally includes vice presidents and above) and (ii) an amount equal to the monthly employer contribution, based on the premiums as of the date of termination, that we would have made to provide health insurance for the applicable executive if he or she had remained employed by us for up to 12 months for our Chief Executive Officer, 9 months for Tier 2 officers and 6 months for Tier 3 officers. The payments under (i) and (ii) will be paid in substantially equal installments in accordance with our payroll practice over 12 months for our Chief Executive Officer, 9 months for Tier 2 officers and 6 months for Tier 3 officers. The Severance Policy will also provide that upon a (A)

termination by us without cause or (B) resignation for good reason, in each case within the change in control period, an eligible executive will be entitled to receive, in lieu of the payments and benefits above and subject to the execution and delivery of an effective and irrevocable release of claims in favor of the company and continued compliance with all applicable restrictive covenants, (I) a lump sum amount equal to the executive's base salary for a period of 18 months for our Chief Executive Officer, 12 months for our Tier 2 officers and 10 months for our Tier 3 officers, (II) a lump sum payment equal to 100% of the executive's annual target bonus in effect immediately prior to the date of termination, pro-rated for the number of days of service provided by the executive during the year of the termination, (III) a lump sum amount equal to the monthly employer contribution, based on the premiums as of the date of termination, that we would have made to provide health insurance for the applicable executive if he or she had remained employed by us for 18 months for our Chief Executive Officer, 12 months for our Tier 2 officers and 10 months for our Tier 3 officers, and (IV) for all outstanding and unvested equity awards of the company that are subject to time-based vesting held by the participant, full accelerated vesting of such awards; provided, that the performance conditions applicable to any outstanding and unvested equity awards subject to performance-based vesting will be deemed satisfied in accordance with the terms of the applicable award agreement.

The payments and benefits provided under the Severance Policy in connection with a change in control may not be eligible for a federal income tax deduction by us pursuant to Section 280G of the Code. These payments and benefits may also subject an eligible executive, including the named executive officers, to an excise tax under Section 4999 of the Code. If the payments or benefits payable in connection with a change in control would be subject to the excise tax imposed under Section 4999 of the Code, then those payments or benefits will be reduced if such reduction would result in a higher net after-tax benefit to the participant.

#### *Clawback Policy*

Our Board of Directors has adopted a policy that, in the event of a material restatement of our financial results, the Compensation Committee of our Board of Directors will review all incentive-based compensation that was paid to our executive officers on the basis of having met or exceeded specific performance targets for performance periods. If the bonuses paid pursuant to such incentive-based compensation would have been lower had the bonuses been calculated based on such restated results, the Company will seek to recoup the portion of the excess compensation that was received unless recovery would be impractical and either the third-party costs associated with recovery would exceed the amount to be recovered or recovery would cause a tax qualified plan to fail to remain tax qualified.

#### *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 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 were in effect immediately prior to the completion of the IPO also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Delaware law, our amended and restated bylaws provides 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 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 is provided for in our amended and restated certificate of incorporation and amended and restated bylaws, we entered 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 this Annual Report on Form 10-K.

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.

## DIRECTOR COMPENSATION

### 2023 Director Compensation Tables

The following table presents the total compensation paid by the Company to non-employee members of our board of directors 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 directors in 2023 for their services as members of the board of directors. Dr. Thomas, our Chief Executive Officer, did not receive any compensation from the Company for his service on our board of directors. See the section titled "Executive Compensation" for more information on the compensation paid to or earned by Dr. Thomas as an employee for the year ended December 31, 2023.

Name	Year	Fees Earned or Paid in Cash (\$)	All Other Compensation(4) (\$)	Total (\$)
Sebastián Bernales	2023	—	—	—
Willard H. Dere(1)(2)	2023	30,000	19,201	49,201
Juergen Eckhardt	2023	—	—	—
Santhosh Palani(3)	2023	—	—	—
Risa Stack(1)(5)	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) Dr. Palani has resigned from our board of directors effective as of January 17, 2024.
- (4) 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.
- (5) Dr. Stack resigned as a member of our board of directors, effective February 8, 2023.

### Non-Employee Director Compensation Policy

Our non-employee director compensation policy was 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	\$	40,000
Additional Annual Retainer for Non-Executive Chairperson of the Board	\$	40,000
Additional Annual Retainer for Committee Membership		
Audit Committee Chairperson	\$	15,000
Audit Committee Member (other than Chairperson)	\$	7,500
Compensation Committee Chairperson	\$	15,000
Compensation Committee Member (other than Chairperson)	\$	7,500
Nominating and Corporate Governance Committee Chairperson	\$	10,000
Nominating and Corporate Governance Committee Member (other than Chairperson)	\$	5,000

In addition, our policy provides 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 \$600,000 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 over three years, with 33% vesting on the first anniversary of the grant date and the remaining 67% vesting in 24 equal monthly vesting thereafter, subject to the non-employee director's continued services to the us. On the date of each annual meeting of stockholders of our company, 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 \$300,000 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 \$1,000,000 in the first calendar year such individual becomes a non-employee director and \$800,000 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.

#### **Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.**

The following table sets forth, as of March 15, 2024, 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 column entitled "Percentage of shares beneficially owned" is based on 37,472,351 shares of our common stock outstanding on March 15, 2024. 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 March 15, 2024 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. Except as otherwise indicated below, the address of each officer, director and five percent stockholder listed below is c/o Metagenomi, Inc., 5959 Horton Street, 7th Floor, Emeryville, California 94608.

	Shares of common stock beneficially owned	Percentage of shares beneficially owned
<b>5% or Greater Stockholders</b>		
Bayer HealthCare LLC(1)	4,050,997	10.81 %
Humboldt Fund I, LP(2)	1,896,445	5.06 %
Entities affiliated with Sozo Ventures(3)	1,892,873	5.05 %
<b>Directors, Named Executive Officers and Other Executive Officers</b>		
Brian C. Thomas, Ph.D.(4)	2,377,284	6.34 %
Juergen Eckhardt, M.D., MBA	—	—
Sebastián Bernales, Ph.D.(5)	3,068,786	8.19 %
Willard Dere, M.D.(6)	51,275	*
Jian Irish, Ph.D., MBA(7)	585,427	1.56 %
Sarah Noonberg, M.D., Ph.D.(8)	42,611	*
All executive officers and directors as a group (11 persons)(9)	6,323,456	16.87 %

\* Less than one percent.

- (1) Information is based solely on a Form 4 filed with the SEC on February 15, 2024 by Bayer HealthCare LLC, Bayer US Holding LP, Bayer World Investments B.V. and Bayer Aktiengesellschaft. Consists of 4,050,997 shares of common stock held by Bayer HealthCare LLC, a Delaware limited liability company. Bayer HealthCare LLC is controlled by Bayer US Holding LP (“Bush LP”), a Delaware limited partnership. Bayer World Investments B.V. (“BWI”), a Dutch private limited company, is the general partner of BUSH LP. BWI is an indirect, wholly owned subsidiary of Bayer Aktiengesellschaft, a publicly-held German stock corporation. Accordingly, Bayer Aktiengesellschaft may be deemed to be an indirect beneficial owner of the shares beneficially directly by Bayer HealthCare LLC. The address of Bayer HealthCare LLC is 100 Bayer Boulevard, Whippany, New Jersey 07981.
- (2) Consists of 1,896,445 shares of common 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.
- (3) Consists of (i) 581,577 shares of common stock held by Sozo Ventures -Truebridge Fund II, L.P. (“Fund II”), (ii) 710,817 shares of common stock held by Sozo Ventures II-S, L.P. (“Fund II-S”), and (iii) 600,479 shares of common stock held by Sozo Ventures III, L.P. (“Fund III”). With respect to Fund II: (i) Sozo Ventures GP II, L.P. (“GP II”) is the sole general partner of Fund II, (ii) Sozo Ventures UGP II, Ltd. (“UGP II”) is the sole general partner of GP II, (iii) UGP II exercises voting and dispositive power over the Company’s securities held by Fund II, (iv) each of Phil Wickham (“Wickham”) and Koichiro Nakamura (“Nakamura”) are the sole directors of UGP II, and (v) each of Wickham and Nakamura may be deemed to share voting and dispositive power over the Company’s securities held by Fund II. With respect to Fund II-S: (i) Sozo Ventures GP II-S, L.P. (“GP II-S”) is the sole general partner of Fund II-S, (ii) Sozo Ventures UGP II-S, Ltd. (“UGP II-S”) is the sole general partner of GP II-S, (iii) UGP II-S exercises voting and dispositive power over the Company’s securities held by Fund II-S, (iv) each of Wickham and Nakamura are the sole directors of UGP II-S, and (v) each of Wickham and Nakamura may be deemed to share voting and dispositive power over the Company’s securities held by Fund II-S. With respect to Fund III: (i) Sozo Ventures GP III, LLC (“GP III”) is the sole general partner of Fund III, (ii) each of Wickham and Nakamura are the sole managing members of GP III, and (iii) each of Wickham and Nakamura may be deemed to share voting and dispositive power over the Company’s securities held by Fund III. The address of Sozo Ventures is 10 California Street, Redwood City, California 94063.
- (4) Consists of (i) 1,431,100 shares of common stock held by Dr. Thomas and (ii) 946,184 shares of restricted common stock held by Dr. Thomas.
- (5) Consists of (i) 769,845 shares of common stock held by Mr. Bernales, (ii) 402,496 shares of common stock held by Praxis Biotech LLC, and (iii) 1,896,445 shares of common 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. Mr. Bernales may be deemed to have voting and dispositive power with respect to the shares held by Praxis Biotech LLC. Mr. Bernales expressly disclaims beneficial ownership of the shares held by Praxis Biotech LLC, except to the extent of his pecuniary interest in such shares. The address for Praxis Biotech LLC is 5904 Doone Valley Ct, Austin, TX 78731.
- (6) Consists of 51,275 shares of restricted common stock held by Dr. Dere.
- (7) Consists of (i) 228,462 shares of restricted common stock held by Dr. Irish, (ii) 178,483 shares of restricted common stock held by the Bruce Irish 2023 Irrevocable Trust FBO Jian Irish, or the Bruce Irish Trust, and (iii) 178,482 shares of restricted common stock held by the Jian Irish 2023 Irrevocable Trust, or the Jian Irish Trust. Jian Irish is a beneficiary of the Bruce Irish Trust and may be deemed to beneficially own the shares held by the Bruce Irish Trust and Jian Irish Trust. The address of the Bruce Irish Trust is 4465 S. Jones Blvd., Las Vegas, NV 89103 and the address of the Jian Irish Trust is 4465 S. Jones Blvd., Las Vegas, NV 89103.
- (8) Consists of 42,611 shares of restricted common stock held by Dr. Noonberg.
- (9) Consists of (i) 4,499,886 shares of common stock, and (ii) 1,823,570 shares of restricted common stock.

### Equity Compensation Plan Information

The following table sets forth additional information as of December 31, 2023 with respect to the shares of common stock that may be issued upon the exercise of options and other rights under our existing equity compensation plans and arrangements in effect as of December 31, 2023.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by security holders(1)	5,431,546	\$ 4.60	2,928,462
Equity compensation plans not approved by security holders	—	—	—
<b>Total</b>	<b>5,431,546</b>	<b>\$ 4.60</b>	<b>2,928,462</b>

- (1) As of December 31, 2023, we did not maintain any equity compensation plans approved by security holders. In connection with the IPO, our board of directors and our stockholders approved the Metagenomi, Inc. 2024 Stock Option and Incentive Plan and the Metagenomi, Inc. 2024 Employee Stock Purchase Plan. Each plan became effective on January 26, 2024. The table above does not include any amounts issuable under either the 2024 Stock Option and Incentive Plan or 2024 Employee Stock Purchase Plan because they were not in effect as of December 31, 2023.
- (2) Our 2019 Equity Incentive Plan, or the 2019 Plan was the only equity compensation plan we had in place as of December 31, 2023.

### Item 13. Certain Relationships and Related Transactions, and Director Independence.

The following is a description of transactions or series of transactions since January 1, 2022, 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 Annual Report on Form 10-K under “Executive Compensation” and “Director Compensation.”

#### 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 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	Units of Series B/ Series B-1 preferred units	Total purchase price
ModernaTX, Inc.(1)	2,982,800	\$ 35,655,978
Bayer HealthCare LLC(2)	1,920,757	\$ 24,529,690
Humboldt Fund I, LP(3)	1,250,532	\$ 14,825,929
Entities affiliated with Sozo Ventures(4)	816,063	\$ 10,442,237

- (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 director on our board of directors, 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 director on our board of directors, 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 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 were terminated upon the closing of our IPO, 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.

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.

#### ***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***

We have entered into agreements to indemnify our directors and executive officers. These agreements, 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. We have adopted a written related party transactions policy that provides that such transactions must be approved by our audit committee. 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 is 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.

#### ***Director Independence***

Under the rules and listing standards of The Nasdaq Stock Market LLC, or the Nasdaq Rules, a majority of the members of our board of directors must satisfy the Nasdaq criteria for "independence." No director qualifies as independent under the Nasdaq Rules unless our board of directors affirmatively determines that the director does not have a relationship with us that would impair independence (directly or as a partner, stockholder or officer of an organization that has a relationship with us). Our board of directors has determined that all members of our board of directors, except Brian C. Thomas and Jian Irish, are independent directors, including for purposes of Nasdaq and the SEC rules. Dr. Thomas and Dr. Irish are not independent under the Nasdaq Rules as a result of their positions as our Chief Executive Officer and Chief Operating Officer, respectively. In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our shares by each non-employee director and the transactions described in this Part III, Item 13 above.

#### **Item 14. Principal Accounting Fees and Services.**

Our independent public accounting firm is PricewaterhouseCoopers LLP, San Jose, California, PCAOB Auditor Firm ID ID 238.

The following table summarizes the aggregate fees for professional services provided by PricewaterhouseCoopers LLP, our independent registered public accounting firm, in the fiscal years ended December 31, 2023 and 2022:

	Fiscal Year Ended	
	2023	2022
Audit Fees(1)	\$ 1,994	\$ 337
Audit-Related Fees	—	—
Tax Fees	—	—
All Other Fees(2)	4	1
<b>Total Fees</b>	<b>\$ 1,998</b>	<b>\$ 338</b>

(1) Audit fees consist of fees billed for professional services performed by PricewaterhouseCoopers LLP for the audit of our annual consolidated financial statements, the review of interim consolidated financial statements, and review of the registration statement on Form S-1 for our IPO, and related services that are normally provided in connection with statutory and regulatory filings or engagements.

(2) All other fees consist of non-audit fees paid to PricewaterhouseCoopers LLP for access to its proprietary accounting disclosure checklist.

The Audit Committee has adopted a policy for the pre-approval of audit and non-audit services rendered by our independent registered public accounting firm, PricewaterhouseCoopers LLP. The policy generally pre-approves specified services in the defined categories of audit services, audit-related services and tax services up to specified amounts. Pre-approval may also be given as part of the Audit Committee's approval of the scope of the engagement of the independent registered public accounting firm or on an individual case-by-case basis before the independent registered public accounting firm is engaged to provide each service. The pre-approval of services may be delegated to one or more of the Audit Committee's members, but the decision must be reported to the full Audit Committee at its next scheduled meeting. By the adoption of this policy, the Audit Committee has delegated the authority to pre-approve services to the Chairperson of the Audit Committee, subject to certain limitations.

