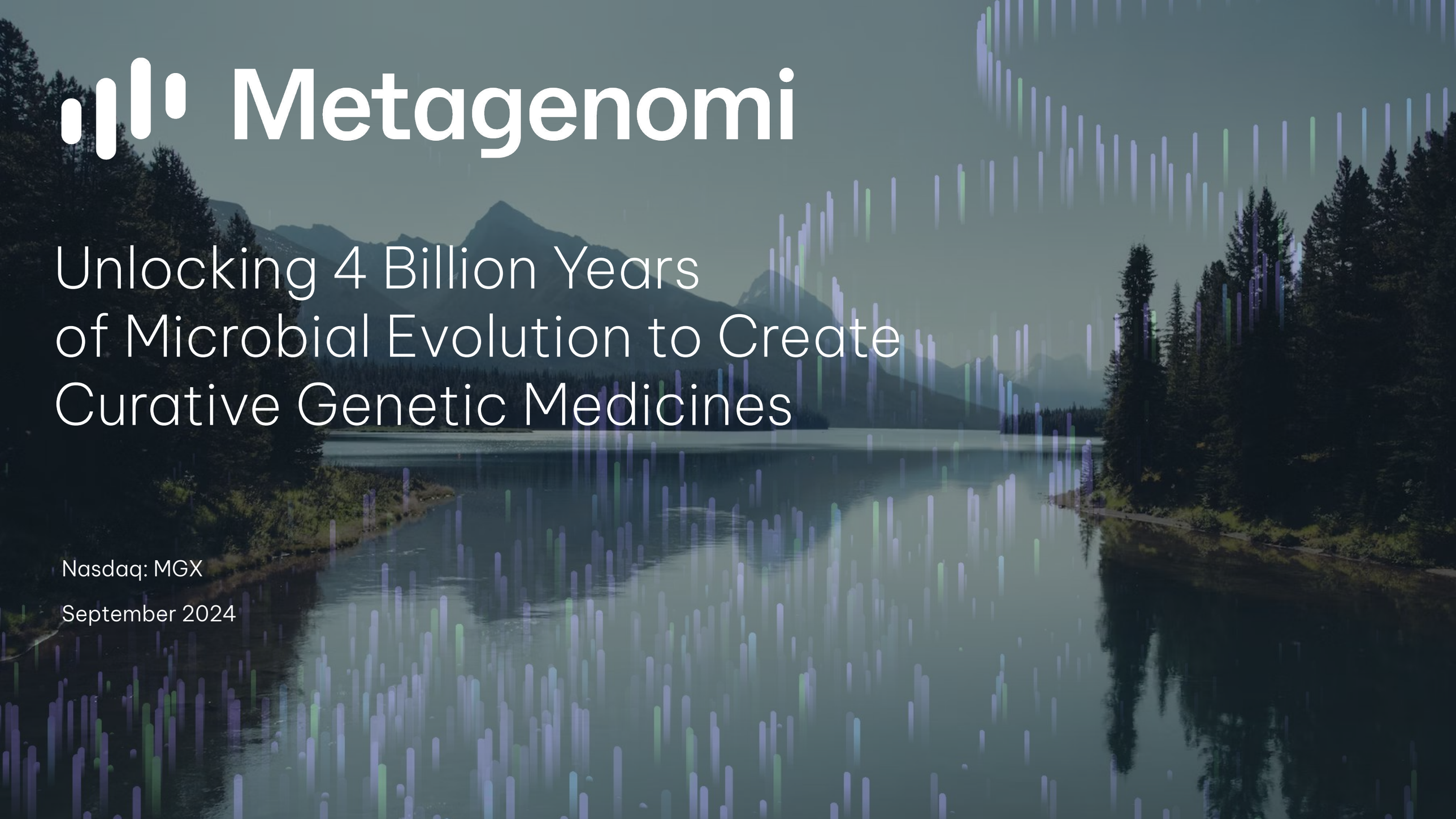


Metagenomi

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

Nasdaq: MGX

September 2024

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.

