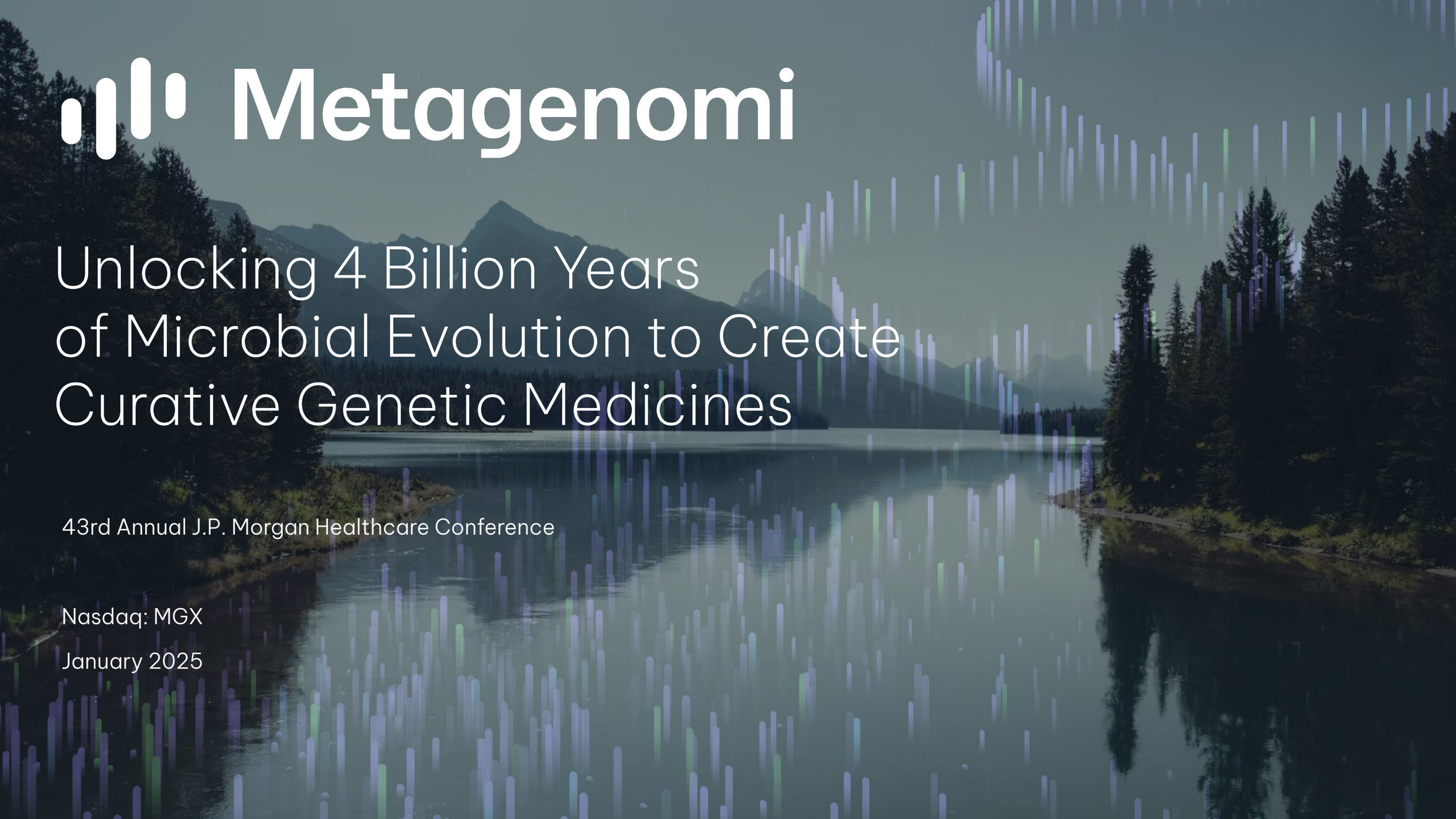


Metagenomi

Unlocking 4 Billion Years of Microbial Evolution to Create Curative Genetic Medicines