**PART IV**

**Item 15. Exhibits, Financial Statement Schedules.**

- (a) *Financial Statements.* The financial statements of Metagenomi Technologies, LLC and the report of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm, are included in a separate section of this Annual Report on Form 10-K beginning on page F-1. All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.
- (b) *Exhibits.* The following is a list of exhibits filed as part of this Annual Report on Form 10-K:

Exhibit Number	Description	Registrant's Form	Date Filed with the SEC	Exhibit Number
2.1+**	<a href="#"><u>Agreement and Plan of Merger by and between Metagenomi Technologies, LLC and Metagenomi, Inc., dated January 24, 2024</u></a>	S-1	02/07/2024	2.1
3.1**	<a href="#"><u>Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect</u></a>	8-K	02/13/2024	3.1
3.3**	<a href="#"><u>Amended and Restated Bylaws, as currently in effect</u></a>	8-K	02/13/2024	3.2
4.1+**	<a href="#"><u>Registration Rights Agreement among the Registrant and certain of its stockholders, dated January 24, 2024</u></a>	S-1	02/07/2024	4.1
4.2**	<a href="#"><u>Form of Common Stock Certificate</u></a>	S-1	02/07/2024	4.2
4.3*	<a href="#"><u>Description of Securities of Registrant</u></a>			*
10.1#**	<a href="#"><u>2024 Stock Option and Incentive Plan and forms of award agreements thereunder</u></a>	S-1	02/07/2024	10.2
10.2#**	<a href="#"><u>2024 Employee Stock Purchase Plan</u></a>	S-1	02/07/2024	10.3
10.3#**	<a href="#"><u>Form of Officer Indemnification Agreement</u></a>	S-1	02/07/2024	10.4
10.4#**	<a href="#"><u>Form of Director Indemnification Agreement</u></a>	S-1	02/07/2024	10.5
10.5†**	<a href="#"><u>Strategic Collaboration and License Agreement by and between the Registrant and ModernaTX, Inc., dated October 29, 2021</u></a>	S-1	02/07/2024	10.6
10.6†**	<a href="#"><u>Collaboration and License Agreement by and between the Registrant and Ionis Pharmaceuticals, Inc., dated November 10, 2022</u></a>	S-1	02/07/2024	10.7
10.7†+**	<a href="#"><u>Development, Option and License Agreement by and between the Registrant and Affini-T Therapeutics, Inc., dated June 14, 2022</u></a>	S-1	02/07/2024	10.8
10.8**	<a href="#"><u>Lease Agreement between EPL Halleck Investors LLC and Metagenomi, Inc., dated January 22, 2021</u></a>	S-1	02/07/2024	10.9
10.9*	<a href="#"><u>Sublease Agreement between Dynavax Technologies Corporation and Metagenomi, Inc., dated March 7, 2024</u></a>			*
10.10**	<a href="#"><u>Lease Agreement between Park Avenue Building LLC and Metagenomi, Inc., dated September 29, 2021</u></a>	S-1	02/07/2024	10.11
10.11#**	<a href="#"><u>Employment Agreement between the Registrant and Brian C. Thomas, dated as of March 20, 2023</u></a>	S-1	02/07/2024	10.12
10.12#**	<a href="#"><u>Offer of Employment between the Registrant and Jian Irish, dated as of January 19, 2021</u></a>	S-1	02/07/2024	10.13
10.13#**	<a href="#"><u>Offer of Employment between the Registrant and Sarah Noonberg, dated as of January 30, 2023</u></a>	S-1	02/07/2024	10.14

Exhibit Number	Description	Registrant's Form	Date Filed with the SEC	Exhibit Number
10.14##**	<a href="#">Form of Confidentiality and Invention Assignment Agreement</a>	S-1	02/07/2024	10.15
10.15##**	<a href="#">Manager Offer Letter between the Registrant and Willard Dere, dated as of August 19, 2021</a>	S-1	02/07/2024	10.16
21.1**	<a href="#">Subsidiaries of the Registrant</a>	S-1	02/07/2024	21.1
23.1*	<a href="#">Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm</a>			*
24.1*	<a href="#">Power of Attorney (included on signature page)</a>			
31.1	<a href="#">Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</a>			*
31.2	<a href="#">Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</a>			*
32.1	<a href="#">Certifications of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002</a>			*
97.1	<a href="#">Metagenomi, Inc. Compensation Recovery Policy</a>			*

\* Filed herewith

\*\* 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.

+ Annexes, schedules and/or exhibits have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The registrant agrees to furnish supplementally a copy of any omitted attachment to the SEC on a confidential basis upon request.

#### Item 16. Form 10-K Summary

None.

## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

### **Metagenomi, Inc.**

Date: March 27, 2024

By: \_\_\_\_\_ /s/ Brian C. Thomas  
**Brian C. Thomas, Ph.D.**  
**Chief Executive Officer**

## POWER OF ATTORNEY AND SIGNATURES

KNOW ALL BY THESE PRESENT, that each individual whose signature appears below hereby constitutes and appoints each of Brian C. Thomas and Pamela Wapnick, as such person's true and lawful attorney-in-fact and agent with full power of substitution and resubstitution, for such person in such person's name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and all documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that any said attorney-in-fact and agent, or any substitute or substitutes of any of them, may lawfully do or cause to be done by virtue hereof

Pursuant to the requirements of the Securities Act, this Annual Report on Form 10-K has been signed by the following person in the capacities and on the date indicated.

<u>NAME</u>	<u>TITLE</u>	<u>DATE</u>
<u>/s/ Brian C. Thomas</u> Brian C. Thomas, Ph.D.	Chief Executive Officer and Director (Principal Executive Officer)	Date: March 27, 2024
<u>/s/ Pamela Wapnick</u> Pamela Wapnick, MBA	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	Date: March 27, 2024
<u>/s/ Jian Irish</u> Jian Irish, Ph.D., MBA	President, Chief Operating Officer and Director	Date: March 27, 2024
<u>/s/ Juergen Eckhardt</u> Juergen Eckhardt, M.D., MBA	Director	Date: March 27, 2024
<u>/s/ Sebastián Bernales</u> Sebastián Bernales, Ph.D.	Director	Date: March 27, 2024
<u>/s/ Willard Dere</u> Willard Dere, M.D.	Director	Date: March 27, 2024



## INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

<a href="#">Report of Independent Registered Public Accounting Firm (PCAOB ID 238)</a>	F-2
<a href="#">Consolidated Balance Sheets as of December 31, 2023 and 2022</a>	F-3
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## **Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Stockholders of Metagenomi, Inc.

### ***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, 2023 and 2022, 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, 2023 and 2022, 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 audits 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  
March 27, 2024

We have served as the Company’s auditor since 2022.

**Metagenomi Technologies, LLC**  
**Consolidated Balance Sheets**  
(in thousands, except units)

	December 31,	
	2023	2022
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 140,603	\$ 184,441
Available-for-sale marketable securities	130,579	177,690
Accounts receivable	2,451	—
Contract assets	—	1,274
Prepaid expenses and other current assets	4,640	3,494
Total current assets	278,273	366,899
Property and equipment, net	21,542	16,522
Long-term investments	10,676	7,806
Operating lease right-of-use assets	43,611	16,736
Other assets	5,492	450
Restricted cash	5,248	6,073
Total assets	\$ 364,842	\$ 414,486
<b>Liabilities, redeemable convertible preferred units and members' deficit</b>		
Current liabilities:		
Accounts payable	\$ 1,791	\$ 2,011
Income tax payable	3,266	1,536
Accrued expenses and other current liabilities	11,472	8,790
Current portion of operating lease liabilities	3,427	1,515
Collaboration advance	837	743
Deferred revenue	48,068	33,942
Total current liabilities	68,861	48,537
Non-current portion of operating lease liabilities	44,802	17,056
Deferred revenue, non-current	30,926	76,185
Other non-current liabilities	5,079	1,033
Total liabilities	149,668	142,811
Commitments and contingencies (Note 8)		
Redeemable convertible preferred units: 41,813,375 units authorized as of December 31, 2023 and 2022; 41,813,375 and 41,478,621 units issued and outstanding as of December 31, 2023 and 2022, respectively. Liquidation preference \$352,044 and \$347,335 as of December 31, 2023 and 2022, respectively.	350,758	346,103
Members' deficit:		
Common units: 66,000,000 units authorized as of December 31, 2023 and 2022; 5,947,500 units issued and outstanding as of December 31, 2023 and 2022	26	26
Profit interests: 14,604,165 units authorized as of December 31, 2023 and 2022; 9,488,776 and 7,516,073 units issued and outstanding as of December 31, 2023 and 2022, respectively	9,431	2,509
Accumulated other comprehensive loss	(97)	(274)
Accumulated deficit	(144,944)	(76,689)
Total members' deficit	(135,584)	(74,428)
Total liabilities, redeemable convertible preferred units and members' deficit	\$ 364,842	\$ 414,486

*The accompanying notes are an integral part of these consolidated financial statements*

**Metagenomi Technologies, LLC**  
**Consolidated Statements of Operations and Comprehensive Loss**  
(in thousands, except units and per unit data)

	Years ended December 31,	
	2023	2022
Collaboration revenue	\$ 44,756	\$ 17,200
Operating expenses:		
Research and development	94,403	43,139
General and administrative	28,845	18,701
Total operating expenses	123,248	61,840
Loss from operations	(78,492)	(44,640)
Other income (expense):		
Interest expense	—	(98)
Interest income	15,468	3,419
Change in fair value of long-term investments	2,870	94
Other income (expense), net	(74)	201
Total other income, net	18,264	3,616
Net loss before provision for income taxes	(60,228)	(41,024)
Provision for income taxes	(8,027)	(2,569)
Net loss	\$ (68,255)	\$ (43,593)
Other comprehensive income (loss):		
Unrealized gain (loss) on available-for-sale marketable securities, net	177	(253)
Comprehensive loss	\$ (68,078)	\$ (43,846)
Net loss per share attributable to common stockholders, basic and diluted (Note 14)	\$ (20.05)	\$ (12.82)
Weighted average common shares outstanding, basic and diluted (Note 14)	3,404,585	3,399,518

*The accompanying notes are an integral part of these consolidated financial statements.*

**Metagenomi Technologies, LLC**  
**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	Units	Amount	Units	Amount			
<b>BALANCE—January 1, 2022</b>	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)
<b>BALANCE—December 31, 2022</b>	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	—	—	—	—	(295,110)	—	—	—	—
Unit-based compensation expense	—	—	—	—	—	6,922	—	—	6,922
Other comprehensive gain	—	—	—	—	—	—	177	—	177
Net loss	—	—	—	—	—	—	—	(68,255)	(68,255)
<b>BALANCE—December 31, 2023</b>	41,813,375	350,758	5,947,500	26	9,488,776	9,431	(97)	(144,944)	(135,584)

*The accompanying notes are an integral part of these consolidated financial statements.*

**Metagenomi Technologies, LLC**  
**Consolidated Statements of Cash Flows**  
(in thousands)

	Years ended December 31,	
	2023	2022
<b>Cash flows from operating activities</b>		
Net loss	\$ (68,255)	\$ (43,593)
Adjustments to reconcile net loss to net cash used in operating activities		
Unit-based compensation expense	6,922	1,962
Depreciation	4,207	1,733
Loss on fixed assets write-off	23	282
Non-cash lease expense	4,207	1,292
Amortization of premiums and discounts on available-for-sale marketable securities	(8,472)	(1,129)
Amortization of non-cash collaboration revenue	(742)	(314)
Non-cash interest expense	—	98
Change in fair value of long-term investments	(2,870)	(94)
Changes in operating assets and liabilities:		
Accounts receivable	(2,451)	—
Contract assets	1,274	(1,274)
Prepaid expenses and other assets	(1,090)	(2,638)
Accounts payable	(84)	721
Income tax payable	1,730	1,536
Deferred revenue and collaboration advance	(30,297)	65,661
Accrued expenses and other current liabilities	1,629	4,529
Operating lease liabilities	(1,186)	(81)
Other non-current liabilities	4,046	1,033
Net cash provided by (used in) operating activities	(91,409)	29,724
<b>Cash flows from investing activities</b>		
Purchases of property and equipment	(9,814)	(13,977)
Purchases of available-for-sale marketable securities	(208,096)	(214,850)
Maturities and sales of available-for-sale marketable securities	263,644	106,627
Net cash provided by (used in) investing activities	45,734	(122,200)
<b>Cash flows from financing activities</b>		
Payments of initial public offering costs	(3,283)	—
Proceeds from issuance of redeemable convertible preferred units, net of issuance costs	4,295	239,594
Net cash provided by financing activities	1,012	239,594
Net (decrease) increase in cash, cash equivalents and restricted cash	(44,663)	147,118
Cash, cash equivalents and restricted cash at beginning of period	190,514	43,396
Cash, cash equivalents and restricted cash at end of period	\$ 145,851	\$ 190,514
<b>Reconciliation of cash, cash equivalents and restricted cash</b>		
Cash and cash equivalents	\$ 140,603	\$ 184,441
Restricted cash	5,248	6,073
Cash, cash equivalents and restricted cash at end of period	\$ 145,851	\$ 190,514

*The accompanying notes are an integral part of these consolidated financial statements*

**Consolidated Statements of Cash Flows (continued)**  
(in thousands)

	Years ended December 31,	
	2023	2022
<b>Supplemental disclosure of non-cash information</b>		
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	\$ 638	\$ 1,247
Operating lease right-of-use assets obtained in exchange for new lease liabilities	\$ 30,836	\$ —
Remeasurement of operating right-of use asset and lease liability	\$ 8	\$ —
Deferred initial public offering costs included in accounts payable and accrued expenses and other current liabilities	\$ 1,841	\$ —
Unpaid finance issuance costs included in accounts payable and accrued	\$ —	\$ 360
Cash paid for income taxes	\$ 2,250	\$ —

*The accompanying notes are an integral part of these consolidated financial statements.*

**Metagenomi Technologies, LLC**  
**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 precision genetic medicines company committed to developing curative therapeutics for patients using our proprietary, comprehensive metagenomics-derived genome editing toolbox.

***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 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, 2023, 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.

On January 24, 2024, the Company completed a series of transactions pursuant to which Metagenomi merged with and into its wholly-owned subsidiary, Metagenomi, Inc., with Metagenomi, Inc. continuing as the surviving corporation (the “Reorganization”). In connection with the Reorganization, (i) all of the outstanding common unitholders received shares of common stock of Metagenomi, Inc., (ii) all of the outstanding preferred unitholders received shares of redeemable convertible preferred stock of Metagenomi, Inc. with the same rights and privileges and (iii) certain holders of profits interest units received shares of common stock and unvested restricted common stock in Metagenomi, Inc. as determined by the applicable provisions of the Amended and Restated Limited Liability Company Agreement dated December 20, 2022, as amended on July 31, 2023 (the “LLC Agreement”) in effect immediately prior to the Reorganization. In connection with the Reorganization, by operation of law, Metagenomi, Inc. acquired all assets of Metagenomi, and assumed all of its liabilities and obligations. The Reorganization is expected to be a non-taxable transaction to Metagenomi, Inc. for U.S. income tax purposes.

***Reverse Stock Split of Metagenomi, Inc.***

On January 26, 2024, following the Reorganization, Metagenomi, Inc. effected a reverse stock split of the shares of common stock at a ratio of 1-for-1.74692 (the “Reverse Stock Split”). The number of authorized shares and par value per share were not adjusted as a result of the Reverse Stock Split.

***Initial Public Offering***

On February 8, 2024, Metagenomi, Inc.’s Form S-1 Registration Statement for its initial public offering (the “IPO”) was declared effective and the common stock of Metagenomi, Inc. began trading on the Nasdaq Global Select Market under the symbol “MGX.” On February 13, 2024, the closing date of IPO, the Company issued 6,250,000 shares of common stock at a price to the public of \$15.00 per share. In connection with the closing of the IPO, the Company received gross proceeds of approximately \$93.8 million and net proceeds of approximately \$81.1 million, after deducting underwriting discounts and commissions and other offering costs totaling approximately \$12.7 million.

Immediately prior to the IPO closing, each share of Metagenomi, Inc.’s redeemable convertible preferred stock then outstanding converted into a number of shares of common stock based on the formula set forth in Metagenomi Inc.’s amended and restated certificate of incorporation in effect immediately prior to the closing of the IPO and giving effect to the reverse stock split.



### ***Liquidity and going concern***

The Company has incurred significant losses from operations since its inception. During the years ended December 31, 2023 and 2022, the Company incurred net losses of \$68.3 million and \$43.6 million, respectively. As of December 31, 2023, the Company had an accumulated deficit of \$144.9 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 TX, Inc. (“Moderna”), Affini-T Therapeutics, Inc. (“Affini-T”) and Ionis Pharmaceuticals, Inc. (“Ionis”) (see Note 7). After the Reorganization, Metagenomi was liquidated and Metagenomi Inc., surviving entity, closed the IPO for approximately \$81.1 million net proceeds. Metagenomi, Inc. 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. Metagenomi, Inc. 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 the Company of \$271.2 million as of December 31, 2023, together with the Metagenomi, Inc. IPO proceeds 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”) and pursuant to the rules and regulations of the Securities and Exchanges Commission (“SEC”) regarding financial reporting. The accompanying consolidated financial statements include the accounts of Metagenomi LLC 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, 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.

### ***Segment and geographical information***

The Company operates and manages its business as one reportable and operating segment, which is the business of developing curative therapeutics for patients using the Company’s proprietary, comprehensive metagenomics-derived genome editing toolbox. 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 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 2023 was marked by significant market uncertainty, increasing inflationary pressures. These market dynamics may continue into 2024 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, 2023 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, asset-backed securities and foreign debt 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 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, 2023 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 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 (expense) in the consolidated statements of operations and comprehensive loss.

