

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

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 13, 2025

Metagenomi, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-41949
(Commission File Number)

81-3909017
(IRS Employer
Identification No.)

5959 Horton Street
7th Floor
Emeryville, California
(Address of Principal Executive Offices)

94608
(Zip Code)

Registrant's Telephone Number, Including Area Code: (510) 871-4880

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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, \$0.0001 par value per share	MGX	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

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

Item 2.02 Results of Operations and Financial Condition.

On May 13, 2025, Metagenomi, Inc. (the “Company”) announced its financial results for the quarter ended March 31, 2025 and additional business updates. A copy of the press release in connection with the announcement is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K (including Exhibit 99.1 attached hereto) is intended to be furnished and shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the “Securities Act”), except as expressly set forth by specific reference in such filing.

Item 7.01 Regulation FD Disclosure.

A copy of the Company’s May 2025 corporate presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information contained in this Item 7.01 (including Exhibit 99.2) is being furnished and shall not be deemed “filed” for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section and shall not be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release Issued by Metagenomi, Inc. on May 13, 2025
99.2	Corporate Presentation of Metagenomi, Inc. dated May 2025
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Metagenomi, Inc.

Date: May 13, 2025

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



Metagenomi Reports Business Updates and First Quarter 2025 Financial Results

- *Nonhuman primate (NHP) study in hemophilia A demonstrated therapeutically relevant factor VIII (FVIII) activity with durable response through approximately 19 months with an encouraging safety profile*
- *Well capitalized with \$226.0 million in cash, cash equivalents and available-for-sale marketable securities as of March 31, 2025 with runway anticipated to support operations into 2027*

EMERYVILLE, Calif., May 13, 2025 (GLOBE NEWSWIRE) – Metagenomi, Inc. (Nasdaq: MGX), a precision genetic medicines company committed to developing curative therapeutics for patients using its proprietary gene editing toolbox, today reported financial results for the quarter ended March 31, 2025, and provided business updates.

“We are excited about the transformative potential of our AI-driven metagenomics platform across multiple indications in our pipeline,” said Brian C. Thomas, PhD, CEO and founder of Metagenomi. “For our lead program in hemophilia A, we are encouraged by the additional durability of response data demonstrating sustained FVIII activity at therapeutically relevant levels throughout our completed study of approximately 19 months in NHPs. Looking ahead, we plan to leverage these findings to inform the strategy for our MGX-001 program moving forward. Further, we remain well capitalized with cash runway anticipated to support our operations through key milestones into 2027.”

First Quarter 2025 Updates

Business Updates

Hemophilia A Program – approximately 19-month durability results in NHP

- Results of the NHP study demonstrate that FVIII activity was consistent at therapeutically relevant levels over the approximately 19-month study duration.
 - Mean FVIII activity of months 12-19 following lipid nanoparticle dosing was 75%, 8% and 29% in animals 1001, 1002 and 1003, respectively.
 - At the 19-month or final measured time point, FVIII levels were 80%, 10% and 32% in each of the three animals, respectively.
 - Plasma FVIII activity levels of 80%, 10% and 32% of normal correlated with gene integration frequency of 5.3%, 0.89% and 2.5% in animals 1001, 1002 and 1003, respectively, as measured in the liver at termination.
 - One animal died prematurely from an intussusception of the colon at 17.8 months post LNP, which was assessed to be unrelated to treatment.
-



Metagenomi

- The FVIII knock-in was achieved with transient elevation of liver transaminases at the time of AAV and LNP administration, and with no other clinically relevant safety findings assessed as related to treatment.
- There was no impact to circulating albumin levels and no significant change in total bilirubin post AAV and LNP.

Additional emerging data relating to MGX-001 using a bioengineered FVIII construct in NHPs has, to date, demonstrated FVIII activity higher than expected. Full data collection is ongoing, and the Company expects to conduct additional studies and/or consider alternatives to this bioengineered FVIII construct.

Platform Technology Updates

- Publication in [Nature Communications](#) describing novel compact CRISPR-associated transposases (CAST) systems which demonstrated integration of a large, therapeutically relevant gene into the genome of human cells, discovered and enabled by Metagenomi's AI-driven metagenomics platform.
 - The study demonstrated integration of multiple cargoes to a known safe-harbor site in the human genome, illustrating the site-specific, programmable, and versatile attributes of the system.
 - Expression of the compact CAST system from a single 'all-in-one' mRNA design represents a first-in-class approach to simplifying delivery for therapeutic applications. Future work will focus on expanding capabilities and optimizing the system for clinical applications, with additional advancements expected in 2025.

Additional details on Metagenomi programs, including the Company's Hemophilia A program, technology platform and anticipated milestones can be found in the corporate presentation on the Metagenomi website, and in the Quarterly Report on Form 10-Q filed on March 13, 2025 with the SEC.



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Upcoming Medical Meetings

Metagenomi plans to participate in the following scientific conferences during the second quarter of 2025:

- ASGCT 28th Annual Meeting in New Orleans, LA
Abstract Titles:
 - In Vivo Genome Editing with an Ultra-Compact Type V Nuclease for All-In-One AAV Delivery
 - Site-Specific Integration of Therapeutic Transgenes with a Type V-K CAST System Engineered for Efficient and Targeted Human Genome Editing
 - A Compact and Potent Type II CRISPR System for CNS Gene Knockdown via AAV DeliveryDate & Time: Tuesday, May 13, 2025, 6:00 p.m. CT
- TIDES USA 2025 Meeting in San Diego, CA
Abstract Title: AI-Guided Metagenomic Discovery of Compact CRISPR Systems for In Vivo Therapeutic Genome Editing
Date & Time: Thursday, May 22, 2025, 2:30 p.m. PT

First Quarter 2025 Financial Results

Cash Position: Cash, cash equivalents, and available-for-sale marketable securities were \$226.0 million as of March 31, 2025, which is anticipated to support operations into 2027.

R&D Expenses: Research and development (R&D) expenses were \$25.1 million for the quarter ended March 31, 2025, compared to \$31.4 million for the comparable period in 2024.

G&A Expenses: General and administrative (G&A) expenses were \$6.8 million for the quarter ended March 31, 2025, compared to \$8.8 million for the comparable period in 2024.