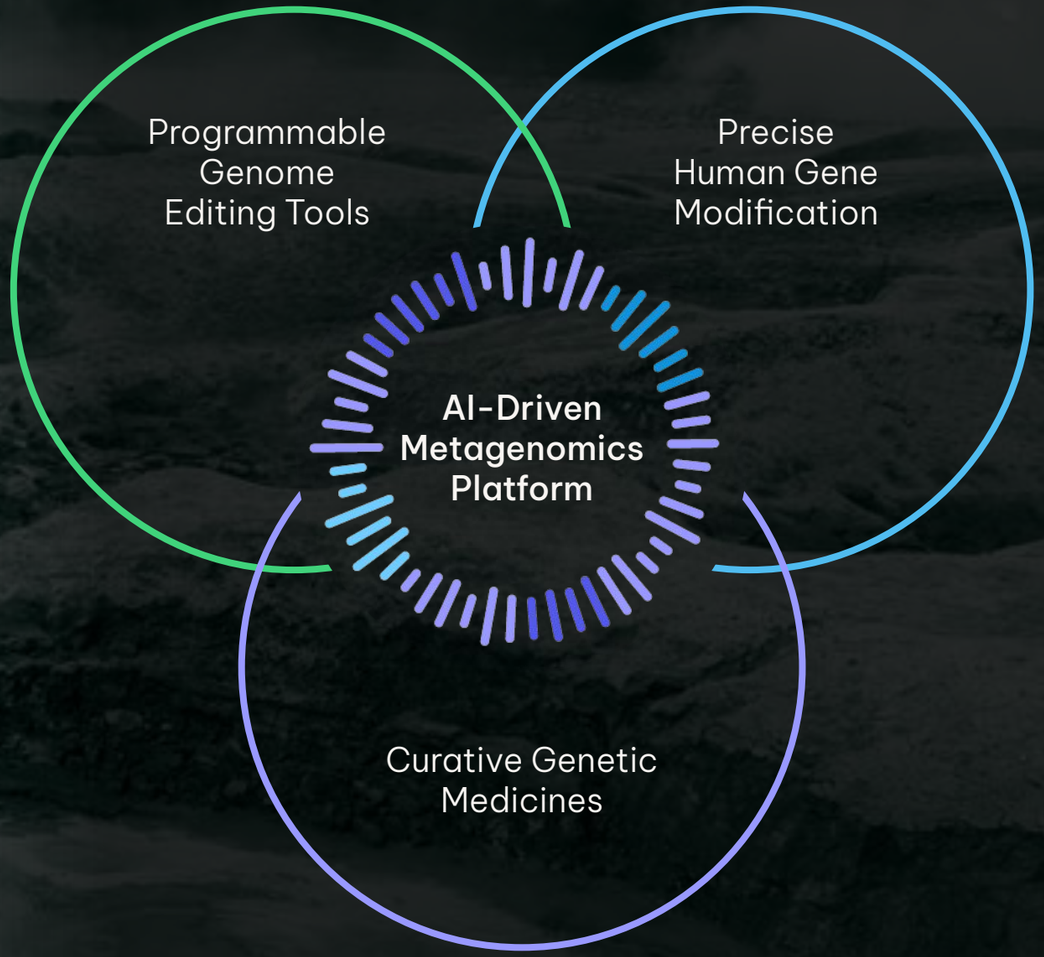
We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short and long term business operations and objectives, and financial needs. These forward-looking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