### **Restricted cash**

Restricted cash of \$5.2 million and \$6.1 million as of December 31, 2023 and 2022, respectively, represents security deposits in the form of a letter of credit issued in connection with the Company's leases (see Note 8).

### **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 concentrations of credit risk. As of December 31, 2023 and 2022, cash consists of cash deposited with three financial institutions, and account balances exceed federally insured limits.

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	
	Years ended December 31,	
	2023	2022
Customer A	49%	*
Customer B	40%	84%
Customer C	11%	15%
	100%	99%

	Accounts receivable	
	Years ended December 31,	
	2023	2022
Customer C	80%	*
Customer B	20%	*
	100%	*

	Contract assets	
	Years ended December 31,	
	2023	2022
Customer C	*	100%
	*	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, 2023 and 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 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 consolidated statements of operations and comprehensive loss. The Company had \$5.1 million and no deferred finance issuance costs capitalized as of December 31, 2023 and 2022, respectively, included in other assets in the consolidated balance sheets.

### ***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, 2023 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, 2023 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; (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, 2023, the Company had no contract assets. 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. 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 share***

The Company calculates basic and diluted net loss per share in conformity with the two-class method required for participating securities. Under the two-class method, basic net loss per share is computed by dividing the net loss by the weighted average number of common shares outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the sum of the weighted average number of common shares outstanding during the period plus the dilutive effects of potentially dilutive securities outstanding during the period. Potentially dilutive securities include unvested common units, profits interests and redeemable convertible preferred units. The dilutive effect of unvested common units and profits interests 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 share is the same as basic net loss per share since the effect of including potential dilutive securities is anti-dilutive and profits interests' participation thresholds were not met. In connection with the Reorganization and in accordance with ASC 260, Earnings Per Share, the conversion of common units has been retrospectively reflected in the Company's net loss per share calculation, see Note 14.

### ***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***

In November 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures. This ASU requires public entities to disclose information about their reportable segments' significant expenses and other segment items on an interim and annual basis. Public entities with a single reportable segment are required to apply the disclosure requirements in ASU 2023-07, as well as all existing segment disclosures and reconciliation requirements in ASC 280 on an interim and annual basis. ASU 2023-07 is effective for fiscal years beginning after December 15, 2023, and for interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the impact of the adoption of this standard on its financial statements.

In December 2023, the FASB issued ASU 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures. This ASU requires public entities, on an annual basis, to provide disclosure of specific categories in the rate reconciliation, as well as disclosure of income taxes paid disaggregated by jurisdiction. ASU 2023-09 is effective for fiscal years beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the impact the adoption of this standard on its financial statements.

## **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 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 preferred stock and common stock shares of Affini-T Therapeutics Inc. ("Affini-T") (see Note 5) are Level 3 financial assets.

The following tables summarize 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 (in thousands):

	<b>December 31, 2023</b>			
	<b>Total</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
<b>Assets:</b>				
Money market funds (included in cash and cash equivalents)	\$ 137,216	\$ 137,216	\$ —	\$ —
U.S. Treasury bills	9,831	—	9,831	—
U.S. Government bonds	2,989	—	2,989	—
Government agency obligations	46,408	—	46,408	—
Corporate debt obligations	10,973	—	10,973	—
Commercial paper	54,727	—	54,727	—
Asset-backed securities	2,171	—	2,171	—
Foreign debt securities	3,479	—	3,479	—
Long-term investments (Note 5)	8,521	—	—	8,521
<b>Total fair value of assets</b>	<b>\$ 276,315</b>	<b>\$ 137,216</b>	<b>\$ 130,578</b>	<b>\$ 8,521</b>

	<b>December 31, 2022</b>			
	<b>Total</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
<b>Assets:</b>				
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
<b>Total fair value of assets</b>	<b>\$ 365,782</b>	<b>\$ 182,441</b>	<b>\$ 177,690</b>	<b>\$ 5,651</b>

(1) Certain prior period amounts have been reclassified to conform to the current period presentation

In addition, restricted cash of \$5.2 million and \$6.1 million as of December 31, 2023 and 2022, 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. As of December 31, 2022, the fair value was estimated based on information available to management including recent financing transactions, capitalization and rights and preferences of outstanding securities. As of December 31, 2023, the Company applied an option-pricing model backsolve method for inferring the total equity value implied by a recent Series A preferred stock financing round of Affini-T. Key assumptions used in the valuation model included an expected holding period of two years, a risk free interest rate of 4.87%, a dividend yield of 0.0% and an estimated volatility of 83.00%. The estimated volatility was calculated based on the historical volatility of a selected peer group of public companies comparable to Affini-T. The estimated fair value of the Company's investment in Affini-T was \$8.5 million and \$5.7 million as of December 31, 2023 and 2022, 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):

	Years ended December 31,	
	2023	2022
Beginning balance	\$ 5,651	\$ 4,262
Change in fair value included in other income (expense)	2,870	94
Fair value of investment received as collaboration consideration (Note 7)	—	1,295
Ending balance	\$ 8,521	\$ 5,651

There were no transfers within the fair value hierarchy during the years ended December 31, 2023 and 2022.

#### 4. AVAILABLE-FOR-SALE MARKETABLE SECURITIES

The following tables summarize the amortized cost, unrealized gains (losses) and estimated fair value of the available-for-sale marketable securities (in thousands):

	December 31, 2023			
	Amortized cost	Unrealized gains	Unrealized losses	Fair value
Money market funds	\$ 137,216	\$ —	\$ —	\$ 137,216
U.S. Treasury bills	9,826	5	—	9,831
U.S. Government bonds	3,005	—	(16)	2,989
Government agency obligations	46,445	4	(41)	46,408
Corporate debt obligations	11,014	—	(41)	10,973
Commercial paper	54,724	4	(1)	54,727
Asset-backed securities	2,177	—	(6)	2,171
Foreign debt securities	3,484	—	(5)	3,479
Total	267,891	13	(110)	267,794
Less: amounts classified as cash equivalents	(137,216)	—	—	(137,216)
Total available-for-sale marketable securities	\$ 130,675	\$ 13	\$ (110)	\$ 130,578

	December 31, 2022			
	Amortized cost	Unrealized gains	Unrealized losses	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, 2023 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, 2023 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, 2023 and 2022, accrued interest receivable was \$1.0 million and \$0.3 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 years ended December 31, 2023 and 2022.

The amortized cost and fair value of available-for-sale marketable securities by contractual maturity were as follows as of December 31, 2023 (in thousands):

	Amortized Cost	Estimated Fair Value
Maturing within one year	\$ 129,822	\$ 129,727
Maturing in one to five years	853	851
Total available-for-sale marketable securities	\$ 130,675	\$ 130,578

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

## 5. LONG-TERM INVESTMENTS

### *Affini-T investment*

As of December 31, 2023 and 2022, 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, 2023 and 2022. The Company is using the fair value method to account for its investments in Affini-T with changes in fair value recorded to other income (expense) in the consolidated statements of operations and other comprehensive loss.

As of December 31, 2021, the Company owned 213,730 shares of Affini-T common stock and a convertible promissory note with the principle amount of \$1.5 million and 6% annual interest rate. In March 2022, Affini-T closed a qualifying round of financing, and the Company's investment in the Affini-T convertible promissory note and accrued interest were converted into 527,035 Series A convertible preferred stock shares of Affini-T.

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.

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 estimated fair value of its investments in Affini-T as \$8.5 million and \$5.7 million as of December 31, 2023 and 2022, respectively (see Note 3). The Company recognized changes in fair value of \$2.9 million and of \$0.1 million for the years ended December 31, 2023 and 2022, respectively.

No impairment loss was recognized on the Company's investment in Affini-T as of December 31, 2023 or 2022.

### ***ViTToria investment***

As of December 31, 2023 and 2022, the Company had investment in shares of preferred stock of ViTToria Biotherapeutics, Inc. (“Vittoria”), a private biotechnology company. During the years ended December 31, 2023 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 accounts for its investment in Vittoria using the measurement alternative method. As of December 31, 2023 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,	
		2023	2022
Laboratory equipment	5	\$ 20,777	\$ 13,455
Leasehold improvements	lesser of useful life or the lease term	3,831	3,531
Computers and related equipment	3-5	648	54
Furniture and fixtures	3-5	374	328
Construction in progress		2,346	1,402
Total property and equipment		27,976	18,770
Less: Accumulated depreciation		(6,434)	(2,248)
Total property and equipment, net		\$ 21,542	\$ 16,522

Depreciation expense was \$4.2 million and \$1.7 million for the years ended December 31, 2023 and 2022, respectively.

Other assets consist of the following (in thousands):

	December 31,	
	2023	2022
Deferred finance issuance costs	\$ 5,124	\$ —
Operating lease deposit	238	237
Long-term prepaid services	130	213
Total other assets	\$ 5,492	\$ 450

Accrued expenses and other current liabilities consist of the following (in thousands):

	December 31,	
	2023	2022
Accrued personnel related expenses	\$ 7,263	\$ 4,819
Accrued legal and professional services	2,627	1,200
Accrued research and development expenses	856	1,684
Accrued purchases of property and equipment	445	896
Other accrued liabilities	281	191
Total accrued expenses and other current liabilities	\$ 11,472	\$ 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 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 use of RNA-mediated integration systems (“RIGS”) with messenger RNA (“mRNA”) and base editing correction with mRNA is within the RT Field exclusive to Moderna within the Term. 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 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 December 31, 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 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 \$18.1 million and \$14.5 million in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, the Company recorded \$0.5 million in accounts receivable on the consolidated balance sheet, related to services performed. As of December 31, 2023 and 2022, deferred revenue related to the Moderna Agreement was \$18.7 million and \$30.2 million, respectively. Collaboration revenue recognized during the years ended December 31, 2023 and 2022 included \$18.1 million and \$14.5 million that was included in deferred revenue as of December 31, 2022 and 2021, respectively. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligations was approximately \$23.7 million as of December 31, 2023, which the Company expects to recognize as revenue over the next two-to-three years.

The Company recognized \$0.3 million and \$0.4 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, 2023. 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 during the year ended December 31, 2022, respectively. As of December 31, 2023, the collaboration advance balance was \$0.7 million and the cost-sharing payable balance was \$0.1 million, which were 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, 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 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 valuation. Affini-T has also agreed to reimburse the Company for expenses incurred while performing research activities under the research plans. As of December 31, 2023, the Company received a total of \$4.3 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, 2023 and 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 collaboration revenue of \$4.7 million and \$2.6 million in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2023 and 2022, 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. As of December 31, 2023, the Company recorded \$2.0 million in accounts receivable on the consolidated balance sheet, related to services performed. There was no contract asset related to services performed as of December 31, 2023. 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. As of December 31, 2023 and 2022, deferred revenue related to the Affini-T Agreement was \$0.2 million and zero, respectively. The value of the transaction price allocated to the remaining unsatisfied portion of the performance obligation was approximately \$1.7 million as of December 31, 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 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 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, its third target ("Target 3") in Wave 1 in November 2023, and its fourth target ("Target 4") in Wave 1 in February 2024. 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 December 31, 2023, the Company received a total of \$2.0 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 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 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, canceled, 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, 2023 and 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, 2023 and 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 collaboration revenue of \$21.9 million and \$0.1 million in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023 and 2022, deferred revenue related to the Ionis Agreement was \$60.0 million and \$79.9 million, respectively. Collaboration revenue recognized during the year ended December 31, 2023 included \$21.9 million that was included in deferred revenue as of December 31, 2022. The value of the transaction price allocated to the remaining performance obligations was approximately \$68.0 million as of December 31, 2023, which the Company expects to recognize as revenue over the next four-to-five years.

## 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 consolidated balance sheets. As of December 31, 2023 and 2022, the balance of this letter of credit was \$2.5 million and \$3.3 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 consolidated balance sheets as of December 31, 2023 and 2022. In addition to base rent, the Company will pay 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 consolidated balance sheet as of December 31, 2023 and 2022. 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 years ended December 31, 2023 and 2022 totaled \$9.6 million and \$3.5 million, respectively, including \$2.8 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,	
	2023	2022
Cash paid for amounts included in the measurement of lease liabilities	\$ 6,561	\$ 2,158
Weighted average remaining lease term (in years)	7.1	8.1
Weighted-average discount rate	11.3 %	10.1 %

The following table summarizes future minimum lease payments as of December 31, 2023 (in thousands):

2024	\$	8,641
2025		9,379
2026		9,673
2027		9,995
2028		10,328
Thereafter		22,955
Total future lease payments		70,971
Less imputed interest		(22,742)
Total lease liability balance		48,229
Less: current operating lease liabilities		(3,427)
Non-current operating lease liabilities	\$	44,802

### 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, 2023 and 2022, 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 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 LLC Agreement. As of December 31, 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, 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>

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 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, 2023 and 2022 the Company's Board of Managers consisted of 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, 2023 and 2022, 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 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 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, 2023 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.

## **10. COMMON UNITS**

As of December 31, 2023 and 2022, 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, 2023 and 2022, the Company reserved common units for future issuance as follows:

	December 31,	
	2023	2022
Outstanding redeemable convertible preferred units	41,813,375	41,478,621
Outstanding profits interests	9,488,776	7,516,073
Units available for grants under 2019 Equity Incentive Plan	5,115,389	7,088,092
Total common units reserved for future issuance	56,417,540	56,082,786

## 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 canceled 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.

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 December 31, 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 year ended December 31, 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	\$ 7.62	
Forfeited and expired	295,110	(295,110)	\$ 3.76	
Outstanding as of December 31, 2023	5,115,389	9,488,776	\$ 2.63	\$ 111,022
Vested and expected to vest	5,115,389	9,488,776	\$ 2.63	\$ 111,022

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, 2023.

During the years ended December 31, 2023 and 2022, the Company granted 2,267,813 and 2,763,356 profits interests with a weighted average grant date fair value of \$6.73 and \$1.9, respectively. The total fair value of the profits interests vested during the years ended December 31, 2023 and 2022 was \$2.8 million and \$1.1 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.

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 years ended December 31, 2023 and 2022:

	From July 31 to December 31, 2023	From January 1 to July 30, 2023	The year ended December 31, 2022
Expected volatility	85.00%	78.57% — 86.33%	79.57% — 82.60%
Expected dividend yield	0%	0%	0%
Expected term (in years)	1.75	2.00 — 4.12	3.51 — 4.00
Risk-free interest rate	5.00%	3.50% — 4.47%	2.65% — 4.33%
Threshold range	\$ 11.84	\$5.75 — \$7.40	\$ 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.

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.

The following table presents the classification of unit-based compensation expense for the years ended December 31, 2023 and 2022 (in thousands):

	Years ended December 31,	
	2023	2022
Research and development expenses	\$ 3,367	\$ 754
General and administrative expenses	3,555	1,208
<b>Total unit-based compensation expense</b>	<b>\$ 6,922</b>	<b>\$ 1,962</b>

The above unit-based compensation expense related to the following unit-based awards for the years ended December 31, 2023 and 2022 (in thousands):

	Years ended December 31,	
	2023	2022
Profits Interests	\$ 6,922	\$ 1,960
Common Units	—	2
<b>Total unit-based compensation expense</b>	<b>\$ 6,922</b>	<b>\$ 1,962</b>

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 was 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 \$1.2 million through December 31, 2023, the remaining \$7.8 million is expected to be recognized over the next 2.8 years as profits interests continue to vest.

There was \$15.5 million unrecognized unit-based compensation expense related to the profits interests as of December 31, 2023 that is expected to be recognized over a weighted-average period of 3.00 years.

## 12. RELATED PARTY TRANSACTIONS

In connection with Series B and Series B-1 financing, the Company reimbursed certain investors for finance issuance costs that they incurred totaling \$0.4 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 was recorded in accrued expenses and other current liabilities in the consolidated balance sheets. The reimbursable Series B-1 financing costs were fully paid during the year ended December 31, 2023.

## 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 consolidated financial statements. All pre-tax losses have been incurred in the United States.