About Hemophilia A

Hemophilia A is the most common X-linked inherited bleeding disorder, caused by a large variety of mutations in the FVIII gene leading to a 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 of severe disease typically occurs in infancy due to exaggerated bleeding in response to minor injury or routine medical procedures. Prevalence is estimated to be up to 26,500 patients in the US and more than 500,000 patients globally according to the World Federation of Hemophilia, with the vast majority of patients being male.



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About Metagenomi

Metagenomi is a precision gene editing company leveraging the power of artificial intelligence and machine learning to develop the next generation of potentially curative genome editing therapeutics. Its metagenomics-derived gene editing toolbox has analyzed over 7.4 billion proteins and has the potential to target any type of genetic mutation across the entire human genome. The Company's innovative and comprehensive platform has full spectrum gene editing, with technologies ranging from ultra-small nucleases and base editors to large gene integrations using CRISPR-associated transposase (CAST) and RNA-Mediated Integration Systems (RIGS). The Company's lead, wholly-owned development program in Hemophilia A is a potentially curative therapy designed to provide life-long protection from bleeding events and joint damage in adults and children. The Company has additional wholly-owned assets in its pipeline for secreted protein deficiencies and partnered assets for cardiometabolic diseases. For more information, please visit <https://metagenomi.co>.

Cautionary Note Regarding Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. Such statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to," "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions include, but are not limited to, any statements relating to our product development programs, including the timing of and our ability to conduct IND-enabling studies, make regulatory filings such as INDs, statements concerning the potential of therapies and product candidates, statements concerning our anticipated cash runway, and any other statements that are not historical facts. Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition, and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to our growth strategy; our ability to obtain, perform under, and maintain financing and strategic agreements and relationships; risks relating to the results of research and development activities; risks relating to the timing of IND submissions and starting and completing clinical trials; uncertainties relating to preclinical and clinical testing; our dependence on third party suppliers; our ability to attract, integrate and retain key personnel; the early stage of products under development; our need for substantial additional funds; government regulation and the current regulatory environment; patent and intellectual property matters; competition; as well as other risks described in "Risk Factors," in our most recent Form 10-K and other risk factors set forth from time to time in our filings with the Securities and Exchange Commission made pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended. We expressly disclaim any obligation or undertaking to release publicly any



Metagenomi

updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Investor Contacts:

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or

Kiki Patel, PharmD
Gilmartin Group
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Condensed Financial Statements

Condensed Balance Sheet Data (Unaudited)

(in thousands)	March 31,		December 31,	
	2025		2024	
Cash, cash equivalents and available-for-sale marketable securities	\$	225,970	\$	248,307
Total assets	\$	297,866	\$	324,599
Total liabilities	\$	85,208	\$	89,742
Redeemable convertible preferred stock	\$	—	\$	—
Total stockholders' equity	\$	212,658	\$	234,857
Total liabilities, redeemable convertible preferred stock and stockholders' equity	\$	297,866	\$	324,599

Condensed Statements of Operations (Unaudited)

(In thousands, except share and per share data)	Three Months Ended			
	March 31,		March 31,	
	2025		2024	
Collaboration revenue	\$	4,127	\$	11,159
Operating expenses:				
Research and development		25,142		31,439
General and administrative		6,805		8,752
Total operating expenses		31,947		40,191
Loss from operations		(27,820)		(29,032)
Other income (expense):				
Interest income		2,887		3,934
Other expense, net		(8)		(50)
Total other income, net		2,879		3,884
Net loss before provision for income taxes		(24,941)		(25,148)
Provision for income taxes		(98)		—
Net loss	\$	(25,039)	\$	(25,148)
Net loss per share attributable to common stockholders, basic and diluted	\$	(0.68)	\$	(1.19)
Weighted average common shares outstanding, basic and diluted		37,019,027		21,137,868



Metagenomi

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

Nasdaq: MGX

May 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.

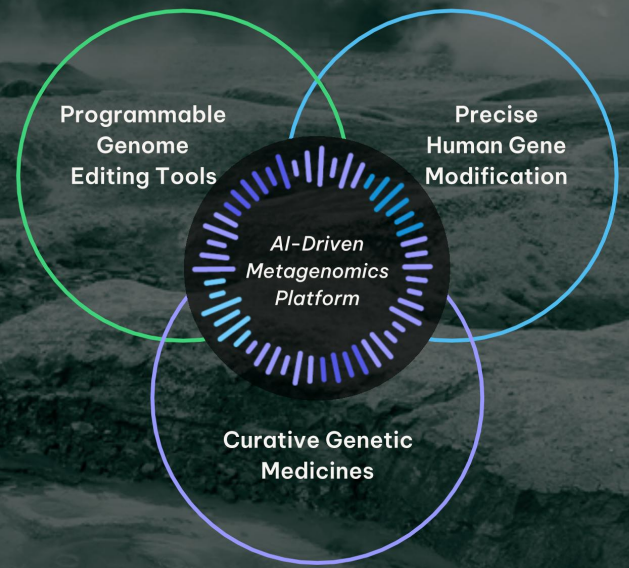
We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short and long term business operations and objectives, and financial needs. These forward-looking 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.

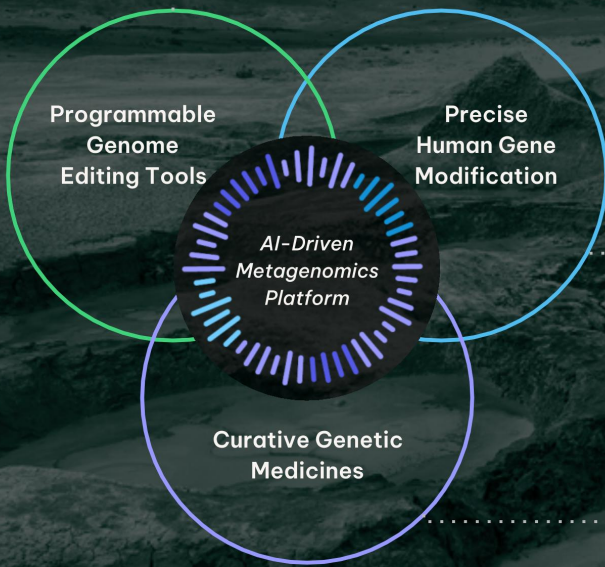
This presentation contains estimates and other information concerning our industry, our business and the markets for our products. Information that is based on estimates, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially 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. These sources include government and industry sources. Industry publications and surveys generally state that the information contained therein has been obtained from sources believed to be reliable. Although we believe the industry and market data to be reliable as of the date of this presentation, this information could prove to be inaccurate. Industry and market data could be wrong because of the method by which sources obtained their data and because information cannot always be verified with complete certainty due to the limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties. While we believe our internal company estimates and research as to such matters is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source and no reliance should be placed on or should be made on any information or statements made in this presentation relating to or based on such internal estimates and research.