43rd Annual J.P. Morgan Healthcare Conference

Nasdaq: MGX

January 2025

Forward Looking Statements

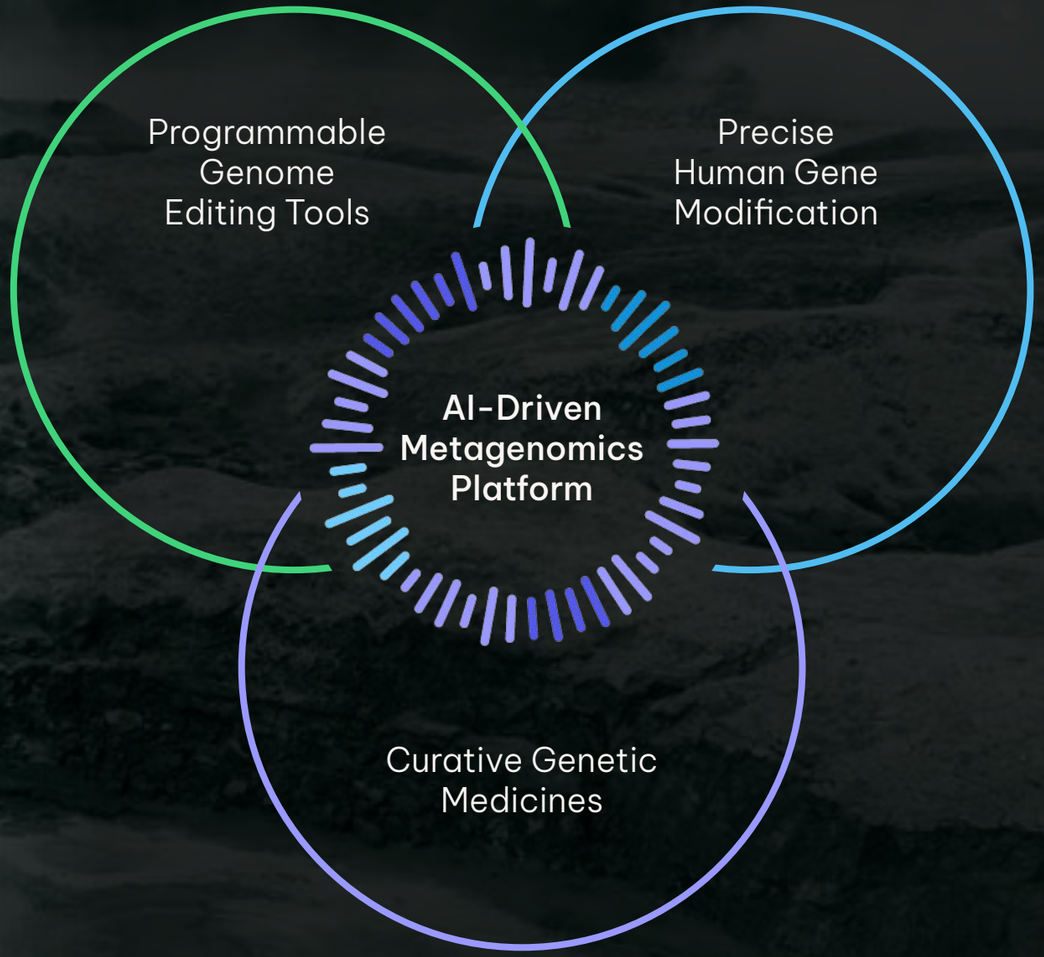
This presentation includes forward-looking statements, including forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained in this presentation are forward looking statements, including statements regarding our cash runway, strategy and plans, industry environment, potential growth opportunities, and the therapeutic potential of our programs. The words “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “ design,” “expect,” “could,” “plan,” “potential,” “predict,” “seek,” “should,” “would,” or the negative version of these words and similar expressions are intended to identify forward-looking statements.

We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short and long term business operations and objectives, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including but not limited to, our ability to develop and advance our programs and product candidates, our ability to maintain and establish collaborations or strategic partnerships, our regulatory approvals and filings, and other risks, uncertainties and assumptions identified in our filings with the Securities and Exchange Commission (the “SEC”), including our most recent Form 10-K and Form 10-Q filed with the SEC, and any subsequent filings with the SEC.

Moreover, we operate in a very competitive and rapidly changing environment and it is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking statements and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations, unless required by law.

Our Vision:

Harness the power of our metagenomics platform to create curative genetic medicines for patients



The metagenomics platform is the foundation of our gene editing toolbox

Proprietary Sampling

Exploring diverse microbe-rich ecosystems to extract DNA from environmental samples

AI-powered Screening

Leveraging AI, ancestral reconstruction, proprietary algorithms, robotics, and automation to reveal novel cellular machinery

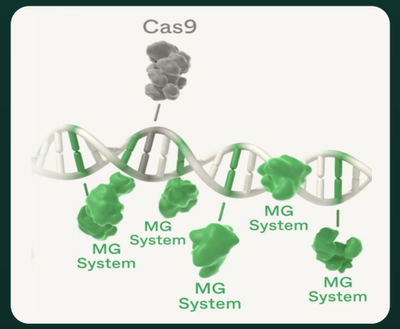
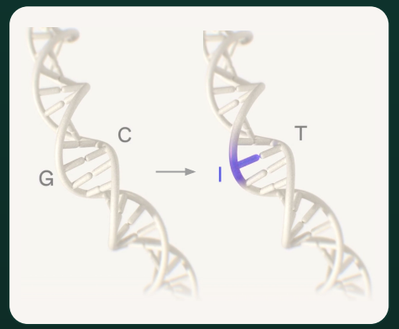
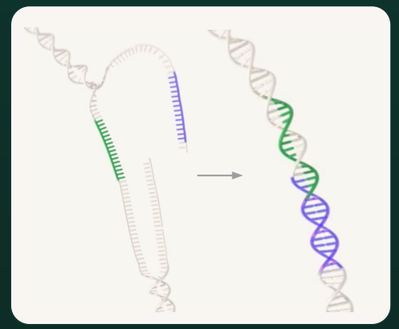
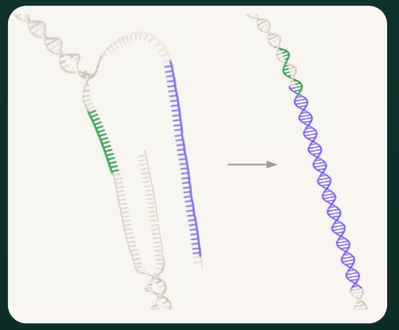
Engineering & Optimization

Designing and optimizing novel gene editing tools to set new standards in targetability, precision, efficiency, and scope of editing capabilities

Complete Genome Editing Capabilities

Building a proprietary toolbox capable of correcting any genetic muta tion anywhere in the human genome