During the year ended December 31, 2023 and 2022, income tax expense consisted of the following (in thousands):

	Years ended December 31,	
	2023	2022
<b>Current:</b>		
Federal	\$ 8,027	\$ 2,569
State	—	—
Total current tax expense	8,027	2,569
<b>Deferred:</b>		
Federal	—	—
State	—	—
Total deferred tax expense	—	—
<b>Total tax expense</b>	<b>\$ 8,027</b>	<b>\$ 2,569</b>

The Company recognized an income tax provision of \$8.0 million for the year ended December 31, 2023 as a result of their taxable income related to an upfront payment received under the Ionis Agreement and capitalization of their research and development expenses under the 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.

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, 2023 and 2022, is as follows:

	Years ended December 31,	
	2023	2022
Statutory rate	21.00 %	21.00 %
Nontaxable LLC losses	0.10 %	(0.13) %
State tax rate	0.00 %	9.73 %
Permanent and other adjustments	(2.32) %	(1.31) %
Change in valuation allowance	(39.19) %	(41.02) %
Research credits	7.08 %	5.47 %
<b>Total</b>	<b>(13.33) %</b>	<b>(6.26) %</b>

Significant components of the deferred tax assets for federal and state income taxes as of December 31, 2023 and 2022, are as follows (in thousands):

	December 31,	
	2023	2022
<b>Deferred Tax Assets:</b>		
Net operating loss carry forwards	\$ 1,226	\$ 655
Research credits	2,985	1,568
Reserves and accruals	1,472	1,326
Lease liability	13,496	5,199
Deferred revenue	21,257	8,465
Capitalized research and development expenses	23,532	8,901
Total deferred tax assets	63,968	26,114
<b>Deferred Tax Liabilities:</b>		
Property and equipment	(3,976)	(2,583)
Right-of-use asset	(12,204)	(4,685)
Total gross deferred tax liabilities	(16,180)	(7,268)
Less: Valuation allowance	(47,788)	(18,846)
<b>Net deferred tax assets</b>	<b>\$ —</b>	<b>\$ —</b>

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 \$28.9 million and \$16.8 million for the years ended December 31, 2023 and 2022, respectively, primarily due to the increase in deferred revenue and capitalization of research and development expenses under Section 174.

As of December 31, 2023, Metagenomi Inc. had less than \$0.1 million and \$17.5 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, 2023, Metagenomi Inc. had \$0 and \$4.7 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, 2023, the Company has completed an IRC Section 382 analysis from inception through the year ended December 31, 2023. 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 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. The Company recognizes interest related to income tax matters as a component of income tax expense. As of December 31, 2023, the amount of accrued interest related to uncertain tax positions was less than \$0.1 million thousand. During the years ended December 31, 2023 and 2022, no penalties were recognized relating to unrecognized tax benefits. In the event Metagenomi Inc. should need to recognize 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, 2023 and 2022, are as follows (in thousands):

	Years ended December 31,	
	2023	2022
Beginning balance	\$ 1,755	\$ 131
Gross increases—tax position in current period	3,731	1,231
Gross increases—tax position in prior periods	1,576	426
Reductions for tax positions of prior years	(1,119)	(33)
Ending balance	\$ 5,943	\$ 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. As of December 31, 2023, the balance of unrecognized tax benefits was \$5.9 million of which \$5.0 million, if recognized, would affect the effective tax rate.

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.

#### 14. NET LOSS PER SHARE

Basic and diluted net loss per share attributable to common stockholders is calculated as follows (in thousands except share and per share amounts):

	Years ended December 31,	
	2023	2022
Numerator:		
Net loss attributable to common stockholders	\$ (68,255)	\$ (43,593)
Denominator:		
Weighted-average common shares outstanding	3,404,585	3,404,585
Less: Weighted-average unvested shares of common stock subject to repurchase	—	(5,067)
Weighted-average common shares outstanding—basic and diluted	3,404,585	3,399,518
Net loss per share attributable to common stockholders—basic and diluted:	\$ (20.05)	\$ (12.82)

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,	
	2023	2022
Redeemable convertible preferred units	41,813,375	41,478,621
Profits interests	9,488,776	7,516,073
Total	51,302,151	48,994,694

\* The table presents the number of units without giving effect of the Reorganization and reverse stock split of Metagenomi, Inc.

#### 15. 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 \$1.4 million and \$0.6 million for the years ended December 31, 2023 and 2022, respectively.

#### 16. SUBSEQUENT EVENTS

##### *Adoption of 2024 Stock Option and Incentive Plan and 2024 Employee Stock Purchase Plan at the IPO effectiveness date*

In January 2024, the board of directors of Metagenomi, Inc. adopted and stockholders approved the amendment and restatement to the Metagenomi, Inc. certificate of incorporation that became effective immediately prior to the closing of the IPO, and the 2024 Stock Option and Incentive Plan (“2024 Plan”) and 2024 Employee Stock Purchase Plan (“ESPP”), which become effective upon the date immediately preceding the date on which Metagenomi Inc.’s registration statement was declared effective by the SEC. In connection with the closing of the IPO, Metagenomi Inc. increased the authorized number of shares of common stock to 500,000,000 shares and was authorized to issue up to 10,000,000 shares of preferred stock. Metagenomi, Inc. initially reserved 6,690,000 and 375,000 shares of common stock under the 2024 Plan and ESPP, respectively, which will increase as defined in the plans.

**Description of the Registrant's Securities Registered Pursuant to  
Section 12 of the Securities Exchange Act of 1934, as amended**

*The following summary of the general terms and provisions of the registered capital stock of Metagenomi, Inc. ("Metagenomi", "we", "our") does not purport to be complete and is subject to, and qualified in its entirety by, reference to our Amended and Restated Certificate of Incorporation, or certificate of incorporation, our Amended and Restated Bylaws, or bylaws, each of which is incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, and applicable provisions of the Delaware General Corporation Law, or the DGCL. Our common stock, par value \$0.0001 per share is registered pursuant to Section 12(b) of the Securities and Exchange Act of 1934 and trades on The Nasdaq Global Select Market under the symbol MGX. The summaries below do not purport to be complete statements of the relevant provisions of the certificate of incorporation, the bylaws or the DGCL.*

**General**

Our authorized capital stock consists of 500,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share, all of which shares of preferred stock are undesignated.

**Common Stock and Non-Voting 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.

Our common stock is listed on The Nasdaq Global Select Market under the trading symbol "MGX."

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

**Preferred Stock**

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 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.

**Registration Rights**

Certain holders of our shares of common stock, are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of a registration rights agreement between us, certain holders of our common stock. The registration rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights.

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### ***Demand Registration Rights***

Holders of certain of our shares of common stock are entitled to demand registration rights. Under the terms of the registration 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 covering all securities eligible for registration that our stockholders request to be included in such registration. We are required to effect only two registrations pursuant to this provision of the registration rights agreement in any twelve-month period.

### ***Short-Form Registration Rights***

Pursuant to the registration 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 registration 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 registration 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 party thereto are entitled to include their shares in the registration. Subject to certain exceptions contained in the registration rights agreement, we may limit the number of shares included in the underwritten offering if we determine in good faith, based on consultation with the underwriters, that marketing factors require a limitation of the number of securities to be underwritten.

### ***Indemnification***

The registration 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, piggyback registration rights, and short form registration rights granted under the registration rights agreement will terminate on the earliest to occur of (a) the third anniversary of our initial public offering or (b) at such time after our initial public offering when the holders' shares may be sold without restriction pursuant to Rule 144 under the Securities Act during any 90 day period.

### ***Anti-Takeover Effects of Delaware Law and Certain Provisions of our Certificate of Incorporation and Amended and Restated Bylaws***

Our certificate of incorporation and bylaws 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 provides 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 provides 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

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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 provides 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 our bylaws 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 of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws 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 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 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 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 provides for 10,000,000 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

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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**

We are subject to the provisions of Section 203 of the DGCL. 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 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% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, (i) shares owned by persons who are directors and also officers, and (ii) 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% 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% 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 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 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.

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**SUBLEASE**

**BASIC SUBLEASE INFORMATION**

**Effective Date:** \_\_\_\_\_ 7 \_\_\_\_\_, 2024

**Sublandlord:** Dynavax Technologies Corporation, a Delaware corporation

**Sublandlord's Address For Notice:** Dynavax Technologies Corp.  
Attn: Chief Financial Officer  
2100 Powell Street, Suite 720  
Emeryville, CA 94608

**With a Copy To:** Cooley LLP  
11951 Freedom Drive, Suite 1400  
Reston, Virginia 20190  
Attn: John G. Lavoie, Esq.  
Email: jlavoie@cooley.com

**Sublandlord's Address For Payment of Rent:** ACH / EFT Payments:  
To be provided

**Subtenant:** Metagenomi, Inc., a Delaware corporation

**Subtenant's Address For Notice and Tenant's Representative:** 5959 Horton Street, 7<sup>th</sup> Floor  
Emeryville, CA 94608  
Attn: Chief Financial Officer  
Email: pamela.wapnick@metagenomi.co

**With a Copy To:** With a copy to:  
legal@metagenomi.co, and  
  
Dalsin Law  
1630 N. Main Street, No. 221  
Walnut Creek, CA 94596  
Attn: Ann M. Dalsin, Esq.  
Email: ann.dalsin@dalsinlaw.com

**Master Landlord:** EmeryStation West, LLC, a California limited liability company

**Building:** The building within the Project with a common address of 5959 Horton Street, Emeryville, California 94608

**Building Address:** 5959 Horton Street  
Emeryville, California 94608

**Subleased Premises:** Approximately seventy-five thousand six hundred sixty-two (75,662) rentable square feet located within the Building, comprising the entirety of the 6<sup>th</sup> and 7<sup>th</sup> floors of the Building, as generally shown in **Exhibit A**

**Subleased Premises Address:** 5959 Horton Street  
Emeryville, California 94608  
6<sup>th</sup> and 7<sup>th</sup> Floor

**Commencement Date:** Immediately upon termination of the (i) Zymergen Sublease and (ii) Sub-Sublease (as such terms are herein defined)

**Expiration Date:** March 31, 2031

**Sublease Term:** The period beginning on the Commencement Date and ending on the Expiration Date.

<b>Base Rent:</b>	From:	To:	Base Rent (per month)
	Commencement Date	June 30, 2024	\$246,677.04
	July 1, 2024	December 31, 2024	\$493,354.07
	January 1, 2025	December 31, 2025	\$510,621.46
	January 1, 2026	December 31, 2026	\$528,493.21
	January 1, 2027	December 31, 2027	\$546,990.47
	January 1, 2028	December 31, 2028	\$566,135.14
	January 1, 2029	December 31, 2029	\$585,949.87
	January 1, 2030	December 31, 2030	\$606,458.12
	January 1, 2031	March 31, 2031	\$627,684.15

**Base Rent Abatement:** One half (50%) of the Base Rent through June 30, 2024 shall be abated as reflected in the above table.

**Subtenant's Share:** Building: 28.94%

**Letter of Credit:** One Million Nine Hundred Seventy-Three Thousand Four Hundred Sixteen and 28/100 Dollars (\$1,973,416.28).

**Sublandlord's Broker:** Not applicable.

**Subtenant's Broker:** Not applicable.

**Permitted Use:** Office, research and development and laboratory use, in each case, to the extent permitted and subject to Section 5 below.

**EXHIBITS**

- A. Outline of Subleased Premises
- B. Master Lease
- C. Sublandlord FF&E
- D. Bill of Sale
- E. Environmental Questionnaire
- F. Intentionally Omitted
- G. Form of Letter of Credit



## RECITALS

WHEREAS, Master Landlord, as landlord, and Sublandlord, as tenant, are parties to that certain Office/Laboratory Lease dated as of September 17, 2018 (the “**Master Lease**”), pursuant to which Master Landlord leases to Sublandlord the Subleased Premises. A copy of the Master Lease is attached to this Sublease as **Exhibit B**.

WHEREAS, Sublandlord, as sublandlord, and Zymergen Inc., a Delaware corporation (“**Zymergen**”), as subtenant, entered into that certain Sublease dated as of July 12, 2019 (the “**Zymergen Sublease**”), pursuant to which Sublandlord subleased to Zymergen the Subleased Premises.

WHEREAS, Zymergen, as sub-sublandlord, and Subtenant, as sub-subtenant, entered into that certain Sublease dated as of November 11, 2022 (the “**Sub-Sublease**”), pursuant to which Zymergen sub-subleased to Subtenant the Subleased Premises.

WHEREAS, pursuant to that certain Termination and Release Agreement dated on or about the date hereof, by and between Master Landlord, Zymergen, Sublandlord and Subtenant, (i) the Zymergen Sublease shall terminate as of the Effective Date hereof; (ii) the Sub-Sublease shall terminate as of the Effective Date hereof; and (iii) Sublandlord and Subtenant shall enter into this Sublease as of the Effective Date hereof, pursuant to which Sublandlord shall sublet to Subtenant, and Subtenant shall sublet from Sublandlord, the Subleased Premises on all of the terms and conditions of this Sublease.

Capitalized terms used herein shall have the meanings given such terms in the Master Lease, unless otherwise defined herein or within the Basic Sublease Information.

## AGREEMENT

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree as follows:

**1. Sublease.** Sublandlord does hereby sublet to Subtenant and Subtenant does hereby sublet from Sublandlord the Subleased Premises, subject to the terms, provisions, and conditions of this Sublease. Subtenant hereby acknowledges the rentable square footage of the Subleased Premises set forth above in the Basic Sublease Information, and Subtenant accepts and agrees that, for all purposes in this Sublease, such amount is not approximate and agrees to be bound by such figure. Notwithstanding the foregoing, in the event the Master Lease provides the right to Master Landlord to remeasure and/or otherwise modify the rentable square footage of the Subleased Premises, the parties agree that the rentable square footage of the Subleased Premises may be modified to reflect such adjustment.

**2. Sublease Contingency; Sublease Term.**

**(a) Sublease Contingency.** Sublandlord and Subtenant expressly acknowledge and agree that this Sublease is subject to the following contingency (the “**Sublease Contingency**”): Master Landlord’s prior written consent to this Sublease, in form provided by Master Landlord and reasonably acceptable to Sublandlord and Subtenant (“**Master Landlord’s Consent**”). Subtenant agrees to cooperate in all reasonable respects in connection with obtaining the Master Landlord’s Consent. If Sublandlord, despite the parties’ good faith efforts, fails to obtain the Master Landlord’s Consent within forty-five (45) days after the Effective Date, then either Sublandlord or Subtenant may terminate this Sublease by giving written notice thereof to the other at any time prior to receipt of the Master Landlord’s Consent. If either party terminates this Sublease pursuant to the immediately preceding sentence, then notwithstanding anything to the contrary set forth herein, this Sublease shall be null and void, of no force or effect, and Sublandlord shall within thirty (30) days after notice of termination is given, return to Subtenant the Prepayment (defined in Section 4 below), and/or Letter of Credit (defined in Section 19 below) to the extent actually delivered by Subtenant to Sublandlord. The return of such sums paid by Subtenant shall be Subtenant’s sole and exclusive remedy in the event of a termination pursuant to this Section 2(a). Furthermore, neither party shall have any liability to the other for any termination or cancellation of this Sublease if Master Landlord’s Consent is not obtained.

**(b) Sublease Term.** The Sublease Term shall commence on the Commencement Date and shall continue in full force and effect for the period of time specified as the Sublease Term in the Basic Sublease Information; provided, however, that in no event shall the Sublease Term extend beyond the term of the Master Lease. Subtenant shall have no right whatsoever pursuant to this Sublease to extend the Sublease Term for any portion of the Subleased Premises, and Subtenant acknowledges and agrees that this Sublease does not incorporate by reference or include any right of Sublandlord in the Master Lease to extend the term of the Master Lease.

**3. Delivery and Condition.** Subtenant accepts the Subleased Premises in its “AS IS, WHERE IS, WITH ALL FAULTS” condition with the furniture, fixtures and equipment existing in the Premises as of the Effective Date remaining. Upon the expiration or earlier termination of the Sublease (including without limitation, in the event the Master Lease terminates prior to the expiration date of this Sublease, and Master Landlord recognizes Subtenant as a direct tenant pursuant to the terms of the Master Landlord’s Consent), Subtenant shall purchase the furniture, fixtures and equipment generally described on **Exhibit C** (the “**Sublandlord FF&E**”), specifically including nine biosafety cabinets and two lab freezers located on the 6<sup>th</sup> Floor Premises from Sublandlord in its “AS IS, WHERE IS, WITH ALL FAULTS” condition for a purchase price of \$1.00, pursuant to a bill of sale to be signed by both parties in the form attached hereto as **Exhibit D**. Subtenant acknowledges that Sublandlord shall have no obligation to perform any improvements, alterations, or other work to the Subleased Premises, or provide Subtenant with any improvement allowance with respect to the Subleased Premises. As of the Possession Date, Subtenant accepted the Subleased Premises in the condition provided for in this Section and waived all claims of defect in or relating to the Subleased Premises.