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

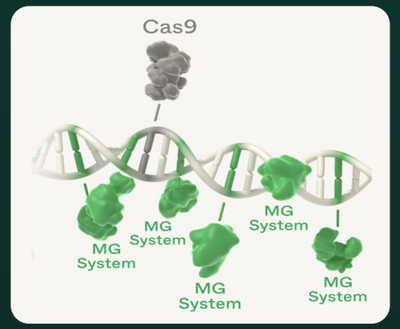
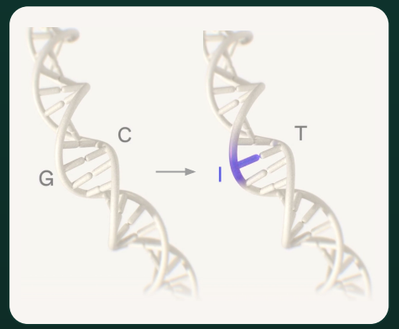
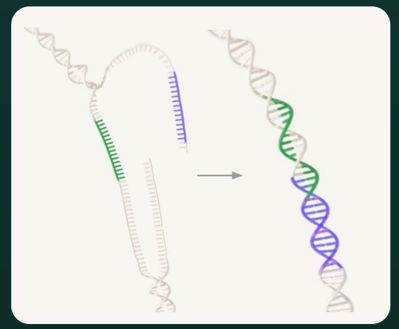
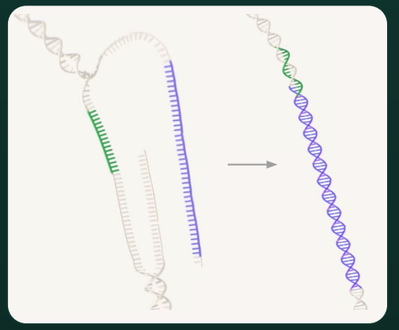
Engineering & Optimization

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*

Precise gene edits unlock development of curative medicines

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 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

AI and automation

Integrated screening and characterization to streamline development

mRNA & gRNA optimization

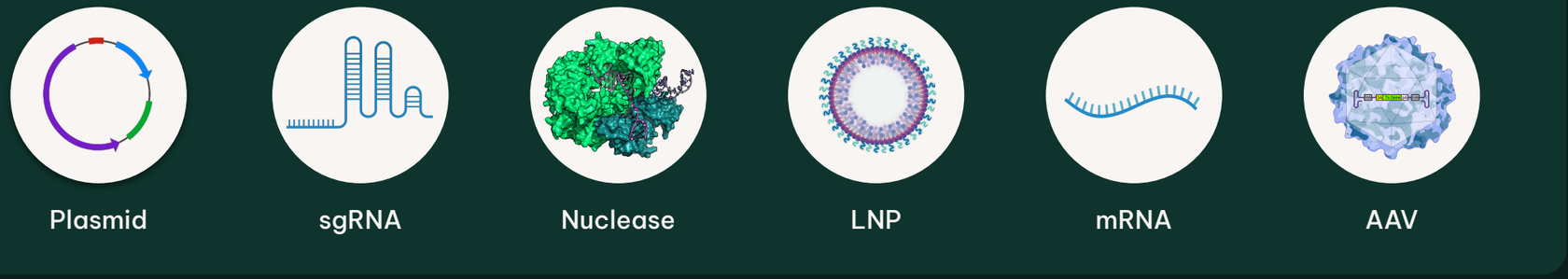
RNA optimizations to enhance genome editing performance

Delivery

LNP and AAV delivery technologies to expand therapeutic targeting

GMP Manufacturing

CMC development and GMP manufacturing to enable pipeline advancement to clinic



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-T™

- 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

Continuing partnering efforts to expand therapeutic impact to patients

- Development Capability
- Complementary Technology
- Market Presence
- Compatible Vision

Broad pipeline built on our metagenomics 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							

*Pipeline as of Q2 earnings (August 13, 2024)