Our Vision:

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



Our Strategy:



Our diverse and modular genome editing toolbox is designed to precisely **target any site in the human genome**, yielding the potential to address the full spectrum of genetic diseases.

Our novel systems, optimized from nature, set new standards in editing **efficiency** and **precision**. Our compact systems also offer advantages for **delivery**.

Investments in **development** and **manufacturing** across a breadth of gene editing technologies, and successful **regulatory** experience enable rapid advancement to the clinic.

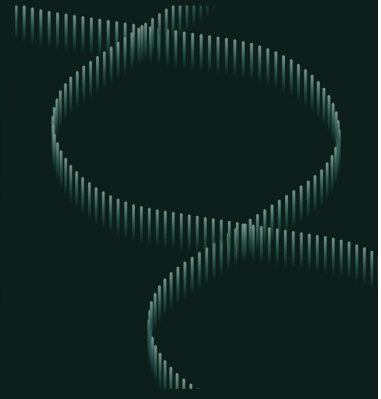
Maximizing impact on care and marketplace value



Hundreds of millions of people
worldwide have diseases that are
potentially treatable with gene editing

Over **180m** with
rare diseases of
genetic origin¹

Over **200m** with
cardiovascular disease tied
to genetic risk factors^{2,3,4}



Hemophilia A

More than 500,000
patients globally⁵

Transthyretin Amyloidosis (TTR)

300,000–500,000 patients
globally with wild-type ATTR⁶

Refractory Hypertension

900,000 patients in the US⁷

1. Wakap, S. N., Lambert, D. M., Ory, A., et al. "Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database." *European Journal of Human Genetics*, 2020; 28: 165–173.

2. Roth, Gregory A., et al. "Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update from the GBD 2019 Study." *Journal of the American College of Cardiology*, vol. 75, no. 25, 22 Dec. 2020, pp. 2993–3021. doi:10.1016/j.jacc.2020.11.010.

3. Khera, A. V., & Kathiresan, S. "Genetics of coronary artery disease: discovery, biology and clinical translation." *Nature Reviews Genetics*, 2017; 18(6): 331–344.

4. Lloyd-Jones, D. M., Nam, B.-H., et al. "Parental cardiovascular disease as a risk factor for cardiovascular disease in middle-aged adults: a prospective study of parents and offspring." *Journal of the American Medical Association (JAMA)*, 2004; 291(18): 2204–2211.

5. Stonebraker, J. S., et al. 2010. Haemophilia. Vol. 16, pp. 20–32.

6. Mohamed-Salem I, et al. "Prevalence..." *Int J Cardiol*, 270:192–196.

7. Yoon, M. et al. 2022. "Prevalence..." *Hypertension Research*, vol. 45, no. 8, pp. 1353–1362.

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

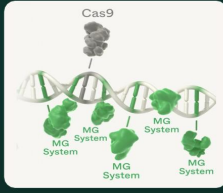
Building a proprietary toolbox capable of correcting any genetic mutation anywhere in the human genome

Our proprietary toolbox enables precise edits of the human genome



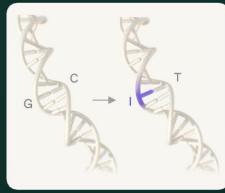
MG Tool

Nuclease



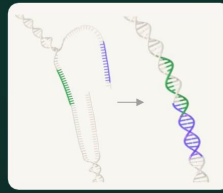
Proprietary library of highly precise and efficient nucleases, including ultra-small systems (SMARTs), provides programmable chassis for other gene editing tools

Base Editors



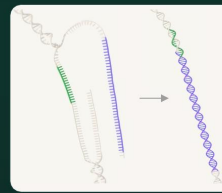
Programmable chassis with additional effector enzymes to cause single nucleotide changes

RIGS: Replacement



RNA-mediated integration systems (RIGS) use programmable chassis with additional reverse transcriptase for edits encoded in RNA templates

RIGS: Integration



RIGS with expanded RNA template for site-specific integration of genes

CAST



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





Disease Target Selection Criteria:

Well understood disease biology

Readily available translational biomarkers

Established development pathways

Important unmet medical need

Choose the right genome editing tool and delivery technology to engineer precision human therapeutics

FOCUS

Liver targeting for hematologic, cardiometabolic and hepatic diseases



Various LNP & AAV delivery options

ADDITIONAL FOCUS

Extrahepatic Disease



Various AAV and novel non-viral delivery options

Internal development, manufacturing, and regulatory capabilities power a fully integrated gene editing company

The ability to develop and characterize complex human gene editing components is essential to pursue a successful regulatory pathway in genetic medicine development

Product Characterization

State-of-the-art screening, optimization, and characterization, streamlining development of highly specific and efficient gene editing systems

GMP Manufacturing

Measured, phase-appropriate investments designed to rapidly and reliably progress Metagenomi's clinical pipeline

Regulatory

Completion of first regulatory engagement for lead program, in addition to supply of gene editing reagents and regulatory support of partner IND filing

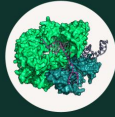
Capabilities span a broad range of technical modalities:



Plasmid



sgRNA



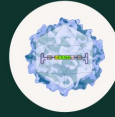
Nuclease



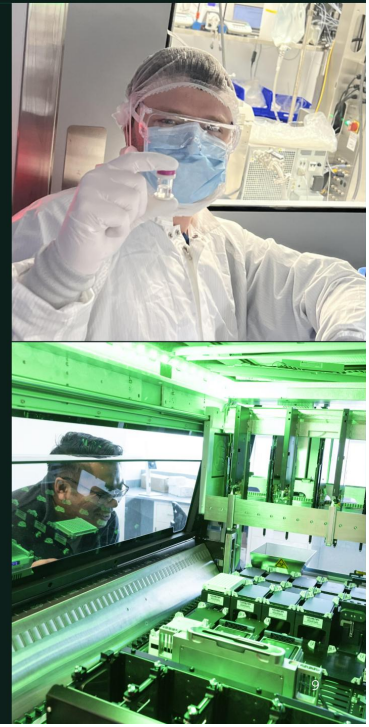
LNP



mRNA



AAV



Strategic collaborations compliment our development capabilities



IONIS

- *in vivo* genome editing therapeutics focusing on cardiometabolic diseases
- Up to 8 targets with 4 co-development and co-commercialization options
- \$80 million cash upfront, plus up to \$2.9B in potential milestone payments and royalties to Metagenomi

affini

- Next-generation cell therapies enhanced by multiplex genome editing targeting TCR *ex vivo* immuno-oncology cell therapies
- Co-founded by world-renowned experts in cancer immunotherapy
- Metagenomi to receive options, milestones and royalties

Partnering efforts to expand therapeutic impact to patients are based on:


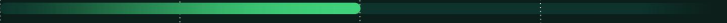
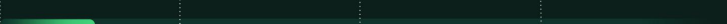

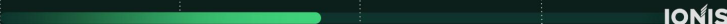

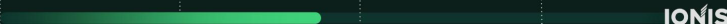
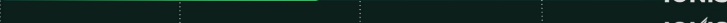
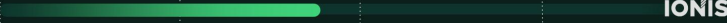
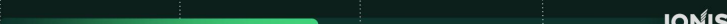
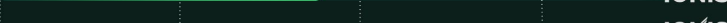
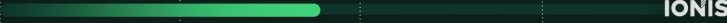
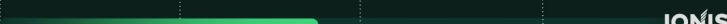

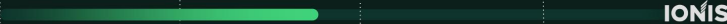
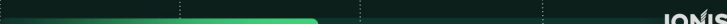

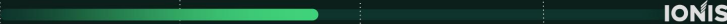
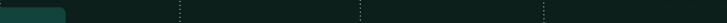
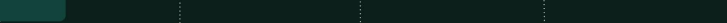
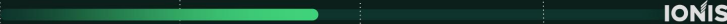
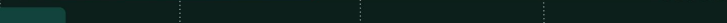
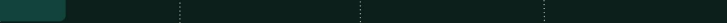
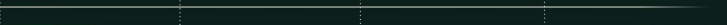
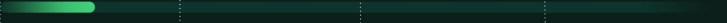
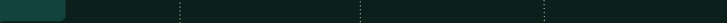
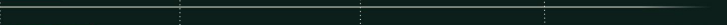
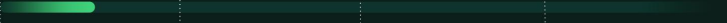
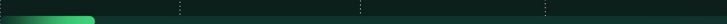
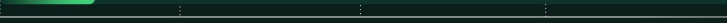

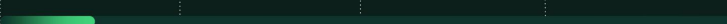
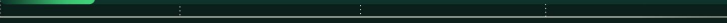
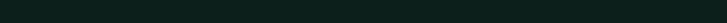

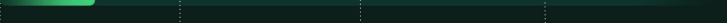
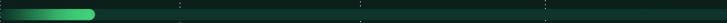
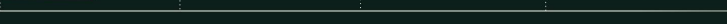
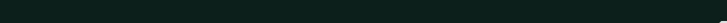

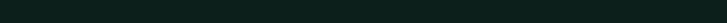
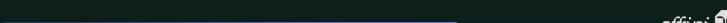
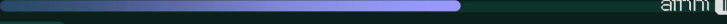

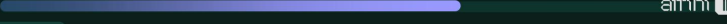
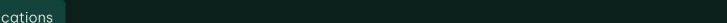
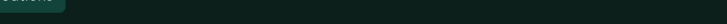
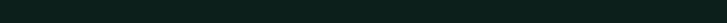

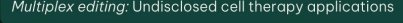
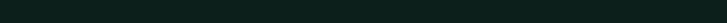
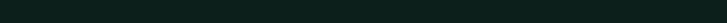
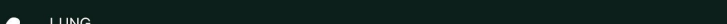
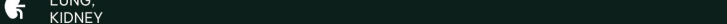
Development Capability

Complementary Technology


Market Presence


Compatible Vision

Broad pipeline built on our next generation gene editing platform

Editing Platform	Delivery	Indication / Editing Target	Discovery	Lead Optimization	IND-Enabling	Clinical	Partner	
 LIVER <i>Knock-in</i> <i>Knockdown</i>	LNP + AAV	Hemophilia A / ALB						
		Undisclosed secreted protein diseases						
	LNP	Transthyretin Amyloidosis / TTR						IONIS
		Refractory Hypertension / AGT						IONIS
		Undisclosed cardiovascular disease						IONIS
		Undisclosed cardiovascular disease						IONIS
Other Program: HAO1								
Small gene corrections	LNP	Alpha 1 Antitrypsin Deficiency / SERPINA1						
Large gene insertion	LNP	Wilson's Disease / ATP7B						
 CELL THERAPY <i>Multiplex editing</i>	Ex vivo	Solid tumor indications / TCR T Cells					affini 	
		Multiplex editing: Undisclosed cell therapy applications						

Additional platform applications:

 NEURO-MUSCULAR
Ultra small systems

 LUNG, KIDNEY
Large gene insertion

*Pipeline as of Q1 2025 earnings (May 13, 2025)

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 ASH¹
- ✓ Initial regulatory engagement with FDA
- ✓ GxP Manufacturing activities initiated

Secreted Protein Deficiencies

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

Cardiometabolic Programs

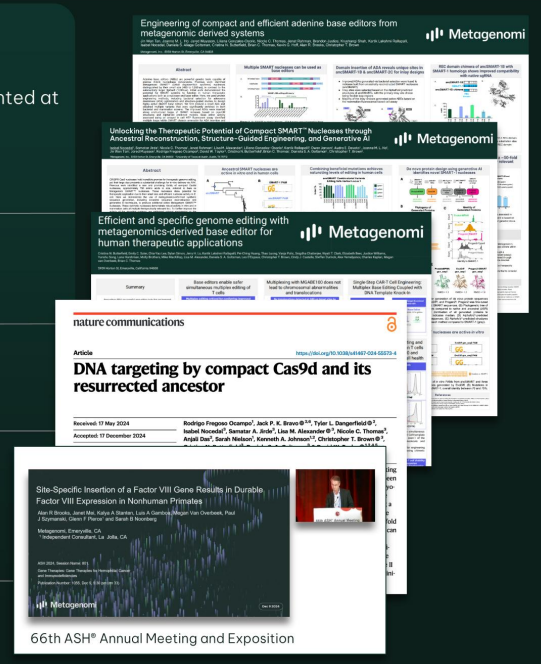
- ✓ All four Wave 1 collaboration targets in lead optimization
- ✓ In vivo rodent PoC achieved for all targets