#### **4. Rent.**

**(a) Terms of Payment.** Subtenant shall pay to Sublandlord, at Sublandlord’s Address for Payment of Rent designated in the Basic Sublease Information, or as otherwise directed by Sublandlord, Base Rent, and Additional Rent, without notice, demand, offset or deduction, in advance, on the first day of each calendar month, except as otherwise expressly set forth in this Sublease. All payments required to be paid by Subtenant to Sublandlord shall be made in federal funds by electronic fund transfer (EFT) or Automated Clearing House (ACH) (or to such other party or at such location as Sublandlord may otherwise from time to time specify in writing) before 11:00 a.m. Pacific Time. If the Sublease Term commences (or ends) on a date other than the first (or last) day of a month, Base Rent shall be prorated on the basis of a thirty (30) day month. Subtenant shall have no right at any time to abate, reduce, or set-off any rent due hereunder except as may be expressly provided in this Sublease.

**(b) Additional Rent.** All sums due from Subtenant to Sublandlord or to any third party under the terms of this Sublease (other than Base Rent and the Letter of Credit) shall be additional rent (“**Additional Rent**”). Additional Rent shall include, without limitation, (i) Subtenant’s Share of all amounts other than base rent payable by Sublandlord to Master Landlord under the Master Lease with respect to the Subleased Premises, including without limitation amounts payable as Rent Adjustment, as defined in the Master Lease; (ii) taxes on personal property, equipment and fixtures located in or about the Subleased Premises; (iii) amounts recoverable due to a failure of performance by Subtenant under this Sublease; and (iv) any other costs or expenses due from Sublessee to Sublessor under this Sublease. “**Subtenant’s Share**” shall be the percentage set forth in the Basic Sublease Information as Subtenant’s Share of the Project and Subtenant’s Share of the Building, as applicable. However, Subtenant’s Share may be reasonably adjusted by Sublandlord in the future for changes in the physical size of the Project made by Sublandlord and/or Master Landlord. Sublandlord may equitably increase Subtenant’s Share for any item of expense or cost reimbursable by Subtenant that relates to an item of maintenance, repair, replacement, or service that benefits only the Subleased Premises. All Additional Rent that is payable to Sublandlord shall be paid at the time, place, and manner as Base Rent pursuant to Section 4(a) above, unless this Sublease expressly provides otherwise. Sublandlord will have the same remedies for a default in the payment of any Additional Rent as for a default in the payment of Base Rent. Together, Base Rent, Additional Rent and any other sums due hereunder from Subtenant are sometimes referred to in this Sublease as “**Rent**”.

#### **(c) Omitted.**

**(d) Late Charge; Interest.** Subject to other provisions of this Sublease, if Subtenant fails to pay any Rent within two (2) business days after notice of late payment (with notice to be given by noon on such first business day), Subtenant shall pay to Sublandlord on demand a late charge equal to ten percent (10%) of such delinquent sum.

The provision for such late charge shall be in addition to all of Sublandlord's other rights and remedies hereunder or at law and shall not be construed as a penalty. No endorsement or statement on a check or letter accompanying a check or payment shall be considered an accord and satisfaction of past due Rent. Subtenant's covenant to pay Rent is independent of every other covenant in this Sublease.

**5. Use; Compliance with Laws; Hazardous Materials.**

(a) The Subleased Premises shall be used for the Permitted Use to the extent permitted by the Master Lease, in accordance with this Sublease, and for no other purpose. Subtenant shall use the Subleased Premises in compliance with all statutes, codes, ordinances, orders, rules and regulations of any municipal or governmental entity, including, without limitation, all applicable federal, state and local laws or regulations governing protection of, damage to the environment, or the treatment, storage or disposal of hazardous materials, and any covenants, conditions and restrictions encumbering the Subleased Premises, the Building and/or the Project (collectively referred to as "**Laws**"). Subtenant shall be responsible for obtaining any permit, business license, or other permits or licenses required by any governmental agency permitting Subtenant's use or occupancy of the Subleased Premises. Sublandlord makes no warranty or representation as to whether or not the Subleased Premises comply with Law and, notwithstanding anything to the contrary contained herein, Sublandlord shall have no obligation to bring the Subleased Premises into compliance with Law, nor any such obligation with respect to the Building or the Project. In the event that Subtenant's use of the Subleased Premises requires modifications or additions to the Subleased Premises, the Building, or the Project in order to be in compliance with Law, Subtenant agrees to make any such necessary modifications and/or additions at its sole cost and expense and in accordance with the terms of Section 8 herein.

(b) Subtenant shall not use, store, transport or dispose of any Hazardous Materials (as defined in the Master Lease) in, under or about the Subleased Premises, Building or the Project, except that Subtenant may keep, store and use in the Subleased Premises those Hazardous Materials, and their respective quantities, specifically listed on the "**Environmental Questionnaire**" attached to this Sublease as **Exhibit E**, in each case, to the extent approved in writing by Sublandlord and (if applicable) Master Landlord, and as otherwise permitted pursuant to the terms and conditions of Section 7.1(g) of the Master Lease incorporated herein. The Environmental Questionnaire may be reasonably updated by written notice by Subtenant to Sublandlord from time to time. Subtenant shall update such Environmental Questionnaire upon reasonable notice from Sublandlord. Any such updates shall be subject to the review and approval of Sublandlord and (if applicable) Master Landlord. Subtenant hereby represents and warrants to Sublandlord that (i) neither Subtenant nor any of its legal predecessors has been required by any prior landlord, sublandlord, lender or governmental authority at any time to take remedial action in connection with Hazardous Materials contaminating a property which contamination was permitted by Subtenant or such predecessor, or resulted from Subtenant's or such predecessor's action or use of the property in question; and (ii) Subtenant is not subject to any enforcement order issued by any governmental authority in connection with the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials (including, without limitation, any order related to the failure to make a required reporting to any governmental authority). If Sublandlord determines that this representation and warranty was not true as of the date of this Sublease, Sublandlord shall have the right to terminate this Sublease in Sublandlord's sole and absolute discretion.

**6. Utilities and Services.**

(a) Subtenant shall be solely responsible for and shall pay when due all (i) water, sewer, gas, electricity, other utilities and utility-type services used on or provided to the Subleased Premises, (ii) environmental health and safety services and hazardous waste management furnished to the Subleased Premises, and (iii) information technology services and support, administrative support, janitorial services, business services, office supplies, food and beverage, and other similar items and services with respect to the Subleased Premises. Subtenant shall contract directly for such services. Sublandlord shall not be liable to Subtenant for interruption in or curtailment of any such utility or service, nor shall any such interruption or curtailment constitute constructive eviction or grounds for rental abatement. In the event the Subleased Premises is not separately metered for a utility service, Subtenant shall have the option, subject to Sublandlord's and Master Landlord's prior written consent and the terms of this Sublease, to cause the Subleased Premises to be separately metered at Subtenant's sole cost and expense. If Subtenant does not elect to cause the Subleased Premises to be separately metered, Subtenant shall pay, upon demand, a reasonable proration of utilities, as determined by Sublandlord. Subtenant hereby waives the provisions of any applicable existing or future

Laws permitting the termination of this Sublease due to an interruption, failure or inability to provide any services or utilities (including, without limitation, the provisions of California Civil Code Section 1932(1)).

(b) To allow for compliance with building performance benchmarking and disclosure laws and regulations (including, but not limited to, compliance with California Public Resources Code §25402.10), Subtenant, promptly upon request, shall deliver to Sublandlord (or, at Sublandlord's option, execute and deliver to Sublandlord an instrument enabling Sublandlord to obtain from such provider) any data about Subtenant's utility consumption. Further, Subtenant authorizes Sublandlord and Master Landlord to disclose such information and data regarding the Subleased Premises as may be requested or required from time to time to comply with Laws and/or energy regulations.

7. **Maintenance and Repairs.** Subtenant acknowledges and agrees that Master Landlord shall be responsible for the maintenance and repair obligations of the "Landlord" under the Master Lease. Subtenant shall look solely to Master Landlord for performance thereof. Subtenant hereby recognizes and agrees that all acknowledgements, reservations of rights, limitations on and waivers of liability, and rights to notice in favor of "Landlord" are incorporated into this Sublease in favor of Master Landlord and Sublandlord, as if the same were restated in this Sublease by Subtenant. In no event shall Sublandlord be obligated to undertake any maintenance, repair or replacement obligations that are otherwise the responsibility of Master Landlord or Subtenant, whether hereunder or under the Master Lease. Notwithstanding anything to the contrary contained herein, if any maintenance, repairs, or replacements are required to be made to the Subleased Premises, the Master Premises, the Building, or the Project due to the acts, omissions or negligence of Subtenant or any Subtenant Party (defined in Section 11 below), then such maintenance, repairs, or replacements shall be at Subtenant's sole cost and expense; provided, further, Subtenant shall be responsible for keeping and maintaining the Subleased Premises in good condition at its sole cost and expense except as explicitly set forth in the Master Lease or herein.

#### 8. **Alterations.**

(a) Any alterations, additions or improvements to the Subleased Premises by or for Subtenant (collectively referred to as "**Alterations**") shall require the prior written consent of Sublandlord and Master Landlord. Alterations shall be subject to and made in accordance with Article 9 of the Master Lease, which is incorporated herein by this reference (provided, however, that all references therein to "Tenant" and "Subleased Premises" shall mean "Subtenant" and the "Subleased Premises", respectively, and all references therein to "Landlord" shall mean "Sublandlord" and "Master Landlord"). Upon the expiration or earlier termination of this Sublease, Subtenant shall remove any or all Alterations made or installed by, or on behalf of, Subtenant and restore the Subleased Premises to the condition required pursuant to Section 17 below; provided, however, (a) rights in favor of Master Landlord to retain, preserve, and/or leave in place all or any portion of such Alterations are incorporated into this Sublease in favor of Master Landlord and Sublandlord, as if the same were restated in this Sublease by Subtenant; and (b) in the event of the exercise of such right, such items shall be and become the property of (as applicable) Sublandlord or Master Landlord upon the expiration or earlier termination of this Sublease. Subtenant shall be solely responsible for the planning, permitting, construction and completion of any Alterations at Subtenant's sole cost and expense. Subtenant shall make all payments for Alterations in a timely manner so as not to permit any mechanic's or other liens to be placed upon the Subleased Premises in connection with any Alterations. Subtenant shall fully discharge any such lien within fifteen (15) days after the date of filing, and if Subtenant fails to do so, Sublandlord may take such action as may be necessary to remove such lien and Subtenant shall promptly pay Sublandlord such amounts expended by Sublandlord in connection therewith. Subtenant shall not damage or deface the furnishings, walls, floors, ceilings or other portions of the Subleased Premises. Any damage to the Subleased Premises, the Building and/or the Project caused by Subtenant or a Subtenant Party shall be promptly repaired by Subtenant, to Sublandlord's and (if applicable) to Master Landlord's satisfaction, all at Subtenant's sole cost and expense. Any provision which permits Master Landlord to recover costs incurred in connection with reviewing and coordination of Alterations shall be construed as requiring Subtenant to pay such costs of Master Landlord and Sublandlord,

(b) It is hereby acknowledged and agreed that it is Subtenant's intention to convert all or a portion of the 7<sup>th</sup> floor of the Premises to laboratory space (the "**Laboratory Conversion Work**"). Subtenant shall have the right, but not the obligation, to undertake the Laboratory Conversion Work at its own cost and expense. Provided Subtenant complies with Article 9 of the Master Lease, Sublandlord consents to Subtenant performing the Laboratory Conversion Work. Notwithstanding anything in this Sublease or Master Lease to the contrary, the Security Deposit and Rent Adjustment shall not be increased due to any Laboratory Conversion Work, nor shall Subtenant nor Sublandlord have

any obligation to remove the Laboratory Conversion Work or restore the Sublease Premises to its condition prior to the Laboratory Conversion Work at the end of the Sublease Term. This paragraph and Sublandlord's consent hereto, shall be subject to Sublandlord's and Subtenant's receipt of consent to the same from Master Landlord.

(c) Notwithstanding anything in this Sublease to the contrary, Sublandlord acknowledges and agrees that certain of the Sublandlord FF&E may be required to be modified, moved or removed by Subtenant in connection with the performance of any Subtenant Alterations and/or the Laboratory Conversion Work. In furtherance of the foregoing, Subtenant shall have the right to remove, move and/or modify the Sublandlord FF&E in connection with an approved Alteration and/or the Laboratory Conversion Work ("**Removable FF&E**") without the prior consent of Sublandlord but upon prior written notice to Sublandlord for Sublandlord's accounting and recordkeeping purposes ("**Removal Notice**"). Further, in the event the cost of removal of any item of Removable FF&E (per instance) exceeds Ten Thousand and No/100 Dollars (\$10,000.00), Subtenant shall have the right to provide Sublandlord with written notice thereof (which notice shall include reasonable backup documentation evidencing such cost), and Sublandlord shall remove the same at Sublandlord's sole cost and expense.

**9. Entry by Sublandlord or Master Landlord.** Sublandlord or Master Landlord may enter the Subleased Premises at any time during the Sublease Term and/or undertake the following all without abatement of Rent or liability to Sublandlord and/or Master Landlord: inspect the Subleased Premises; to make and operate repairs, alterations, improvements, or additions to the Subleased Premises; show the Subleased Premises to prospective purchasers and investors and existing and prospective lenders; and (if applicable), during the last nine (9) months of the Subleased Term, place signs for the rental of, and show the Subleased Premises to prospective tenants and/or subtenants. Subtenant acknowledges that any prior notice of entry into the Subleased Premises may be given orally; however, no notice shall be required in case of an emergency.

**10. Assignment and Subletting.** Subtenant shall not assign, sublease, or transfer any interest in this Sublease or allow any third party to use any portion of the Subleased Premises (collectively or individually, a "**Transfer**"), without the prior written consent of Sublandlord and Master Landlord. Each Transfer (including a proposed Transfer) shall be subject to Article 10 of the Master Lease which is incorporated herein by this reference (provided, however, that all references therein to "Tenant" and "Subleased Premises" shall mean "Subtenant" and the "Subleased Premises", respectively, and all references therein to "Landlord" shall mean "Sublandlord" and "Master Landlord"). Any Transfer without the prior written consent of Sublandlord and Master Landlord shall be an incurable default by Subtenant and, in addition to any other rights and remedies, shall entitle Sublandlord to terminate this Sublease immediately. Subtenant shall not be released from any of its obligations under this Sublease or those provisions of Master Lease incorporated herein, and shall continue to be liable as a principal, not as a guarantor or surety, and to the same extent as though no Transfer had been made. Subject to all of the foregoing, no permitted Transfer shall be effective until there has been delivered to Sublandlord a counterpart of the Transfer instrument in which the transferee agrees to be and remain jointly and severally liable with Subtenant for the payment of Rent pertaining to the Subleased Premises and for the performance of all of the terms and provisions of this Sublease and those provisions of Master Lease incorporated herein. Notwithstanding anything to the contrary herein or otherwise, Subtenant shall not collaterally assign, mortgage, pledge, hypothecate or otherwise encumber the Subleased Premises, this Sublease, the Master Lease, or any of Subtenant's rights hereunder without the prior written consent of Sublandlord and Master Landlord, which consent Sublandlord and/or Master Landlord may withhold in its/their sole discretion. Subtenant hereby waives (for itself and all persons claiming under Subtenant) the provisions of California Civil Code Section 1995.310.