Our proprietary toolbox enables precise edits of the human genome

MG Tool	Nuclease	Base Editors	RIGS: Replacement	RIGS: Integration	CAST
					
	Proprietary library of highly precise and efficient nucleases, including ultra-small systems (SMARTs), provides programmable chassis for other gene editing tools	Programmable chassis with additional effector enzymes to cause single nucleotide changes	RNA-mediated integration systems (RIGS) use programmable chassis with additional reverse transcriptase for edits encoded in RNA templates	RIGS with expanded RNA template for site-specific integration of genes	CRISPR-associated transposases (CAST) use DNA templates to allow for site-specific gene integration
Genomic Correction	*Knockdown, knock-in, exon skipping*	*Single nucleotide changes*	*1-100 base pair replacement, insertion, or deletion*	*>100 base pair integrations*	*>10,000 base pair integrations*

Broad pipeline built on our gene editing platform

Editing Platform	Delivery	Indication / Editing Target	Discovery	Lead Optimization	IND-Enabling	Clinical	Partner
LIVER	LNP + AAV	Hemophilia A / ALB					
Knock-in		Undisclosed secreted protein diseases					
Knockdown	LNP	Transthyretin Amyloidosis / TTR					IONIS
		Refractory Hypertension / AGT					IONIS
		Undisclosed cardiovascular disease					IONIS
		Undisclosed cardiovascular disease					IONIS
		Other Program: Primary Hyperoxaluria Type 1 / HAO1					
Small gene corrections	LNP	Alpha 1 Antitrypsin Deficiency / SERPINA1					
Large gene insertion	LNP	Wilson's Disease / ATP7B					
CELL THERAPY	Ex vivo	Solid tumor indications / TCR T Cells					affini
Multiplex editing		*Multiplex editing:* Undisclosed cell therapy applications					
NEURO-MUSCULAR	LNP / AAV	*Programs in Research:* Familial ALS, Duchenne Muscular Dystrophy, Charcot Marie Tooth Disease					
Ultra small systems							
LUNG, KIDNEY	LNP / AAV	*Programs in Research:* Undisclosed renal diseases, Cystic Fibrosis					
Large gene insertion							

2024 milestones and key publications

Hemophilia A Program

- ✓ Declared MGX-001, wholly-owned Development Candidate (DC)
- ✓ Factor VIII activity sustained in NHP study for more than 16 months presented at ASH [1]
- ✓ Initial regulatory engagement with FDA
- ✓ GxP Manufacturing activities initiated

Secreted Protein Deficiencies

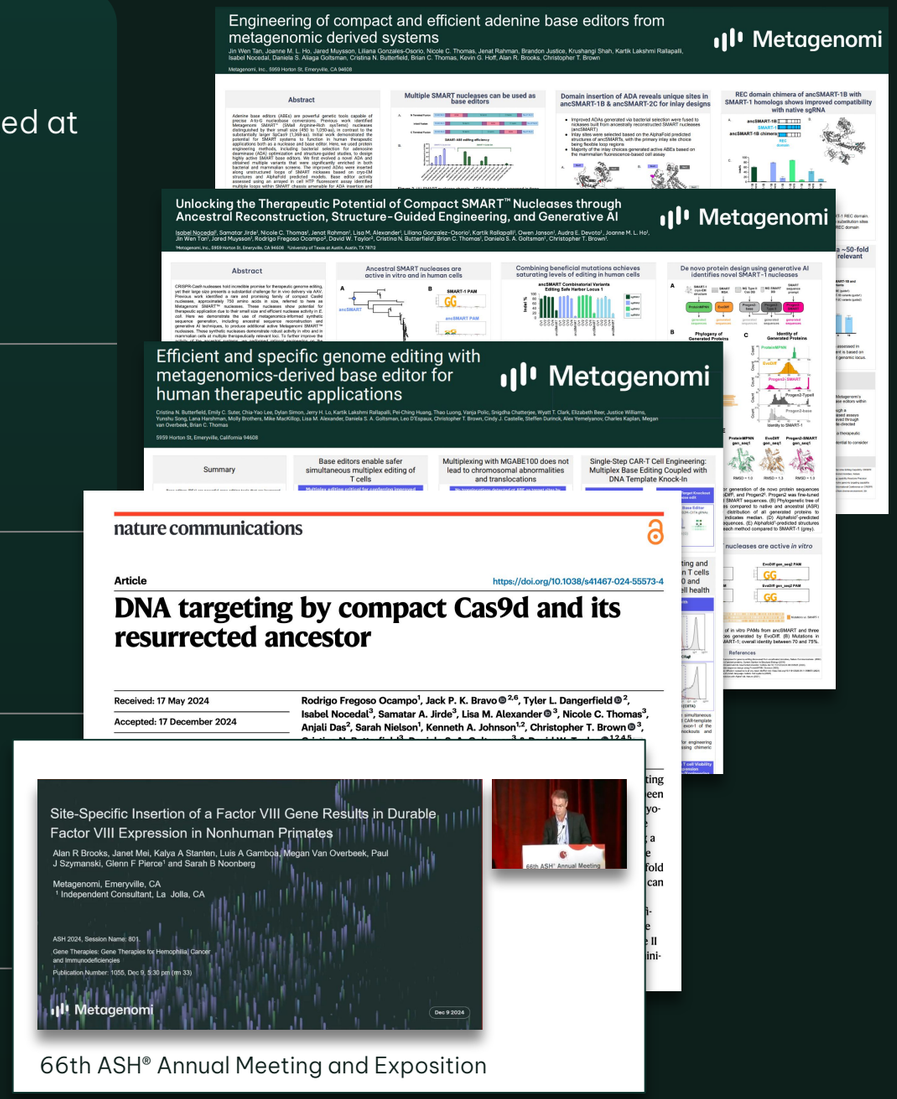
- ✓ In vivo proof-of-concept (PoC) achieved with initial targets