Other Therapeutic Programs / Technology Development

- ✓ AI-enabled nuclease and base editor development presented at CSHL²
- ✓ Multiplex base editing data presented at ESGCT³
- ✓ 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>



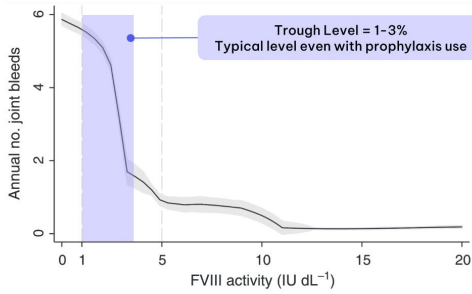
Anticipated milestones allow advancement towards the clinic



	2025	2026	
Hemophilia A Program	<ul style="list-style-type: none">• Complete ongoing NHP durability study• Conduct Pre-IND and ex-US regulatory meetings	<ul style="list-style-type: none">• IND / CTA filings	
Secreted Protein Deficiencies	<ul style="list-style-type: none">• Disclose lead indication for secreted protein deficiency platform• Achieve NHP PoC	<ul style="list-style-type: none">• Nominate DC	
Cardiometabolic Programs	<ul style="list-style-type: none">• Nominate 1-2 DCs• Disclose indications for remaining Wave 1 targets	<ul style="list-style-type: none">• Initiate IND enabling activities• Additional DCs for Wave 1 targets	
Other Therapeutic Programs / Technology Development	<ul style="list-style-type: none">• Continue to advance early-stage pipeline for multiple future IND filings		

IND = Investigational New Drug
CTA = Clinical Trial Authorization

Pipeline Overview



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



International Hemophilia Training Center, 2024. Hemophilia Joint Bleeds. <https://www.ihc.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 US¹
- More than **500,000** patients globally²

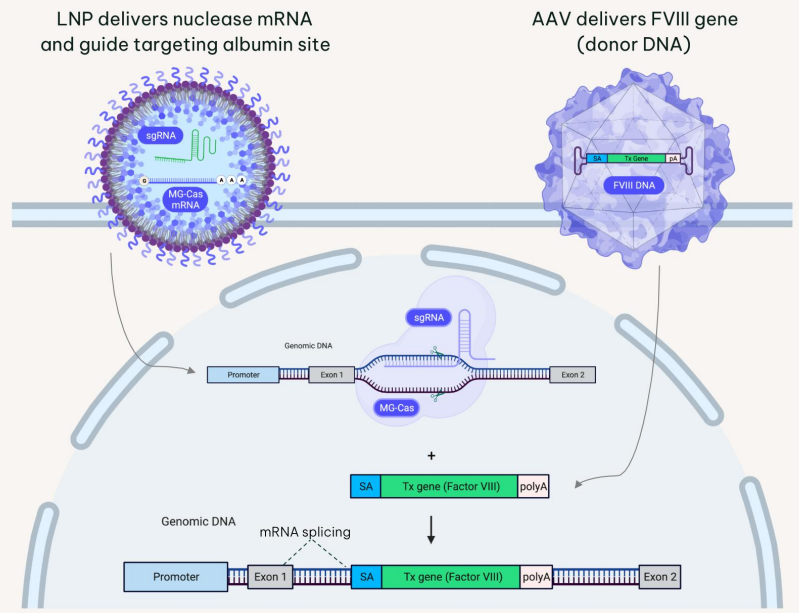
1. Soucie, J.M., et al. 2020. Haemophilia. Vol. 26, no. 3, pp. 487-493.
2. Stonebraker, J. S., et al. 2010. Haemophilia. Vol. 16, pp. 20-32.

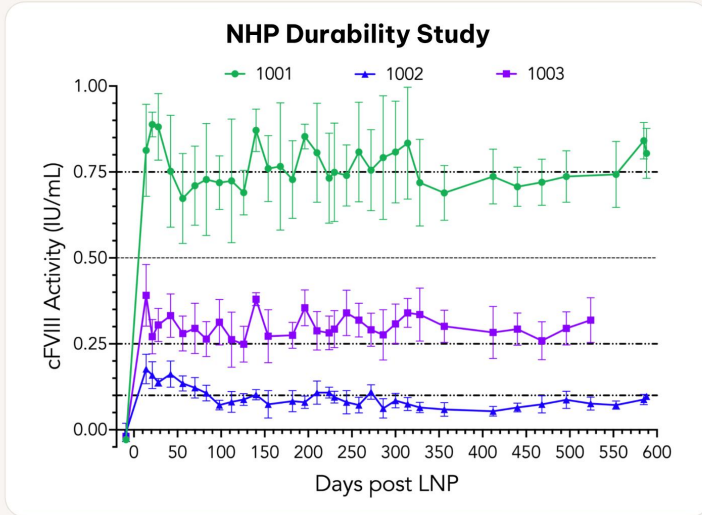


Genome Editing Approach

- 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

Durable, therapeutic levels of FVIII achieved in non-human primate (NHP) study with tolerable safety findings





FVIII 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.

Animal 1003 died from "intussusception of the colon" on day 540 (17.8 mo) post LNP, considered unrelated to the treatment.