**11. Indemnity and Waiver of Claims.** Subtenant shall indemnify, defend (by counsel acceptable to Sublandlord) and hold Sublandlord and all of Sublandlord's affiliates, and each of their respective, owners, investors, partners, principals, members, trustees, officers, directors, shareholders, agents, contractors, employees and lenders ("**Sublandlord Parties**") harmless from and against all liabilities, damages, claims, and expenses, including, without limitation, reasonable attorneys' fees (if and to the extent permitted by Law), which may be imposed upon, incurred by or asserted against Sublandlord or any of the Sublandlord Parties, arising directly or indirectly out of (a) the use or occupancy of the Subleased Premises, the conduct of Subtenant's business or any activity, work or things done, permitted or suffered by Subtenant or any of Subtenant's affiliates, or their respective employees, agents, customers, visitors, invitees, licensees, contractors, assignees (individually, a "**Subtenant Party**", and collectively, the "**Subtenant Parties**"), or (b) a breach or default in the performance of any obligation on Subtenant's part to be performed hereunder, except to the extent caused by Sublandlord's gross negligence or willful misconduct. Subtenant hereby waives all claims against Sublandlord and the Sublandlord Parties for (i) any injury or damage to person or

property (or resulting from the loss of use thereof) in or about the Subleased Premises or the Building by or from any cause whatsoever (including, without limiting the foregoing, rain or water leakage of any character from the roof, windows, walls, basement, pipes, plumbing works or appliances, the Project, the Building and/or the Subleased Premises not being in good condition or repair, gas, fire, oil, or electricity), except to the extent caused by Sublandlord's gross negligence or willful misconduct, and (ii) any failure to prevent or control any criminal or otherwise wrongful conduct by any third party or to apprehend any third party who has engaged in such conduct. Notwithstanding any provision in this Sublease to the contrary, neither Sublandlord nor any Sublandlord Parties, nor Master Landlord nor any of their owners, partners, principals, members, trustees, officers, directors, shareholders, agents, employees and lenders, shall be liable for (and Subtenant hereby waives any claims for) any injury or damage to, or interference with, Subtenant's business, including consequential damage, loss of profits, loss of rents or other revenues, loss of business opportunity, loss of goodwill or loss of use, or for any form of punitive damage. Subtenant and Subtenant parties shall only be liable to Sublandlord, Sublandlord Parties and Master Landlord for any consequential damage, compensation or claims for inconvenience or loss of business, rents or profits as a result of any injury or damage (a) (i) caused directly by an act or omission of Subtenant or any of Subtenant's invitees, agents or employees, and (ii) Master Landlord has brought an action against Sublandlord for same; or (b) to the extent resulting from a holdover (which is governed by Section 18 of this Sublease).

**12. Insurance.** The provisions of Article 16 of the Master Lease pertaining to insurance shall be incorporated into this Sublease, subject to the following terms. For purposes of this Sublease, (i) the term "**Tenant**" in Article 16 of the Master Lease shall be deemed to mean Subtenant; (ii) the term "**Landlord**" in Section 16.3 of the Master Lease shall be deemed to mean Master Landlord; (iii) the term "**Landlord**" in Sections 16.1, 16.2, 16.4 and 16.5 of the Master Lease shall be deemed to mean Master Landlord and Sublandlord (it being understood that Sublandlord and Sublandlord Parties shall be named, as applicable, as additional insureds and loss payees, that Sublandlord shall be entitled to all applicable notices related to such insurance and to evidence of all such insurance, and that the release and waiver of subrogation in Section 16.4 of the Master Lease shall also apply as between Sublandlord and Subtenant; and (iv) the term "Premises" shall mean the "Subleased Premises." The insurance certificate to be provided by Subtenant shall be subject to approval by Sublandlord and Master Landlord (the "**Insurance Certificate**").

**13. Damage or Destruction and Condemnation.** The provisions of Article 13 of the Master Lease pertaining to damage or destruction and condemnation, respectively, shall be incorporated into this Sublease, subject to the following terms. For purposes of this Sublease, the term "Tenant" in Article 13 of the Master Lease shall be deemed to mean Subtenant and the term "Landlord" therein shall be deemed to mean Master Landlord and the term "Premises" shall mean the "Subleased Premises", except that (a) in no event shall Sublandlord have any obligation to Subtenant to restore the Subleased Premises if damaged, destroyed or condemned as described in Article 13 of the Master Lease; and (b) Subtenant shall have no right to (i) terminate this Sublease due to casualty damage to or condemnation of all or any portion of the Subleased Premises unless Sublandlord has such right under the Master Lease, or (ii) any insurance proceeds or condemnation awards received by Sublandlord under the Master Lease, all of which shall be deemed to be the property of Sublandlord. Subtenant hereby (A) waives (I) any and all provisions of applicable Laws that provide alternative rights for the parties in the event of damage or destruction (including, without limitation, the provisions of California Civil Code Section 1932, Subsection 2, and Section 1933, Subsection 4, and any successor statute or laws of a similar nature), and (II) any rights it may have pursuant to any applicable Laws in the event of a condemnation (including, without limitation, Section 1265.130 of the California Code of Civil Procedure and any successor statutes); and (B) agrees that the provisions of this Section 13 shall govern the parties' rights in the event of any casualty and/or condemnation.

**14. Events of Default.** The occurrence of any of the following shall constitute a material breach of this Sublease and a default by Subtenant ("**Default**"): (i) Subtenant's failure to pay Rent within three (3) days of the date due; provided, however that Sublandlord will give Subtenant notice and an opportunity to cure any failure to pay Rent within three (3) days of any such notice not more than twice in any twelve (12) month period; provided, further, that any such notice shall be in lieu of, and not in addition to, any notice required under California Code of Civil Procedure Section 1161; (ii) all those items of default set forth in the Master Lease where the obligation is incorporated in this Sublease, including, without limitation, the Defaults listed in Article 11 of the Master Lease, which remain uncured after the cure period provided in the Master Lease; (iii) Subtenant shall attempt or there shall occur any Transfer in contravention of this Sublease or the Master Lease; or (iv) Subtenant's failure to perform any other term, provision or covenant of this Sublease, which failure remains uncured after fifteen (15) days written notice thereof; provided that, subject to Section 16(b) below, if the failure is of a nature that reasonably requires more than fifteen (15) days, to cure,

the cure period shall be extended so long as the cure is commenced within such period and diligently prosecuted to completion.

**15. Remedies.** Upon any Default by Subtenant under the terms of this Sublease, beyond any applicable notice and cure period, Sublandlord shall have the remedies set forth in Article 11 of the Master Lease (which rights are hereby incorporated by reference into the terms of this Sublease) as if Sublandlord were Master Landlord, including, without limitation, the right to terminate this Sublease, in which case Subtenant shall immediately surrender the Subleased Premises to Sublandlord. If Subtenant fails to surrender the Subleased Premises, Sublandlord may, in compliance with applicable Laws and without prejudice to any other right or remedy, enter upon and take possession of the Subleased Premises. In addition to the right to terminate this Sublease and collect damages, Sublandlord shall have the right to pursue any other remedy provided under the Master Lease or that is now or hereafter available at law or in equity. No right or remedy conferred upon or reserved to Sublandlord is intended to be exclusive of any other right or remedy, and each and every right and remedy shall be cumulative and in addition to any other right or remedy given hereunder or now or hereafter existing by agreement, Laws, or in equity.

**16. Sublandlord Representations, Warranties and Covenants; Master Lease.**

(a) Sublandlord represents and warrants the following is true and correct as of the Effective Date: (i) Sublandlord is the tenant under the Master Lease and has the capacity to enter into this Sublease with Subtenant subject to the Sublease Contingency, (ii) the Master Lease attached as **Exhibit B**, is a true, correct, and complete copy of the Master Lease, is in full force and effect, and has not been further modified, amended, or supplemented except as expressly set out herein, (iii) Sublandlord has not received any notice, and has no actual knowledge of any default by Sublandlord under the Master Lease, including without limitation as to any covenants related to Hazardous Materials, (iv) Sublandlord has no actual knowledge, of any default by Master Landlord under the Master Lease. Sublandlord covenants that it will maintain the Master Lease during the entire Sublease Term, subject, however, to any earlier termination of the Master Lease without the fault of Sublandlord. Sublandlord hereby covenants not to enter into any amendment or other agreement with respect to the Master Lease without the prior written consent of the Subtenant.

(b) Subtenant takes possession of the Subleased Premises, and enters into this Sublease, subject and subordinate to all of the terms, covenants, conditions, and restrictions of the Master Lease, except as otherwise expressly provided for herein. Subtenant's use of the Subleased Premises, the Building, and the Project shall be subject and subordinate to all of the terms, covenants, conditions, and restrictions of the Sublease and the Master Lease, except as otherwise expressly provided for herein. Subtenant shall not, and shall not permit Subtenant Parties to, by act or omission cause a breach of any of the terms, covenants, conditions, and restrictions contained in this Sublease or the Master Lease. Except as specifically set forth herein, with respect to any obligation of Subtenant to be performed under this Sublease, wherever the Master Lease grants to Sublandlord a specified number of days after notice or other time condition to perform its corresponding obligation under the Master Lease (excluding the payment of Rent), Subtenant shall have one-fourth fewer days (rounded to the nearest whole day) to perform the obligation, including without limitation curing any defaults. Any default notice or other notice of any obligations (including any billing or invoice for any Rent or any other expense or charge due under the Master Lease) from Master Landlord which is received by Subtenant (whether directly or as a result of being forwarded by Sublandlord) shall constitute such notice from Sublandlord to Subtenant under this Sublease without the need for any additional notice from Sublandlord.

(c) It is expressly understood, acknowledged and agreed by Subtenant that all of the other terms, conditions and covenants of this Sublease shall be those stated in the Master Lease except as excluded or modified below in this Section 16(c). Except as otherwise set forth in this Sublease, Subtenant shall be subject to, bound by and comply with all of said Sections of the Master Lease with respect to the Subleased Premises and shall satisfy all applicable terms and conditions of the Master Lease for the benefit of Sublandlord and Master Landlord, it being understood and agreed (except as otherwise expressly set forth in this Sublease), however, that (i) wherever in the Master Lease the word "Tenant" appears, for the purposes of this Sublease, the word "Subtenant" shall be substituted, wherever the word "Landlord" appears, for the purposes of this Sublease, the word "Sublandlord" shall be substituted, wherever the word "Lease" appears, for purposes of this Sublease, the word "Sublease" shall be substituted, and wherever the word "Premises" appears, for the purposes of this Sublease, the word "Subleased Premises" shall be substituted, and wherever the word "Term" appears, for purposes of this Sublease, the words "Sublease Term" shall be substituted; (ii) Sublandlord shall have no liability to Subtenant with respect to (w) representations and warranties made by Master Landlord under the Master Lease, (x) any indemnification obligations of Master Landlord under the

Master Lease, (y) obligations or liabilities of Master Landlord under the Master Lease with respect to compliance with laws, condition of the Subleased Premises or Hazardous Materials, or (z) obligations under the Master Lease to repair, maintain, restore, or insure all or any portion of the Subleased Premises, regardless of whether the incorporation of one or more provisions of the Master Lease might otherwise operate to make Sublandlord liable therefor; (iii) in any case where "Tenant" is to indemnify, release or waive claims against "Landlord", such indemnity, release or waiver shall be deemed to run from Subtenant to Master Landlord and Sublandlord; (iv) whenever the provisions of the Master Lease incorporated as provisions of this Sublease require the written consent of Master Landlord, said provisions shall be construed to require the written consent of Master Landlord and Sublandlord; (v) whenever the provisions of the Master Lease incorporated as provisions of this Sublease require the written consent of Tenant, said provisions shall be construed to require the written consent of Subtenant; and (vi) in any case where Master Landlord is to indemnify, release or waive claims against "Tenant", such indemnity, release or waiver shall be deemed to run from Master Landlord and Sublandlord to Subtenant. In the event of any conflict between this Sublease, on the one hand, and the Master Lease, on the other hand, the terms of this Sublease shall control as between Sublandlord and Subtenant. Subtenant hereby acknowledges that it has read and is familiar with all the terms of the Master Lease. In addition to any other provisions contained in this Sublease which specifically state that certain provisions of the Master Lease are not incorporated into this Sublease or are otherwise modified as described in such other provisions, the terms and provisions of the following Sections and portions of the Master Lease are not incorporated into this Sublease or are modified as provided for below: (A) the following provisions of the Master Lease are expressly not incorporated herein by reference: the definition of "Base Rent," "Applicable Monthly Base Rent," "Security Deposit," "Sublease Term," and "Commencement Date," are not a part of this Sublease; the definition of "Monthly Base Rent," "Security Deposit," "Lease Term" and "Commencement Date," as the same appear in the Master Lease, are not part of this Sublease; Section 2.1, Section 2.2, Section 2.3, Section 2.6, Section 2.7, Section 2.8, Article 3, Article 5, Article 22 and Section 24(b), all of the Master Lease, are not part of (and not incorporated into) this Sublease; the references to "Landlord" in Section 8.1, Section 16.3, Article 14 and Article 15 of the Master Lease shall be deemed to mean "Master Landlord,"; and Exhibits B, B-1 and B-2 to the Master Lease are not part of (and are not incorporated into) this Sublease.

(d) Sublandlord shall have no liability to Subtenant on account of any failure of Master Landlord to observe or perform any of the terms, covenants or conditions of the Master Lease required to be observed or performed by Master Landlord. Sublandlord, upon Subtenant's written request, shall use commercially reasonable efforts to cause the Master Landlord to perform its obligations under the Master Lease (including without limitation by notifying Master Landlord of Master Landlord's failure to perform its obligations under the Master Lease if Master Landlord fails to perform same within thirty (30) days after Master Landlord has been requested to do so in writing by Subtenant) and shall use commercially reasonable efforts to cooperate with Subtenant in its efforts to obtain such performance at no cost to Sublandlord. In no event shall Sublandlord be required to initiate any legal proceedings or to incur any expense or liability in connection with such efforts.

(e) If (i) Subtenant shall fail to perform any of its obligations hereunder and such failure shall continue beyond any cure period provided for herein, or (ii) Master Landlord shall give any notice of failure or default under the Master Lease arising out of any failure by Subtenant to perform any of its obligations hereunder, then, in any such case, Sublandlord shall have the right (but not the obligation) to enter the Subleased Premises and perform or endeavor to perform such obligation, at Subtenant's expense. Subtenant shall, within ten (10) days of Sublandlord's demand, reimburse Sublandlord for all such costs and expenses incurred by Sublandlord in doing so (plus a sum for overhead to Sublandlord equal to five percent (5%) of such costs and expenses) as Rent.

(f) Subtenant shall promptly execute, acknowledge and deliver to Sublandlord, any certificate or other document evidencing the status of the Sublease or subordination of this Sublease to the Master Lease, that Sublandlord or Master Landlord may reasonably request, in accordance with the Master Lease or this Sublease.

## **17. Surrender of Subleased Premises.**

(a) Subtenant shall remove from the Subleased Premises on or before the expiration or earlier termination of this Sublease (i) any Alterations that are required to be removed pursuant to Section 8 of this Sublease, other than the Laboratory Conversion Work, (ii) any other improvements, alterations or fixtures in the Subleased Premises that were performed by or on behalf of Subtenant and that are required to be removed at the expiration of the term of the Master Lease pursuant to the terms therein, and (iii) Subtenant's personal property, including, without



limitation, any property that would be considered “**Required Removables**” pursuant to the terms of the Master Lease. In addition, Subtenant shall quit and surrender the Subleased Premises to Sublandlord on or before the expiration or earlier termination of this Sublease, broom clean, and in at least the same order, condition and repair as on the date received, ordinary wear and tear excepted and in accordance with the terms of the Master Lease. Conditions existing because of Subtenant’s failure to perform maintenance, repairs or replacements shall not be deemed “ordinary wear and tear.” If Subtenant fails to timely remove any Alterations, improvements or fixtures that are required to be removed, or any of Subtenant’s personal property, Sublandlord, at Subtenant’s sole cost and expense, shall be entitled (but not obligated) to remove such Alterations, improvements and/or fixtures and/or remove, store or dispose of Subtenant’s personal property. Sublandlord shall not be responsible for the value, preservation or safekeeping of Subtenant’s personal or other property. On the basis of the foregoing, Subtenant waives and releases its rights under Sections 1980 et. seq. and 1993 et. seq. of the California Civil Code, or any similar Laws now or hereafter in effect.

(b) At least thirty (30) days prior to Subtenant’s surrender of possession of any part of the Subleased Premises, Subtenant shall provide Sublandlord with a facility decommissioning and Hazardous Materials closure plan for the Subleased Premises (“**Exit Survey**”) prepared by an independent third-party, state-certified professional with appropriate expertise, which Exit Survey must be reasonably acceptable to Sublandlord. The Exit Survey shall comply with the American National Standards Institute’s Laboratory Decommissioning guidelines (ANSI/AIHA Z9.11-2008) or any successor standards published by ANSI or any successor organization (or, if ANSI and its successors no longer exist, a similar entity publishing similar standards). In addition, at least ten (10) days prior to Subtenant’s surrender of possession of any part of the Subleased Premises, Subtenant shall (i) provide Sublandlord with written evidence of all appropriate governmental releases obtained by Subtenant in accordance with Laws, including laws pertaining to the surrender of the Subleased Premises, (ii) place laboratory equipment decontamination forms on all decommissioned equipment to assure safe occupancy by future users, and (iii) conduct a site inspection with Sublandlord. In addition, Subtenant agrees to remain responsible after the surrender of the Subleased Premises for the remediation of any recognized environmental conditions, including those set forth in the Exit Survey and comply with any recommendations set forth in the Exit Survey. Subtenant’s obligations under this Addendum shall survive the expiration or earlier termination of the Sublease.