Cardiometabolic Programs

- ✓ All four Wave 1 collaboration targets in lead optimization
- ✓ In vivo rodent PoC achieved for all targets

Other Therapeutic Programs / Technology Development

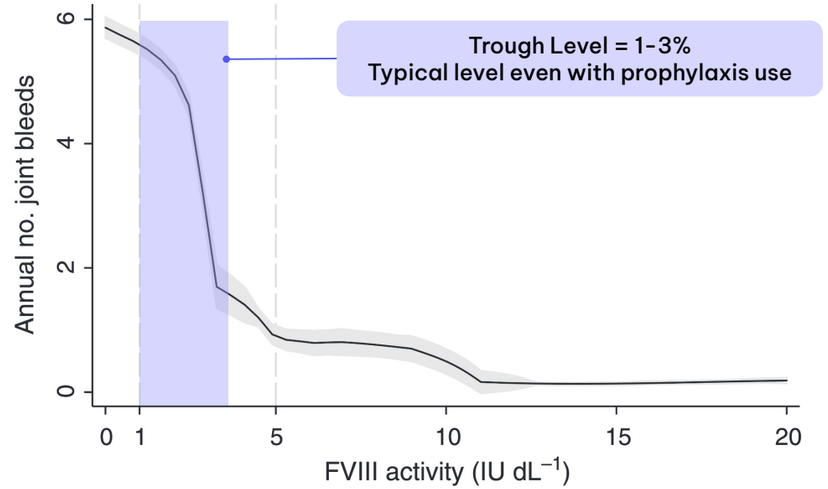
- ✓ AI-enabled nuclease and base editor development presented at CSHL [2]
- ✓ Multiplex base editing data presented at ESGCT [3]
- ✓ Ultra-small nucleases published in *Nature Communications* [4]



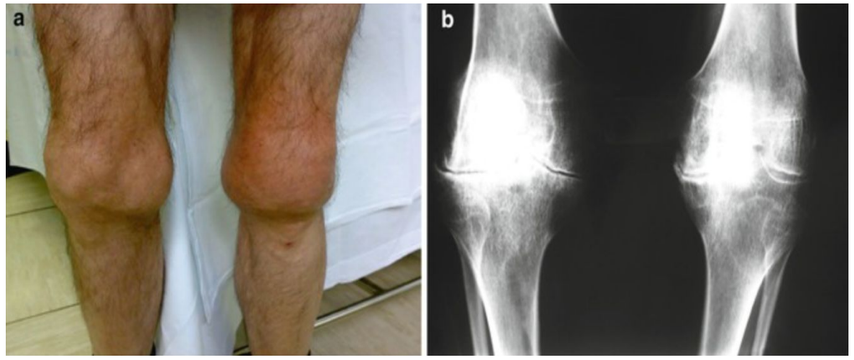
1. American Society of Hematology (ASH) 66th Annual Meeting and Exposition, San Diego, December 2024
2. 10th meeting on Genome Engineering: CRISPR Frontiers at Cold Spring Harbor Laboratory, New York, August 2024
3. European Society of Gene and Cell Therapy (ESGCT) 31st Annual Congress in Rome, Italy, October 2024
4. https://doi.org/10.1038/s41467-024-55573-4

All posters and publications can be found at https://metagenomi.co/news/posters-publications

A life-altering bleeding disorder



Adapted from Den Uijl et al, 2011. Haemophilia. Vol. 17, pp. 849-853



International Hemophilia Training Center, 2024. Hemophilia Joint Bleeds. https://www.ihtc.org/hemophilia-joint-bleeds. Accessed 23 Aug. 2024.

Disease Background

- Most common X-linked inherited bleeding disorder; vast majority of patients are male
- Caused by large variety of mutations in the Factor VIII (FVIII) gene leading to loss of functional FVIII protein
- Intracranial bleeding is of greatest concern as this can lead to major morbidity and mortality
- Bleeding into joints leads to cumulative joint damage and is a major cause of morbidity
- Diagnosis typically occurs in infancy due to exaggerated bleeding in response to minor injury or routine medical procedures