Animal	Integration at study termination ¹	Mean FVIII levels (IU/ml) over specific time periods			
		3-6 months post LNP (d83-d182)		12-19 months post LNP (d356-d588)	
		Mean +/- Stdev	Mean	Stdev	Mean
1001	5.3 +/- 0.49	0.748	0.055	0.747	0.051
1002	0.89 +/- 0.23	0.087	0.013	0.075	0.014
1003	2.5 +/- 0.84	0.288	0.045	0.292	0.020

¹ Integration in forward orientation (copies per 100 haploid genomes, average of 5 liver lobes)

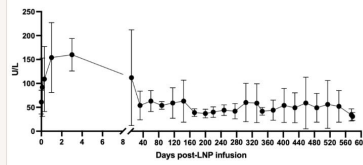
- Plasma FVIII activity levels unchanged over ~19 months of the study
- Plasma FVIII activity levels at the end of the study were:
 - 1001: 0.80 IU/ml (80% of normal FVIII values)
 - 1002: 0.10 IU/ml (10 % of normal FVIII values)
 - 1003: 0.32 IU/mL (32% of normal FVIII values)
- Plasma FVIII activity levels correlate with gene integration frequency measured in the liver at termination



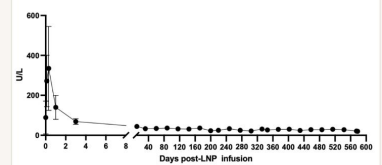
SUMMARY OF SAFETY FINDINGS

- Integration of the FVIII gene at the albumin locus had no impact on circulating albumin levels
- Transient elevation of liver function tests after the infusion of AAV and LNP with no significant change in total bilirubin
- Animal 1003 died from "intussusception of the colon" on day 540 (17.8 mo) post LNP, considered unrelated to the treatment
- Animals exhibited normal weight gain

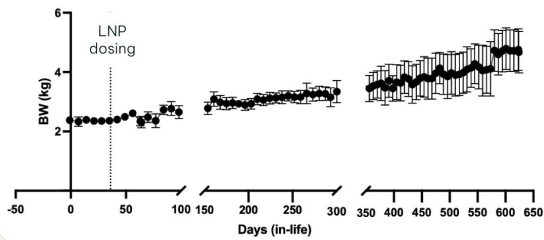
Alanine transaminase (ALT) levels post LNP infusion



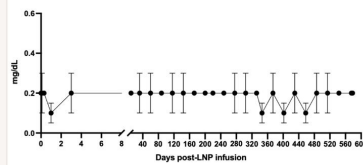
Aspartate transaminase (AST) levels post LNP infusion



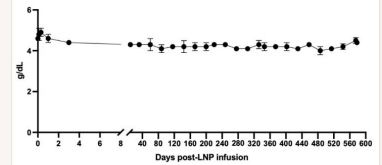
Body Weight



Total bilirubin levels post LNP infusion



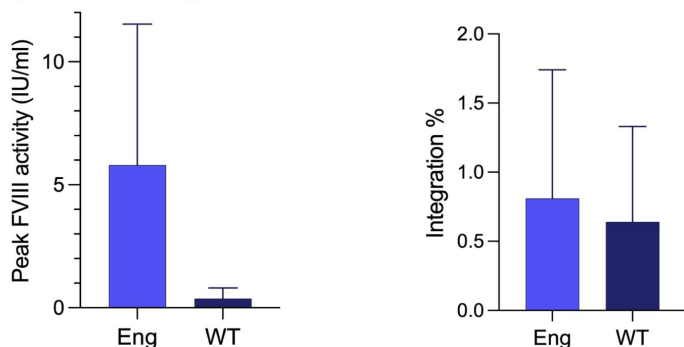
Albumin levels post LNP infusion



All graphs are mean and standard deviation for N=3 NHP's
Animal 1003 died from "intussusception of the colon" on day 540 (17.8 mo) post LNP, considered unrelated to the treatment.



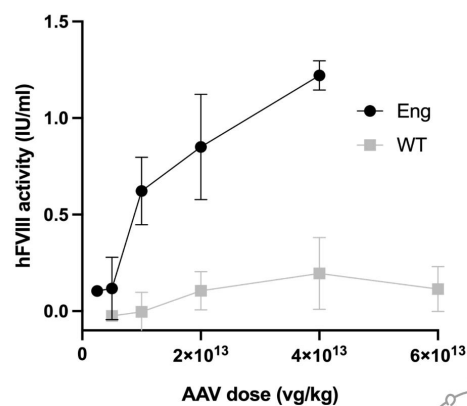
Bioengineered FVIII yields significantly higher plasma FVIII activity despite similar integration frequency in NHPs



LNP dose 1 mg/kg, AAV doses 5e12 and 2e13 vg/kg (data combined)
Mean +/- SD (N=6). Integration in liver measured at termination (d49)
Peak FVIII activity occurred between d5 and d17 post LNP and then declined in parallel with the appearance of anti-human FVIII antibodies
All animals developed varying degrees of anti-human FVIII antibodies that may have contributed to inter-animal variability in peak FVIII activity



Mouse dose dependent FVIII activity



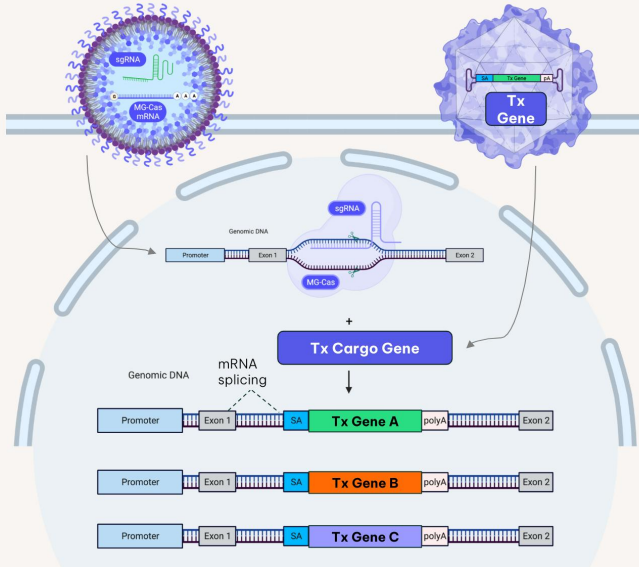
- **No off-target editing identified to date with MGX-001 development candidate.**
- **Significantly higher plasma FVIII activity from the bioengineered FVIII despite similar integration frequency is expected to enable therapeutic FVIII activity at lower AAV doses with associated safety benefit.***

*Emerging data relating to MGX-001 from NHP studies using this bioengineered construct has, to date, demonstrated FVIII activity higher than expected. While we have not received all of the data from the studies, we expect to conduct additional studies and/or consider alternatives to this bioengineered B-domain deleted FVIII construct.