Recent and upcoming milestones drive towards the clinic

	Recent milestones achieved	2H' 2024	2025
Hemophilia A Program	✓ Generated robust proof-of-concept data in multiple NHP studies ✓ Engaged with FDA for regulatory advice ✓ Nominated Development Candidate	• Confirm 12-month durable expression of Factor VIII in NHP study • Initiate GMP manufacturing and related IND enabling activities	• Continue IND enabling activities to support an IND filing in 2026
Cardiometabolic Programs	✓ Advanced all four targets in wave one of Ionis collaboration in lead optimization	• Demonstrate *in vivo* proof-of-concept supporting Development Candidate nominations	• Nominate one to two Development Candidates
Other Therapeutic Programs	✓ Established GMP genome editing reagents for cell therapy and regulatory filing to support Affini-T IND	• Present multiplex base editing data at scientific meeting for cell therapy applications	• Continue to advance early-stage pipeline for multiple future IND filings

Cash runway into 2027

Technology innovations continue...

Technology milestones achieved

2021-2022

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

2023

- ✓ 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**

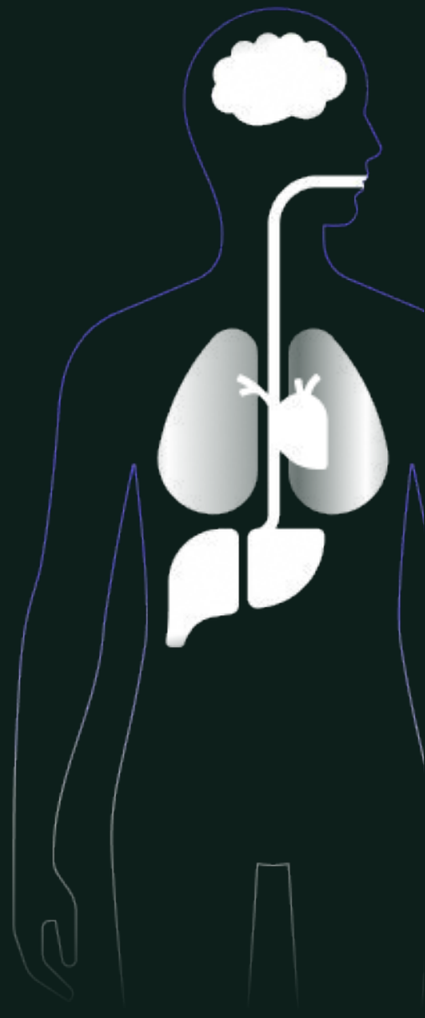
2024

- ✓ **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 (presentation pending)
- ✓ **CAST:** *in vitro* PoC for large gene integration (publication submitted)

Future Technology Milestones

2025 and beyond

- **RIGS or Base Editing:** *In vivo* PoC for small gene correction
  Example disease: A1AT deficiency
- **RIGS:** *in vivo* PoC for site-specific large gene integration with non-viral, single vector delivery
  Example disease: Wilson's
- **RIGS + CAST:** *in vivo* PoC for large gene integration
  Example diseases: Cystic Fibrosis, Duchenne Muscular Dystrophy



Metagenomi

Pipeline Overview

Hemophilia A
MGX-001

A novel, durable, knock-in approach for expression of Factor VIII (FVIII)

THERAPEUTIC CHALLENGES

Available treatments do not eliminate breakthrough bleeds which can result in progressive joint damage

Available gene therapy for adults lacks durability

Available gene therapy not feasible for infants or children

OUR APPROACH (MGX-001)