Prevalence

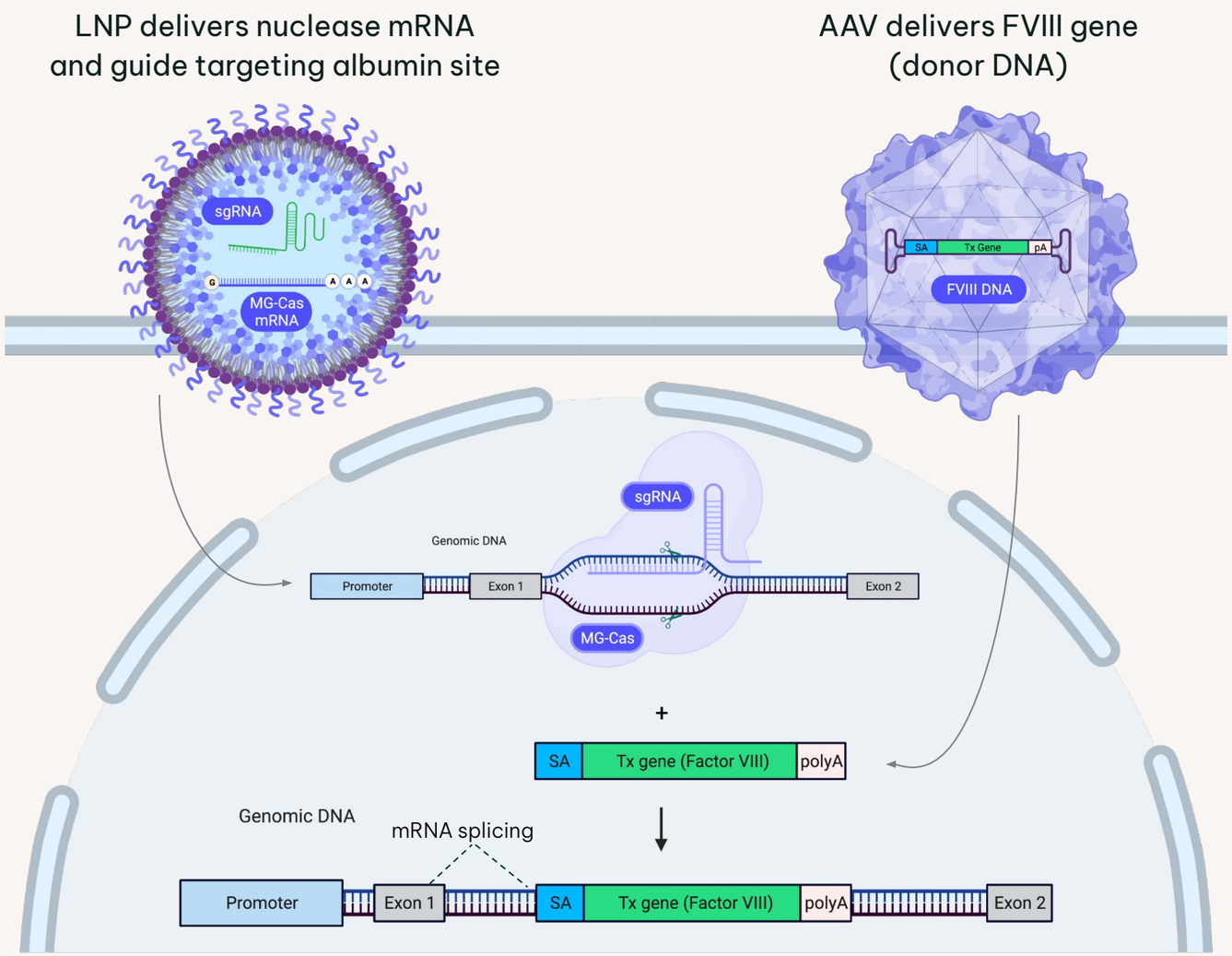
- Up to **26,500** patients in US [1]
- More than **500,000** patients globally [2]

1. Soucie, J.M., et al, 2020. Haemophilia. Vol. 26, no. 3, pp. 487-493.
2. Stonebraker, J. S., et al, 2010. Haemophilia. Vol. 16, pp. 20-32.

An investigational gene editing therapeutic for hemophilia A

Genome editing approach

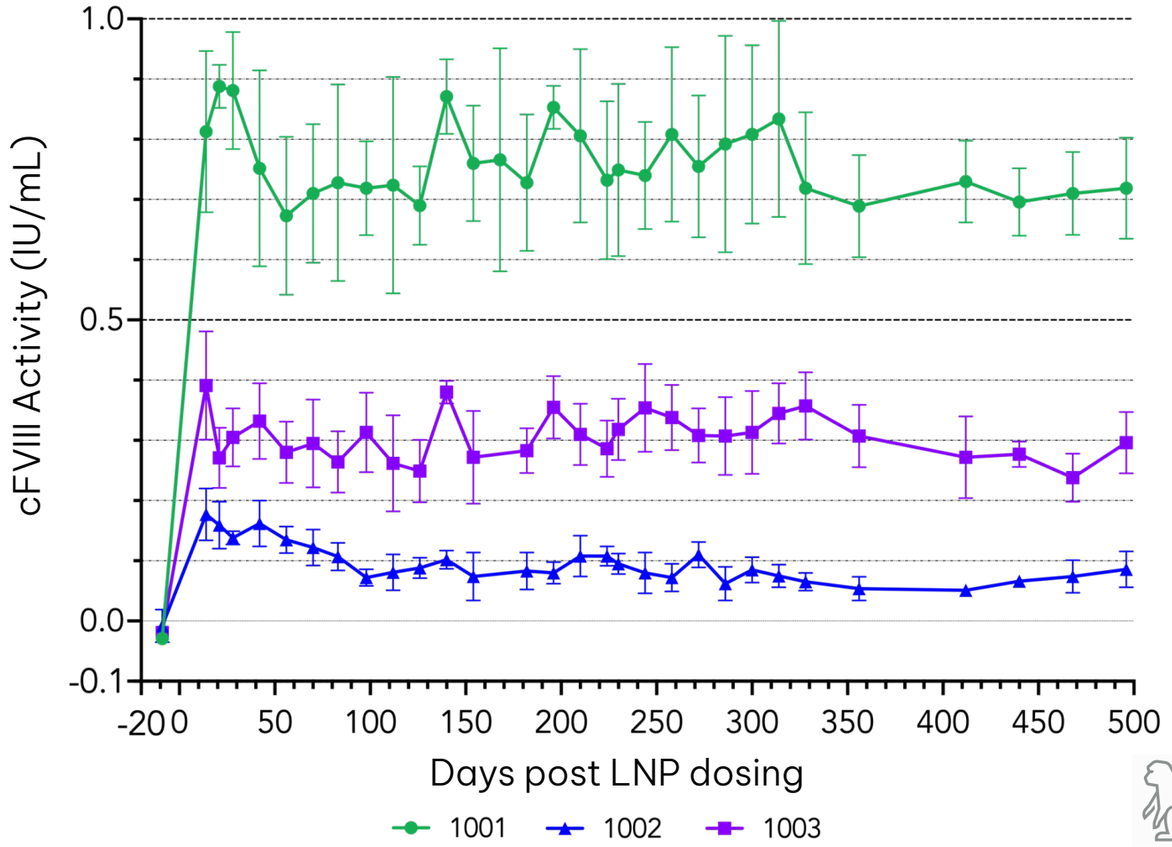
- MG nuclease creates efficient and specific cut at safe harbor locus in albumin gene
- Factor VIII donor DNA is inserted at cut site
- Strength of albumin promoter provides high level of FVIII expression even at low integration rates
- Mechanistically different from AAV gene therapy
  - Integrated vs episomal FVIII gene
  - Native promoter vs exogenous promoter