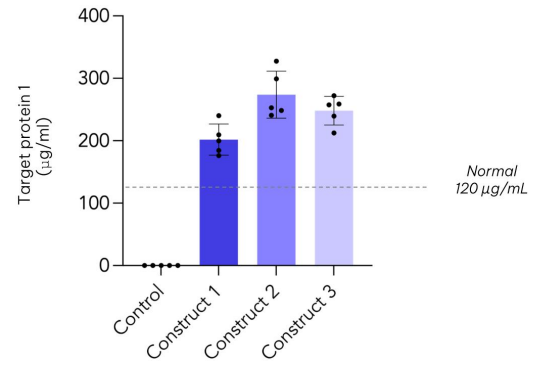
Leveraging the MGX-001 approach from the Hemophilia A program to accelerate timelines and reduce costs to IND

LNP delivers nuclease mRNA and guide targeting albumin site

AAV delivers Transgene (donor DNA)



Normal circulating levels of a target protein can be achieved in mice 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



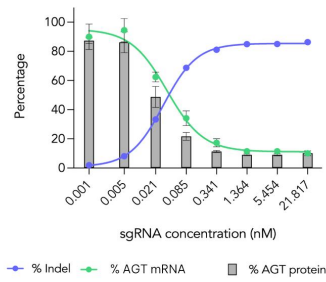


Refractory hypertension is characterized as uncontrolled hypertension despite the use of five or more drugs and is a significant risk for major cardiovascular events¹

Prevalence: 900,000 adults with refractory hypertension in the US²

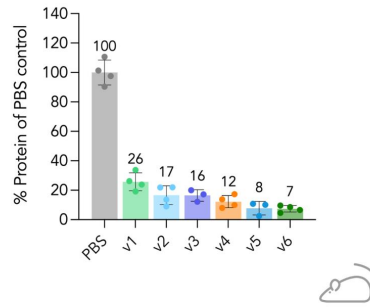
Dose dependent editing, mRNA and protein knockdown in primary human hepatocytes

>85% editing, 90% mRNA and protein knockdown



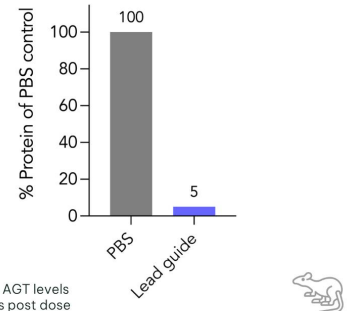
mRNA, gRNA, and LNP were optimized to increase potency

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



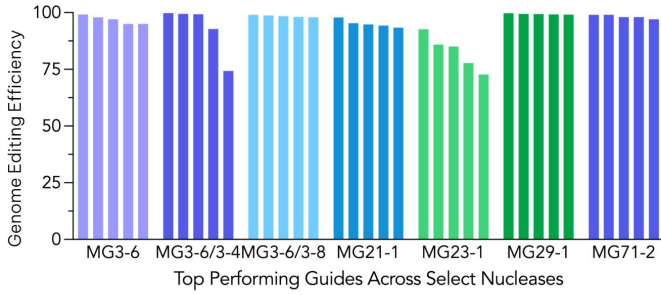
1. Acelejado, M. C., et al. 2019. Treatment...Circulation Research, 124(7), 1061-1070
2. Yoon, M. et al. 2022. "Prevalence..." Hypertension Research, vol. 45, no. 8, pp. 1353-1362

Technology Platform

Highly efficient nucleases designed for any target in the human genome

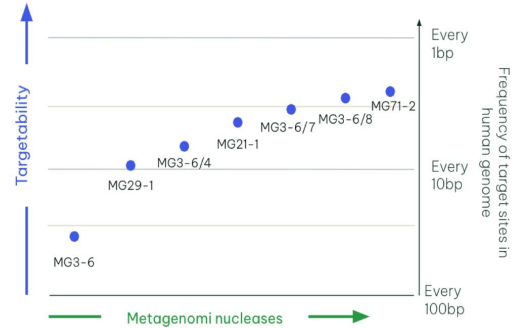
Our nucleases, selected for their native high-efficiency, expand targeting options within genes of interest

Efficient across multiple guides and targets



Editing efficiency in mammalian cells determined based on the frequency of InDels detected by next generation sequencing ("NGS") at genomic sites targeted by each nuclease

Estimated potential to target every codon in the human genome



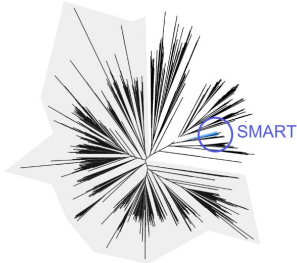
Targetability is the average distance between nuclease target sites in the human genome

Generative AI trained on proteins from nature informs optimization of efficient SMART nucleases



Search our metagenomics database for novel compact nucleases

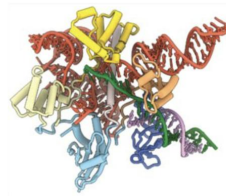
Protein sequence comparisons highlight novelty of SMART CRISPR systems



*Phylogenetic tree comparing CRISPR nucleases
*Gray shaded area indicates previously known nucleases including SpCas9

Characterize small CRISPR-associated nucleases (SMall ARGinine-rich sysTEms: "SMART")

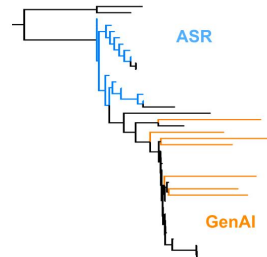
SpCas9 1376 amino acids
SMART 748 amino acids



*Protein structure defined in collaboration with David Taylor, UT Austin

Design SMART nucleases with generative AI and ancestral sequence reconstruction (ASR)

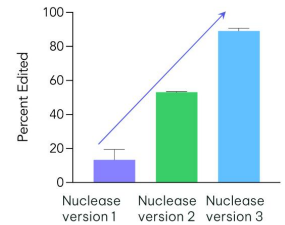
De novo SMART proteins from ASR and GenAI are unique from natural systems



*Phylogenetic tree comparing natural and de novo designed SMART nuclease protein sequences

Optimize SMART nucleases with fine-tuned AI models and protein structure

Editing efficiency improved to >90% with engineered SMART nucleases <750aa

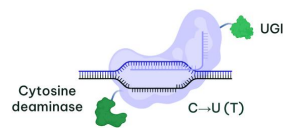
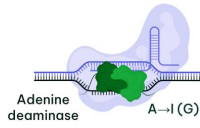