**18. Holding Over.** Subtenant shall have no right to holdover in the Subleased Premises beyond the expiration or earlier termination of this Sublease. If Subtenant does not surrender and vacate the Subleased Premises as and when provided for herein, Subtenant shall be deemed to be holding over as a tenant at sufferance, and the parties agree that the Rent during such holdover period shall be one hundred seventy five percent (175%) of the Rent in effect immediately prior to such holding over. No holding over by Subtenant shall operate to extend the Sublease Term. Notwithstanding the foregoing, and in addition to all other rights and remedies on the part of Sublandlord, if Subtenant fails to surrender the Subleased Premises upon the expiration or earlier termination of this Sublease, in addition to any other liabilities to Sublandlord accruing therefrom, Subtenant shall be liable to Sublandlord for any obligations imposed by Master Landlord pursuant to the Master Lease as a result of such holding over, and Subtenant shall be responsible for all damages suffered by Sublandlord resulting from or occasioned by such holding over, including, without limitation, consequential damages (notwithstanding any limitations thereon under the Master Lease).

**19. Letter of Credit.** Subtenant shall deliver to Sublandlord, at Subtenant’s sole cost and expense, an unconditional, irrevocable, standby letter of credit (the “**Letter of Credit**”) with an initial expiration date no earlier than one (1) year after the Effective Date of this Sublease in the amount set forth in the Basic Lease Information (the “**Letter of Credit Amount**”), in the form attached hereto as **Exhibit G** or in other such form as is reasonably acceptable to Sublandlord. The Letter of Credit shall secure the full and faithful performance of each provision of this Sublease to be performed by Subtenant pursuant to the following terms and conditions.

(a) The Letter of Credit shall state on its face that, notwithstanding the stated expiration date, the term of the Letter of Credit shall be automatically renewed for successive, additional one (1) year periods during the Sublease Term through the date that is at least ninety (90) days after the last day of the Sublease Term, unless, at least ninety (90) days prior to any such date of expiration, the issuing bank shall have given written notice to Sublandlord, by certified mail, return receipt requested at the Sublandlord’s Address For Notice stated in the Basic Sublease Information or such other address as Sublandlord shall have given to the issuing bank, that the Letter of Credit will not be renewed. The failure of Subtenant to cause the Letter of Credit to be renewed or reissued at least sixty (60) days prior to the expiration thereof shall constitute Default under this Sublease.

**(b)** The Letter of Credit shall be issued by a financial institution reasonably acceptable to Sublandlord, which financial institution shall be a bank that accepts deposits, maintains accounts, will negotiate letters of credit, and whose deposits are insured by the FDIC. The Letter of Credit must be presentable in Emeryville, California or such other United States location reasonably acceptable to Sublandlord. If the financial institution that issues the Letter of Credit makes a general assignment for the benefit of creditors, or commences any case, proceeding or other action seeking to have an order for relief entered on its behalf as a debtor or to adjudicate it as bankrupt or insolvent, or seeking reorganization, arrangement, adjustment, liquidation, dissolution or composition of it or its debts or seeking appointment of a receiver, trustee, custodian or other similar official for it or for all or of any substantial part of its property, or loses or has its charter revoked, goes into receivership, or is otherwise taken over by any regulatory agency which oversees such issuer, then Subtenant shall, promptly, but in no event later than ten (10) days after the occurrence of such event, deliver a replacement Letter of Credit to Sublandlord in the full Letter of Credit Amount and otherwise in accordance with the requirements set forth in this Section 19, and promptly upon Sublandlord's receipt of the replacement Letter of Credit, Sublandlord shall return to Subtenant the Letter of Credit being replaced.

**(c)** If Subtenant fails to perform fully and timely all or any of Subtenant's covenants and obligations set forth in this Sublease, including, without limitation, Subtenant's failure to renew the Letter of Credit at least ninety (90) days prior to the expiration thereof, or if Subtenant has filed a voluntary petition under the federal bankruptcy code or an involuntary petition has been filed against Subtenant under the federal bankruptcy code, Sublandlord may, without notice to Subtenant, execute one or more drafts on the Letter of Credit and apply all or any portion of the Letter of Credit toward fulfillment of Subtenant's unperformed covenants and/or obligations, including any Rent payable by Subtenant that is not paid when due; provided, however, that a failure of Subtenant to renew the Letter of Credit in accordance with this Section 19 shall entitle Sublandlord to execute a draft for the entire amount of the Letter of Credit and such proceeds shall be deemed the property of Sublandlord until such time as Subtenant delivers a replacement Letter of Credit to Sublandlord in the full Letter of Credit Amount and otherwise in accordance with the requirements set forth in this Section 19, and promptly upon Sublandlord's receipt of the replacement Letter of Credit, Sublandlord shall apply the amount of proceeds drawn from the issuing bank upon Subtenant's failure to renew the Letter of Credit against the next due installment(s) of Base Rent under this Sublease. Any proceeds drawn shall constitute the property of Sublandlord and need not be segregated from Sublandlord's other assets. If, as a result of any application or use by Sublandlord of all or any part of the Letter of Credit, the amount of the Letter of Credit shall be less than the Letter of Credit Amount, Subtenant shall, within ten (10) days thereafter, provide Sublandlord with additional letter(s) of credit in an amount equal to the deficiency, and any such additional (or replacement) letter of credit shall comply with all of the provisions of this section and if Subtenant fails to comply with the foregoing, notwithstanding anything to the contrary contained in the Sublease, the same shall constitute an immediate Default by Subtenant.

**(d)** Ninety (90) days after Subtenant vacates the Subleased Premises, upon the expiration or sooner termination of this Sublease, if Subtenant is not then in default, Sublandlord shall return to Subtenant the Letter of Credit (and any unapplied cash balance of the Letter of Credit that had been previously drawn upon); provided that Sublandlord may retain the Letter of Credit (or previously drawn proceeds therefrom) until such time as any Rent (including Additional Rent) due from Subtenant for known defaults in accordance with this Sublease has been determined and paid in full by Subtenant.

**(e)** In no event or circumstance shall the Letter of Credit or any renewal thereof or any proceeds thereof be deemed to be or treated, or intended to serve as a "security deposit" within the meaning of any applicable law or statute. Subtenant hereby waives the provisions of any Laws which establishes the time frame by which Sublandlord must refund collateral or security for performance of a subtenant's obligations under a sublease. Subtenant agrees and acknowledges that Subtenant has no property interest whatsoever in the Letter of Credit or the proceeds thereof and that, in the event Subtenant becomes a debtor under any chapter of the Federal Bankruptcy Code, neither Subtenant, any trustee, nor Subtenant's bankruptcy estate shall have any right to restrict or limit Sublandlord's claim and/or rights to the Letter of Credit and/or the proceeds thereof by application of Section 502(b)(6) of the federal bankruptcy code or otherwise.

**(f)** Should the Permitted Use be amended to accommodate a change in the business of Subtenant or to accommodate a sub-subtenant or assignee, Sublandlord shall have the right to increase the Letter of Credit to the extent necessary, in Sublandlord's reasonable judgment, to account for any increased risk to the Subleased Premises or increased wear and tear that the Subleased Premises may suffer as a result thereof. If a change in control of

Subtenant occurs during the Sublease and following such change the financial condition of Subtenant is, in Sublandlord's reasonable judgment, materially reduced, Subtenant shall deposit such additional monies with Sublandlord as shall be sufficient to cause the Letter of Credit to be at a commercially reasonable level based on said change in financial condition.

(g) Subtenant acknowledges that Sublandlord has the right to transfer its interests in this Sublease. Subtenant agrees that in the event of any such transfer, Sublandlord shall have the right to transfer, assign and/or endorse the Letter of Credit to Sublandlord's master lessors, or other transferees or assignees. Subtenant shall look solely to such parties for the return of the Letter of Credit in accordance with the terms of this Sublease. Subtenant agrees further that, upon Sublandlord's written request, it shall have the Letter of Credit issued, at Subtenant's sole cost and expense, in favor of Sublandlord's master lessor or other transferee or assignee to be held by any such party in accordance with the terms of this Sublease.

## 20. Parking; Signage.

(a) **Parking.** Subtenant shall have Subtenant's proportionate share of such parking rights as Sublandlord may have in connection with the Subleased Premises, as set forth in the Master Lease. Sublandlord shall have the right to pass through to Subtenant any charges payable to Master Landlord under the Master Lease for such parking rights. Subtenant shall pay as Additional Rent all such amounts at the same time and in the same manner as Subtenant pays Base Rent pursuant to Section 4 above.

(b) **Signage.** Subtenant shall not, without the prior written consent of Sublandlord (which consent may be granted or withheld in its sole and absolute discretion) and Master Landlord, post, project, affix, exhibit or display any signs, notices, window or door lettering, placards, decorations, or advertising media of any type which can be viewed from the exterior of the Subleased Premises. Subtenant shall have the right to display, at Subtenant's sole cost and expense, signs bearing Subtenant's name and/or logo at specific locations within the Subleased Premises, subject to the prior written consent of Sublandlord (which consent shall not be unreasonably withheld, conditioned or delayed). Subtenant shall be entitled to Subtenant's signage rights and proportionate share of any Building standard identification signage allowed to the "Tenant" under the Master Lease at Subtenant's sole cost and expense, and subject to Laws and Sublandlord's and Master Landlord's prior written approval, of the design and location of such signage. Upon the expiration or earlier termination of this Sublease, Subtenant shall be responsible for removing any signage described above, repairing any damage caused by such removal, and restoring the area to its prior condition. Subtenant shall in no event be entitled to any exterior Building signage.

21. **Limitation of Liability.** None of the Sublandlord Parties shall have any personal liability for any obligation of Sublandlord under this Sublease or arising in connection herewith or with the operation, management, leasing, subleasing, repair, renovation, alteration or any other matter relating to the Project, the Building or the Subleased Premises, and Subtenant hereby expressly waives and releases such personal liability on behalf of itself and all persons claiming by, through or under Subtenant. Whenever Sublandlord transfers its interest, Sublandlord shall be automatically released from further performance under this Sublease and from all further liabilities and expenses hereunder subject to assumption by the transferee of Sublandlord's interest of all liabilities and obligations of Sublandlord hereunder from the date of such transfer.

## 22. Miscellaneous.

(a) All demands, approvals, consents or notices shall be in writing and delivered by hand or sent by registered or certified mail with return receipt requested, or sent by overnight or same day courier service at the party's respective Address(es) for Notice set forth above in the Basic Sublease Information. Each notice shall be deemed to have been received or given on the earlier to occur of (i) actual delivery or the date on which delivery is refused, (ii) three (3) business days after notice is deposited in the U.S. mail, one (1) business day after notice is deposited with an overnight or same day courier service in the manner described above or the date on which delivery is refused. Any party may, at any time, change its notice address (other than to a post office box address) by giving the other parties written notice of the new address.

(b) Either party's failure to declare a default immediately upon its occurrence or delay in taking action for a default shall not constitute a waiver of the default, nor shall it constitute an estoppel. If either party institutes a

suit against the other for violation of or to enforce any covenant, term or condition of this Sublease, the prevailing party shall be entitled to all of its costs and expenses, including, without limitation, reasonable attorneys' fees.

(c) This Sublease shall be interpreted and enforced in accordance with the Laws of the state in which the Subleased Premises is located.

(d) Subtenant represents and warrants to Sublandlord that it has not dealt with any broker in connection with this Sublease, other than Subtenant's Broker (if any) identified in the Basic Sublease Information. Subtenant agrees to indemnify, defend and hold Sublandlord and Sublandlord Parties party harmless from any commissions due to any broker claiming by, through or under Subtenant.

(e) The Basic Sublease Information set forth above and any Addenda, Exhibits and Schedules attached hereto are incorporated into and made a part of the Sublease. Each reference in this Sublease to any of the Basic Sublease Information shall mean the respective information above. In the event of any conflict between the Basic Sublease Information and the provisions of the Sublease, the provisions of the Sublease shall control. This Sublease constitutes the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements and understandings related to the Subleased Premises. This Sublease may be modified only by a written agreement signed by Sublandlord and Subtenant and consented to by Master Landlord.

(f) Subtenant represents and warrants that the execution, delivery, and performance by Subtenant of its obligations under this Sublease have been duly authorized and will not violate any provision of Laws, any order of any court or other agency of government, or any indenture, agreement or other instrument to which it is a party or by which it is bound.

(g) This Sublease may be executed in multiple counterparts, and by each party on separate counterparts, each of which shall be deemed to be an original but all of which shall together constitute one agreement. Signature pages may be detached from the counterparts and attached to a single copy of this document to physically form one document. This Sublease may be executed in so-called "pdf" format and each party has the right to rely upon a pdf counterpart of this Sublease signed by the other party to the same extent as if such party had received an original counterpart.

(h) Subtenant represents and warrants that neither it, nor any Subtenant Party, (i) is directly or indirectly owned or controlled by any individual or entity included on the List of Specially Designated Nationals and Blocked Persons or the Foreign Sanctions Evaders List maintained by the Office of Foreign Assets Control, Department of the Treasury ("**OFAC**") or any other governmental entity imposing economic sanctions and trade embargoes, (ii) is directly or indirectly owned or controlled by any individual or entity who is located, organized, or resident in a country or territory that is, or whose government is, the target of sanctions imposed by OFAC or any other governmental entity ("**Sanctioned Territory**"); and (iii) shall provide any technology or technical information shared between the parties to any Sanctioned Territory or entity or individual that is a citizen of a Sanctioned Territory; Subtenant shall notify Sublandlord promptly upon knowledge of a violation of the foregoing (i) through (iii).

**23. California Civil Code Section 1938 Statement.** To Sublandlord's actual knowledge, the Subleased Premises has not undergone an inspection by a certified access specialist. For purposes of the preceding sentence, Sublandlord's actual knowledge shall mean and be limited to the actual knowledge of the person who is Sublandlord's Chief Financial Officer (not any other person) on the Effective Date, without any duty of inquiry or investigation, and such Chief Financial Officer shall have no personal liability if such representation is untrue. California Civil Code Section 1938 provides in relevant part as follows: "A Certified Access Specialist (CASP) can inspect the subject premises and determine whether the subject premises comply with all of the applicable construction-related accessibility standards under state law. Although state law does not require a CASp inspection of the subject premises, the commercial property owner or lessor may not prohibit the lessee or tenant from obtaining a CASp inspection of the subject premises for the occupancy or potential occupancy of the lessee or tenant, if requested by the lessee or tenant. The parties shall mutually agree on the arrangements for the time and manner of the CASp inspection, the payment of the fee for the CASp inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the premises." Nothing in this paragraph or California Civil Code Section 1938 shall relieve or modify Subtenant's obligations with respect to (a) compliance with Laws, including without limitation any construction-related accessibility standards, as set forth elsewhere in this Sublease, including,

without limitation, Section 5(a) and Section 8 above, or (b) payment of Additional Rent as set forth in Section 4 above. Subtenant hereby agrees that any Subtenant-initiated CASp inspection (x) shall be at Subtenant's sole cost and expense, and (y) shall take place during normal business hours following reasonable prior written notice to Sublandlord and Master Landlord. Any information contained in a CASp report shall be maintained as confidential. Subtenant, at its sole cost and expense, shall be responsible for making any improvements, alterations, modifications and/or repairs to or within the Subleased Premises to correct violations of construction-related accessibility standards, including, without limitation, any violations disclosed by such CASp inspection; and if such CASp inspection identifies any improvements, alterations, modifications and/or repairs necessary to correct violations of construction-related accessibility standards relating to those items of the Building and/or the Project located outside the Subleased Premises then, at the Master Landlord's election, either Subtenant or the Master Landlord shall perform such improvements, alterations, modifications and/or repairs as and to the extent required by applicable laws to correct such violations, in either instance at Subtenant's sole cost and expense.