Robust in vivo data supports advancing to the clinic

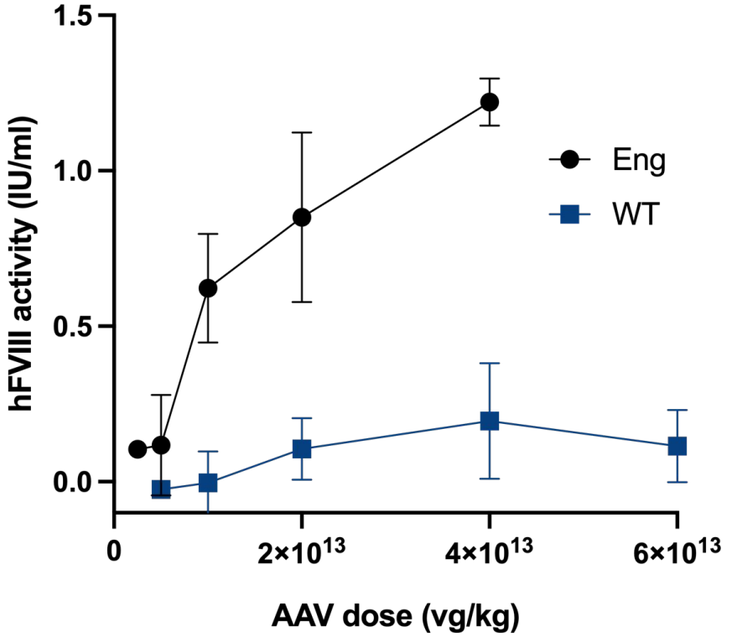
Durable FVIII activity achieved in non-human primates (NHP)

Wild-type FVIII activity levels sustained for 16.5 months
(Data cutoff: 11-13-24)



Mouse dose dependent FVIII activity

Bioengineered FVIII construct used in MGX-001 has higher activity than wild-type FVIII



Factor VIII activity values are the mean and standard deviation of at least 3 independent assay runs with each sample run in at least duplicate in each assay

The day 168 plasma sample for 1002 and 1003 were excluded because they appear to have been switched (mis-labelled) at the CRO

Data source: "Site-Specific Insertion of Factor VIII Gene Results in Durable Factor VIII Expression in Nonhuman Primates," oral presentation at American Society of Hematology (ASH) 66th Annual Meeting and Exposition, San Diego, December 2024

No off-target editing observed across multiple hepatocyte donors

Potential OT site discovery

Three orthogonal methods:

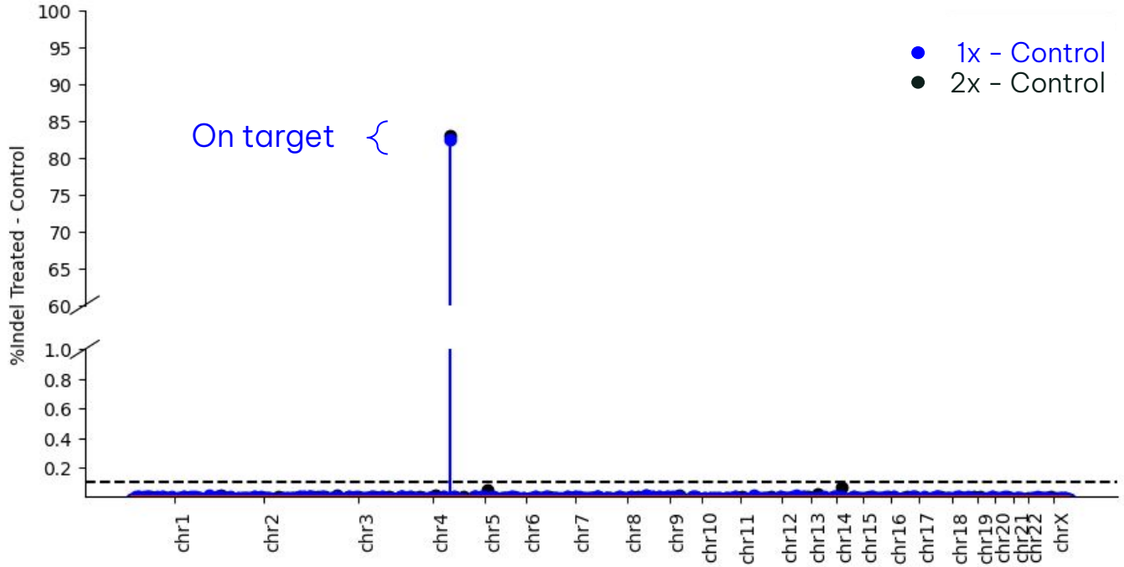
- In silico prediction
- In cell assay
- Biochemical (in vitro) assay