*Gene editing in human cells with engineered SMART nucleases measured by NGS
*Compact size enables all-in-one AAV delivery

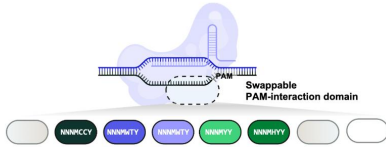
Base editing platform with broad targetability achieves efficient multiplex editing for cell engineering



ABE (Adenine Base Editor) CBE (Cytosine Base Editor)



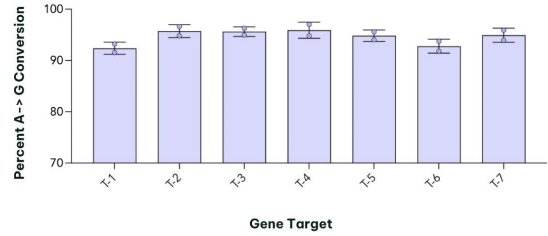
Reprogrammed chassis increases genome targetability of Base Editors



ABE: SpCas9 = 18% and MG3-6 = 95% targetability
 CBE (not shown): SpCas9 = 5% and MG3-6 = 53%
 *SpCas9 analysis with NGG PAM

■ Targetable
 ■ Nontargetable

ABE are efficient for multiplexed base editing in primary T cells

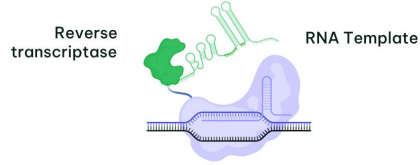


1. Top guides for seven cell therapy targets were tested in a multiplexed fashion (7-plex edits)
1. Edits durable over 11 days and do not impact cell viability or expansion (not shown)

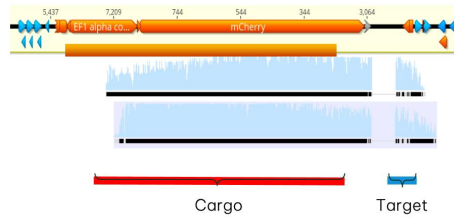
Next generation technology for programmable large genome integration to address complex genetic diseases



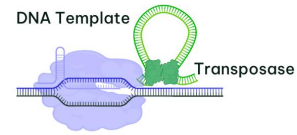
RIGS (RNA-Mediated Integration Systems)



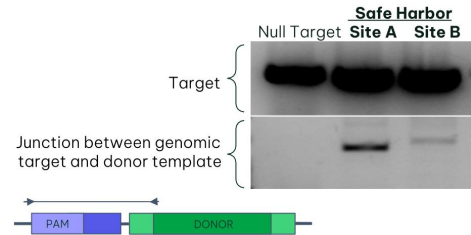
First-ever report of targeted integration of >900 bp with all-RNA delivery



CAST (DNA-Mediated Integration Systems)



Demonstrated large targeted genome integration using compact CAST in human cells





Technology milestones achieved

Future Technology Milestones

- ✓ MGX Toolbox with **large selection of nucleases**
- ✓ Theoretical ability to **target any codon** in the human genome

2021-2022

- ✓ Discovered **large gene integration systems** (CAST and RIGS)
- ✓ Discovered **compact systems (SMART)**
- ✓ Developed **base editing** platform
- ✓ Proof-of-concept (PoC) for **in vivo liver editing with nuclease**

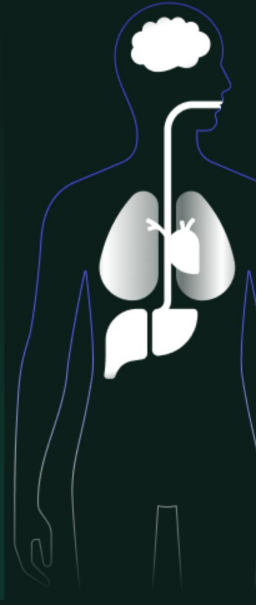
2023

- ✓ **Compact systems:** *in vitro* PoC for neuromuscular target
- ✓ **RIGS:** *in vitro* PoC for small gene correction in liver targets
- ✓ **Multiplex base editing:** PoC for cell therapy
- ✓ **CAST:** *in vitro* PoC for large gene integration

2024


- **Targeted Corrections:** *in vivo* PoC with RIGS or base editors
Example disease: A1AT deficiency
- **Large Integrations:** *in vivo* PoC with RIGS, CAST, or novel technology
Example diseases: Wilson's, Cystic Fibrosis, Phenylketonuria

2025 and beyond



Corporate Highlights

Most recent and upcoming anticipated milestones drive toward the clinic

	Recent milestones achieved	2025	2026 
Hemophilia A Program	<ul style="list-style-type: none"> ✓ MGX-001 Development Candidate (DC) ✓ Factor VIII activity sustained in NHP study for >16 months presented at ASH¹ ✓ Initial regulatory engagement with FDA ✓ GxP Manufacturing activities initiated 	<ul style="list-style-type: none"> • Complete ongoing NHP durability study • Conduct Pre-IND and ex-US regulatory meetings 	<ul style="list-style-type: none"> • IND / CTA filings
Secreted Protein Deficiencies	<ul style="list-style-type: none"> ✓ In vivo proof-of-concept (PoC) achieved with initial targets 	<ul style="list-style-type: none"> • Disclose lead indication for secreted protein deficiency platform • Achieve NHP PoC 	<ul style="list-style-type: none"> • Nominate DC
Cardiometabolic Programs	<ul style="list-style-type: none"> ✓ All four Wave 1 collaboration targets in lead optimization ✓ In vivo rodent PoC achieved for all targets 	<ul style="list-style-type: none"> • Nominate 1-2 DCs • Disclose indications for remaining Wave 1 targets 	<ul style="list-style-type: none"> • Initiate IND enabling activities • Additional DCs for Wave 1 targets
Other Therapeutic Programs / Technology Development	<ul style="list-style-type: none"> ✓ AI-enabled nuclease and base editor presented at CSHL² ✓ Multiplex base editing data presented at ESGCT³ ✓ Ultra-small nucleases published in <i>Nature Communications</i>⁴ 	<ul style="list-style-type: none"> • Continue to advance early-stage pipeline for multiple future IND filings 	

IND = Investigational New Drug
CTA = Clinical Trial Authorization

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>

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



Thank you

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IR@metagenomi.co