**24. Anti-Corruption.** Neither Subtenant nor any of its directors, officers, employees, or any agent, representative, subcontractor or other third party acting for or on Subtenant's behalf (collectively, "**Representatives**"), shall, directly or indirectly, offer, pay, promise to pay, or authorize such offer, promise or payment, of anything of value, to any person, governmental agency, or other entity for the purposes of obtaining any improper advantage in connection with this Sublease. Not by way of limitation of Section 5 of this Sublease, neither Subtenant nor any of its directors, officers or employees shall violate any applicable laws, rules and regulations concerning or relating to public or commercial bribery or corruption ("**Anti-Corruption Laws**"). Within five (5) business days of Sublandlord's written request, Subtenant shall execute and deliver a compliance certification (which certification may be limited to Subtenant's knowledge) with respect to Subtenant's compliance with Anti-Corruption Laws and this Section 24. If Subtenant shall breach the foregoing at any time during the Sublease Term, a Default will be deemed to have occurred, without the necessity of notice to Subtenant.

**25. Confidential Information.** During the Sublease Term, Sublandlord and Subtenant may each receive, obtain, or be given access to, whether directly or indirectly, including through audio or visual observation, information that relates to their respective business, finances, and/or technology (collectively, "**Proprietary Information**"), which such Proprietary Information shall include, without limitation, the existence and contents of this Sublease, the Master Lease, the Subleased Premises, the Building and the Project. Sublandlord and Subtenant shall each (i) not use the Proprietary Information for any purpose, except as is necessary to perform its obligations hereunder, (ii) not disclose any Proprietary Information, or component thereof, to any third party, (iii) within their respective organization, only disclose Proprietary Information to those Sublandlord Parties and Subtenant Parties, as applicable, who need such Proprietary Information for the purposes of performing the obligations hereunder and who are bound by obligations of confidentiality with respect to such Proprietary Information at least as protective as those contained herein, and (iv) use best efforts to protect the confidentiality of the Proprietary Information. Sublandlord and Subtenant shall each notify the other of any unauthorized use or disclosure of Proprietary Information and to take all actions reasonably necessary to prevent further unauthorized use or disclosure thereof. Sublandlord and Subtenant each also recognizes and agrees that they have no expectation of privacy with respect to Sublandlord's or Subtenant's, as applicable, telecommunications, networking or information processing systems (including, without limitation, stored computer files, email messages and voice messages) and that their respective activity, and any files or messages, on or using any of those systems may be monitored at any time without notice.

**26. No Publicity.** Sublandlord and Subtenant each hereby acknowledges and agrees that it shall not use, without the other's prior written approval, which may be withheld in such party's sole discretion, the name of the other party, its affiliates, trade names, trademarks or trade dress, products, or any signs, markings, or symbols from which a connection to such party may be reasonably inferred or implied, in any manner whatsoever, including, without limitation, press releases, marketing materials, or advertisements.

**[Signature Page Follows]**

IN WITNESS WHEREOF, Sublandlord and Subtenant have executed this Sublease effective as of Effective Date above written, on the dates set forth below.

**SUBLANDLORD:**

**DYNAVAX TECHNOLOGIES CORP.,**  
a Delaware corporation

By: /s/ Kelly MacDonald  
Name: Kelly MacDonald  
Title: CFO

**SUBTENANT:**

**METAGENOMI, INC.**  
a Delaware corporation

By: /s/ Jian Irish  
Name: Jian Irish  
Title: Chief Operating Officer

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-276983) of Metagenomi, Inc. of our report dated March 27, 2024 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP  
San Jose, California  
March 27, 2024

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**CERTIFICATION PURSUANT TO  
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,  
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Brian C. Thomas, certify that:

1. I have reviewed this Form 10-K for the Annual Period Ended December 31, 2023 of Metagenomi, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 27, 2024

By: \_\_\_\_\_ /s/ Brian C. Thomas

**Brian C. Thomas, Ph.D.**  
**Chief Executive Officer**  
**(Principal Executive Officer)**



**CERTIFICATION PURSUANT TO  
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,  
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Pamela Wapnick, certify that:

1. I have reviewed this Form 10-K for the Annual Period Ended December 31, 2023 of Metagenomi, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 27, 2024

By: \_\_\_\_\_ /s/ Pamela Wapnick  
**Pamela Wapnick, MBA**  
**Chief Financial Officer**  
**(Principal Financial Officer and Principal Accounting Officer)**

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**CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO  
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Metagenomi, Inc. (the "Company") for the fiscal year ended December 31, 2023 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of their knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 27, 2024

By: \_\_\_\_\_ /s/ Brian C. Thomas  
**Brian C. Thomas, Ph.D.**  
**Chief Executive Officer**  
**(Principal Executive Officer)**

Date: March 27, 2024

By: \_\_\_\_\_ /s/ Pamela Wapnick  
**Pamela Wapnick, MBA**  
**Chief Financial Officer**  
**(Principal Financial Officer and Principal Accounting Officer)**

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**METAGENOMI, INC.**  
**COMPENSATION RECOVERY POLICY**

**Adopted as of January 26, 2024**

Metagenomi, Inc., a Delaware corporation (the “Company”), has adopted a Compensation Recovery Policy (this “Policy”) as described below.

**1. Overview**

The Policy sets forth the circumstances and procedures under which the Company shall recover Erroneously Awarded Compensation from Covered Persons (as defined below) in accordance with rules issued by the United States Securities and Exchange Commission (the “SEC”) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and the Nasdaq Stock Market. Capitalized terms used and not otherwise defined herein shall have the meanings given in Section 3 below.

**2. Compensation Recovery Requirement**

In the event the Company is required to prepare a Financial Restatement, the Company shall recover reasonably promptly all Erroneously Awarded Compensation with respect to such Financial Restatement.

**3. Definitions**

- a. “Applicable Recovery Period” means the three completed fiscal years immediately preceding the Restatement Date for a Financial Restatement. In addition, in the event the Company has changed its fiscal year: (i) any transition period of less than nine months occurring within or immediately following such three completed fiscal years shall also be part of such Applicable Recovery Period and (ii) any transition period of nine to 12 months will be deemed to be a completed fiscal year.
  - b. “Applicable Rules” means any rules or regulations adopted by the Exchange pursuant to Rule 10D-1 under the Exchange Act and any applicable rules or regulations adopted by the SEC pursuant to Section 10D of the Exchange Act.
  - c. “Board” means the Board of Directors of the Company.
  - d. “Committee” means the Compensation Committee of the Board or, in the absence of such committee, a majority of independent directors serving on the Board.
  - e. “Covered Person” means any Executive Officer. A person’s status as a Covered Person with respect to Erroneously Awarded Compensation shall be determined as of the time of receipt of such Erroneously Awarded Compensation regardless of such person’s current role or status with the Company (e.g., if a person began service as an Executive
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Officer after the beginning of an Applicable Recovery Period, that person would not be considered a Covered Person with respect to Erroneously Awarded Compensation received before the person began service as an Executive Officer, but would be considered a Covered Person with respect to Erroneously Awarded Compensation received after the person began service as an Executive Officer where such person served as an Executive Officer at any time during the performance period for such Erroneously Awarded Compensation).

- f. “Effective Date” means January 5, 2024.
- g. “Erroneously Awarded Compensation” means the amount of any Incentive-Based Compensation received by a Covered Person on or after the Effective Date and during the Applicable Recovery Period that exceeds the amount that otherwise would have been received by the Covered Person had such compensation been determined based on the restated amounts in a Financial Restatement, computed without regard to any taxes paid. Calculation of Erroneously Awarded Compensation with respect to Incentive-Based Compensation based on stock price or total shareholder return, where the amount of Erroneously Awarded Compensation is not subject to mathematical recalculation directly from the information in a Financial Restatement, shall be based on a reasonable estimate of the effect of the Financial Restatement on the stock price or total shareholder return upon which the Incentive-Based Compensation was received, and the Company shall maintain documentation of the determination of such reasonable estimate and provide such documentation to the Exchange in accordance with the Applicable Rules. Incentive-Based Compensation is deemed received, earned or vested when the Financial Reporting Measure is attained, not when the actual payment, grant or vesting occurs.
- h. “Exchange” means the Nasdaq Stock Market LLC.
- i. An “Executive Officer” means any person who served the Company in any of the following roles at any time during the performance period applicable to Incentive-Based Compensation and received Incentive-Based Compensation after beginning service in any such role (regardless of whether such Incentive-Based Compensation was received during or after such person’s service in such role): the president, principal financial officer, principal accounting officer (or if there is no such accounting officer, the controller), any vice president in charge of a principal business unit, division, or function (such as sales, administration, or finance), any other officer who performs a policy making function, or any other person who performs similar policy making functions for the Company. Executive officers of parents or subsidiaries of the Company may be deemed executive officers of the Company if they perform such policy making functions for the Company.
- j. “Financial Reporting Measures” mean measures that are determined and presented in accordance with the accounting principles used in preparing the Company’s financial statements, any measures that are derived wholly or in part from such measures (including, for example, a non-GAAP financial measure), and stock price and total shareholder return.

- k. “GAAP” means generally accepted accounting principles in the United States of America.
- l. “Incentive-Based Compensation” means any compensation provided, directly or indirectly, by the Company or any of its subsidiaries that is granted, earned, or vested based, in whole or in part, upon the attainment of a Financial Reporting Measure and any other equity-based compensation provided by the Company or any of its subsidiaries, including, without limitation, stock options, restricted stock awards, restricted stock units and stock appreciation rights.
- m. A “Financial Restatement” means a restatement of previously issued financial statements of the Company due to the material noncompliance of the Company with any financial reporting requirement under the securities laws, including any required restatement to correct an error in previously-issued financial statements that is material to the previously-issued financial statements or that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period.
- n. “Restatement Date” means, with respect to a Financial Restatement, the earlier to occur of: (i) the date the Board concludes, or reasonably should have concluded, that the Company is required to prepare the Financial Restatement or (ii) the date a court, regulator or other legally authorized body directs the Company to prepare the Financial Restatement.

#### **4. Exception to Compensation Recovery Requirement**

The Company may elect not to recover Erroneously Awarded Compensation pursuant to this Policy if the Committee determines that recovery would be impracticable, and one or more of the following conditions, together with any further requirements set forth in the Applicable Rules, are met: (i) the direct expense paid to a third party, including outside legal counsel, to assist in enforcing this Policy would exceed the amount to be recovered, and the Company has made a reasonable attempt to recover such Erroneously Awarded Compensation; or (ii) recovery would likely cause an otherwise tax-qualified retirement plan to fail to be so qualified under applicable regulations.

#### **5. Recovery from Participating Employees**

In addition to (and without limiting) the provisions of paragraph 2 above, in the event the Company is required to prepare a Financial Restatement after the Effective Date, the Company may recover from any current or former employee of the Company who is not a Covered Person (each a “Participating Employee”) and who received Incentive-Based Compensation from the Company during the three completed fiscal years immediately preceding the date on which the Board or the Audit Committee of the Board (the “Audit Committee”) determines that the Company is required to prepare a Financial Restatement, the amount that exceeds what would have been paid to the Participating Employee under the Financial Restatement; provided that, this paragraph 5 will apply only to the extent the Board (or a duly established committee thereof), in its sole discretion, determines that the Participating Employee committed any act or omission that materially

contributed to the circumstances requiring the Financial Restatement and such act or omission involved any of the following: (i) misconduct, wrongdoing or a violation of any of the Company's rules or of any applicable legal or regulatory requirements in the course of the Participating Employee's employment by the Company; or (ii) a breach of a fiduciary duty to the Company or its stockholders by the Participating Employee.

## **6. Recovery Where Intentional Misconduct**

In addition to (and without limiting) the provisions of paragraphs 2 and 5 above, in the event the Company is required to prepare a Financial Restatement after the Effective Date and the Board (or a duly established committee thereof), in its sole discretion, determines that a Covered Person's or a Participating Employee's act or omission contributed to the circumstances requiring the Financial Restatement and such act or omission involved any of the following: (i) willful, knowing or intentional misconduct or a willful, knowing or intentional violation of any of the Company's rules or any applicable legal or regulatory requirements in the course of the Covered Person's or the Participating Employee's employment by the Company or (ii) fraud in the course of the Covered Person's or the Participating Employee's employment by the Company, the Company will use reasonable efforts to recover from such Covered Person or Participating Employee up to 100% (as determined by the Board or a duly established committee thereof in its sole discretion) of the Incentive-Based Compensation received by such Covered Person or Participating Employee from the Company during the three fiscal years preceding the date on which the Company determined that it is required to prepare a Financial Restatement.

## **7. Tax Considerations**

To the extent that, pursuant to this Policy, the Company is entitled to recover any Erroneously Awarded Compensation that is received by a Covered Person, the gross amount received (i.e., the amount the Covered Person received, or was entitled to receive, before any deductions for tax withholding or other payments) shall be returned by the Covered Person.

## **8. Method of Compensation Recovery**

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[1] Institutional Shareholder Services ("ISS") has stated that, in order to receive points for having a clawback policy on the ISS Equity Plan Scorecard ("EPSC"), the clawback policy should authorize recovery upon a financial restatement and cover all or most equity-based compensation for all NEOs (including both time- and performance vesting equity awards). Accordingly, a clawback policy that adheres to the minimum requirements of the SEC's finalized clawback rules will not receive EPSC points. Glass Lewis has been increasingly focusing attention on the specific terms of recoupment policies beyond whether a company maintains a clawback that simply satisfies the minimum legal requirements and has stated that recoupment policies that empower companies to recover compensation without regard to a restatement "may inform our overall view" of the compensation program in the future. To address these proxy advisory firm expectations and for other reasons, before effectiveness of the new SEC compensation recovery rules, many companies adopted clawback policies that were broader than the SEC's rules while, at the same time, being discretionary in nature (unlike the mandatory aspects of the SEC requirements). Paragraphs 5 and 6 are optional expanded clawback provisions for the Board's consideration. Paragraph 5 extends the Policy to a broader universe of employees. Paragraph 6 expands the universe of reasons why a clawback could be invoked.

The Committee shall determine, in its sole discretion, the method for recovering Erroneously Awarded Compensation hereunder, which may include, without limitation, any one or more of the following:

- a. requiring reimbursement of cash Incentive-Based Compensation previously paid;
- b. seeking recovery of any gain realized on the vesting, exercise, settlement, sale, transfer or other disposition of any equity-based awards;
- c. cancelling or rescinding some or all outstanding vested or unvested equity-based awards;
- d. adjusting or withholding from unpaid compensation or other set-off;
- e. cancelling or offsetting against planned future grants of equity-based awards; and/or
- f. any other method permitted by applicable law or contract.

Notwithstanding the foregoing, a Covered Person will be deemed to have satisfied such person's obligation to return Erroneously Awarded Compensation to the Company if such Erroneously Awarded Compensation is returned in the exact same form in which it was received; provided that equity withheld to satisfy tax obligations will be deemed to have been received in cash in an amount equal to the tax withholding payment made.

## **9. Policy Interpretation**

This Policy shall be interpreted in a manner that is consistent with the Applicable Rules and any other applicable law. The Committee shall take into consideration any applicable interpretations and guidance of the SEC in interpreting this Policy, including, for example, in determining whether a financial restatement qualifies as a Financial Restatement hereunder. To the extent the Applicable Rules require recovery of Incentive-Based Compensation in additional circumstances besides those specified above, nothing in this Policy shall be deemed to limit or restrict the right or obligation of the Company to recover Incentive-Based Compensation to the fullest extent required by the Applicable Rules.

## **10. Policy Administration**

This Policy shall be administered by the Committee; provided, however, that the Board shall have exclusive authority to authorize the Company to prepare a Financial Restatement. In doing so, the Board may rely on a recommendation of the Audit Committee of the Board. The Committee shall have such powers and authorities related to the administration of this Policy as are consistent with the governing documents of the Company and applicable law. The Committee shall have full power and authority to take, or direct the taking of, all actions and to make all determinations required or provided for under this Policy and shall have full power and authority to take, or direct the taking of, all such other actions and make all such other determinations not inconsistent with the specific terms and provisions of this Policy that the Committee deems to be necessary or appropriate to the administration of this Policy. The interpretation and construction by the

Committee of any provision of this Policy and all determinations made by the Committee under this policy shall be final, binding and conclusive.

**11. Compensation Recovery Repayments not Subject to Indemnification**

Notwithstanding anything to the contrary set forth in any agreement with, or the organizational documents of, the Company or any of its subsidiaries, Covered Persons are not entitled to indemnification for Erroneously Awarded Compensation or for any losses arising out of or in any way related to Erroneously Awarded Compensation recovered under this Policy.