⇒ 481 potential sites

Interrogate all 481 sites for editing

- PHH edited at a dose that results in saturating editing and a dose 2x higher
- Perform sensitive amplicon sequencing

No off-target editing observed

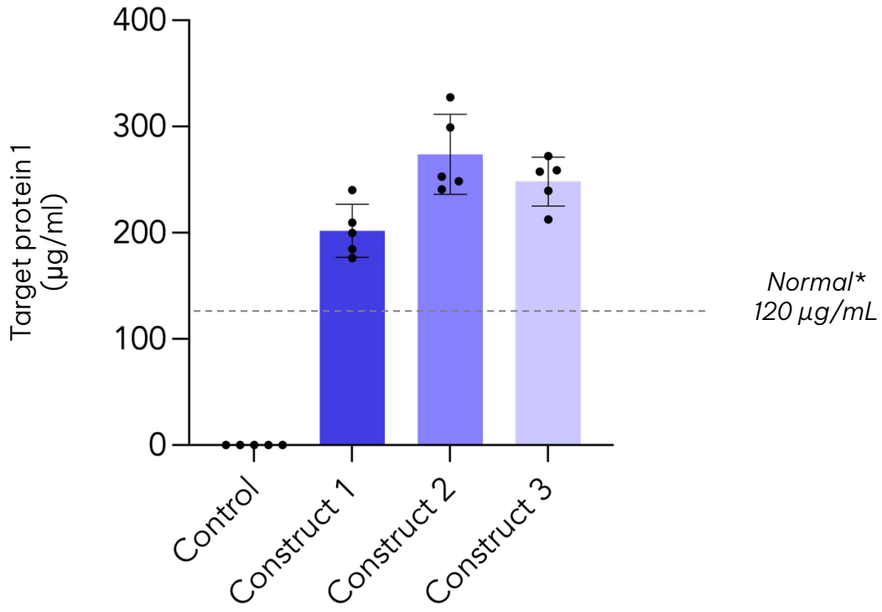


Data Source: "Specific and efficient genome editing with metagenomics-derived tools for in vivo and ex vivo therapeutic applications", Nature Conference: RNA bench to bedside, December 11, 2024

Secreted Protein Deficiencies

Addressing secreted protein diseases with large gene insertion

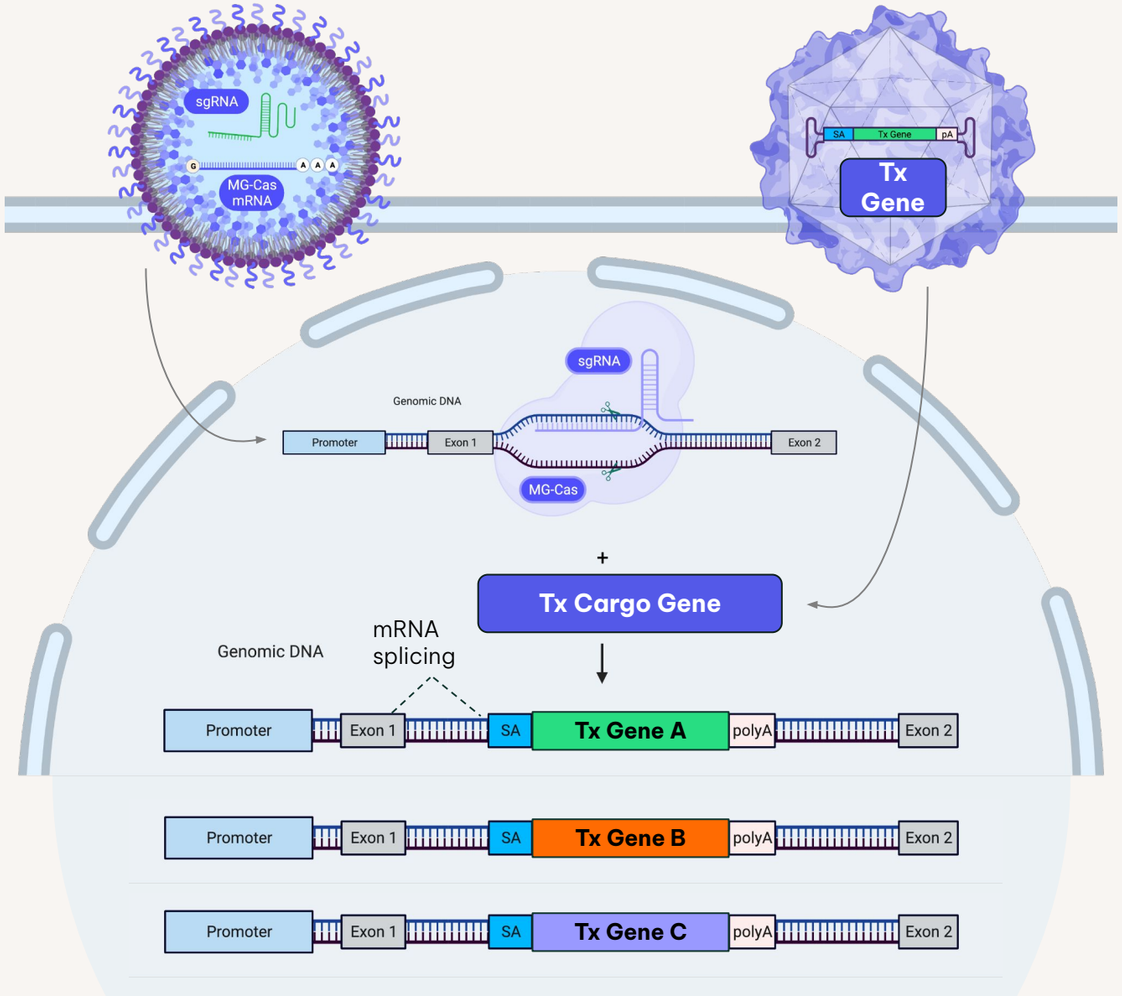
Target protein in mice can achieve normal circulating levels with multiple construct designs



- >200% of normal human protein expression achieved in mouse plasma
- Insertion assessed with multiple DNA template constructs
- LNP and AAV dose titration can be used to fine tune therapeutic window

LNP delivers nuclease mRNA and guide targeting albumin site

AAV delivers donor DNA



Refractory Hypertension

Rodent proof-of-concept achieved

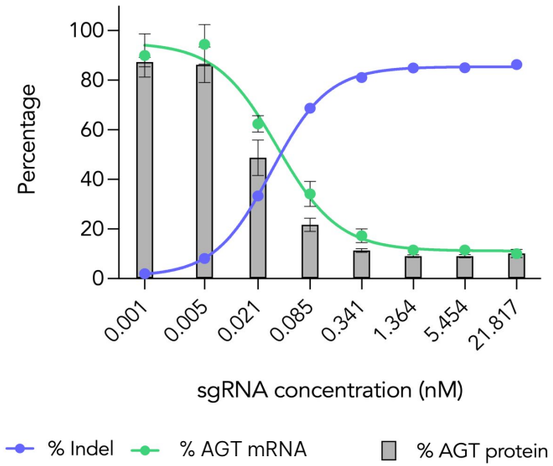
Partnered with IONIS

Refractory hypertension is characterized as uncontrolled hypertension despite the use of five or more drugs and is a significant risk for major cardiovascular events[1]

Prevalence: 900K adults with refractory hypertension in the US[2]

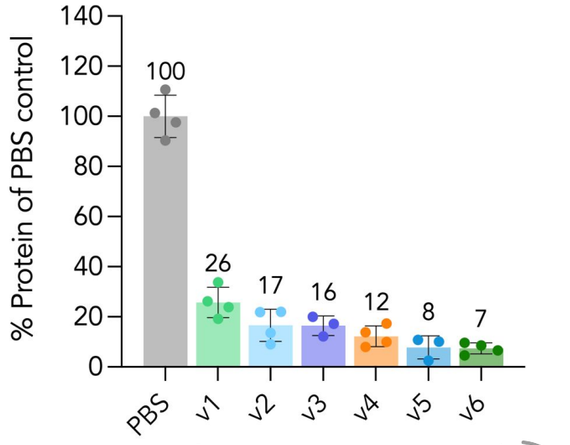
Dose dependent editing, mRNA and protein knockdown in primary human hepatocytes

>85% editing, 90% mRNA and protein knockdown



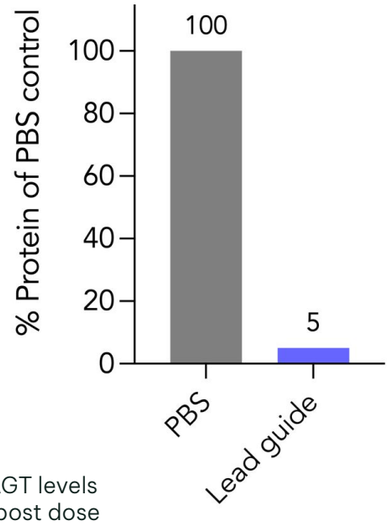
mRNA, gRNA, and LNP were optimized to increase potency

Human AGT transgenic mice
LNP dosed at 0.1 mg/kg



95% protein knockdown in spontaneous hypertensive rats

Evaluation of blood pressure reduction planned in longer term study



Plasma AGT levels
2 weeks post dose

1. Acelajado, M. C., et. al. 2019. Treatment…Circulation Research, 124(7), 1061–1070
2. Yoon, M. et al. 2022. “Prevalence...” Hypertension Research, vol. 45, no. 8, pp. 1353–1362

Anticipated milestones allow advancement towards the clinic

	2025	2026
Hemophilia A Program	• Complete ongoing NHP durability study • Conduct Pre-IND and ex-US regulatory meetings	• IND / CTA filings
Secreted Protein Deficiencies	• Disclose lead indication for secreted protein deficiency platform • Achieve NHP PoC	• Nominate DC
Cardiometabolic Programs	• Nominate 1-2 DCs • Disclose indications for remaining Wave 1 targets	• Initiate IND enabling activities • Additional DCs for Wave 1 targets
Other Therapeutic Programs / Technology Development	• Continue to advance early-stage pipeline for multiple future IND filings	

IND = Investigational New Drug
CTA = Clinical Trial Authorization

Metagenomi: Pipeline advancing, positioned for success

Driving towards clinic with wholly-owned MGX-001 in hemophilia A

Leveraging MGX-001 to establish secreted protein deficiencies platform

Advancing cardiometabolic programs with Ionis

Progressing additional wholly owned therapeutic candidates

Realizing the potential of our AI-enabled gene editing capabilities

Well capitalized with cash runway into 2027

Harnessing the power of our metagenomics platform to create curative genetic medicines for patients