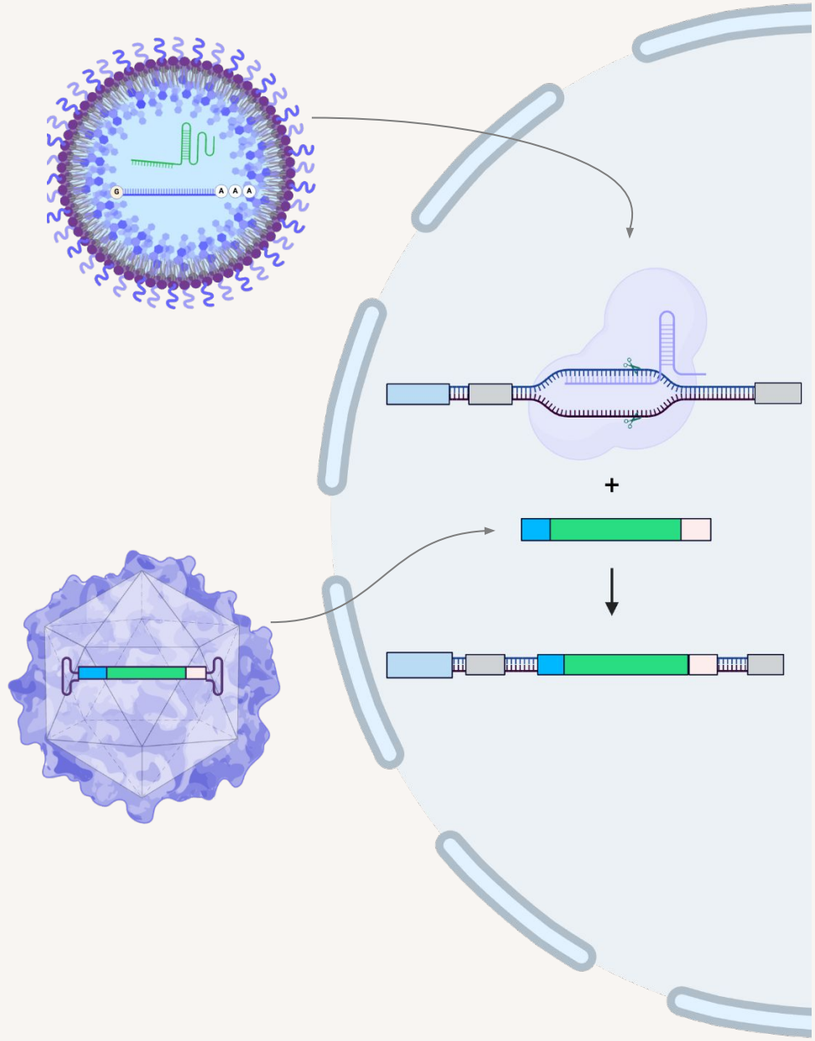
Highly efficient and specific nuclease creates precise cut at albumin safe harbor gene locus after delivery by LNP

AAV vector delivers FVIII DNA template inserted into nuclease cut site by naturally occurring DNA repair process

POTENTIAL BENEFIT

Lifelong, stable FVIII expression due to insertion in safe harbor gene locus

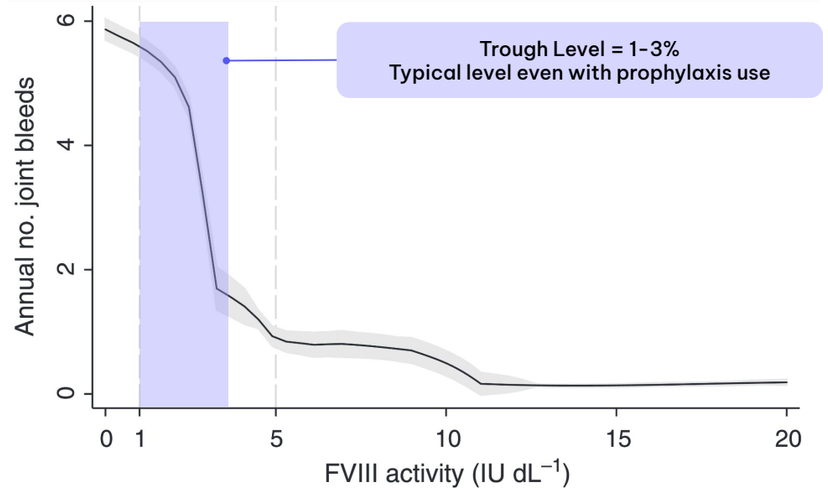
Eliminate need for life long therapy for both adults and children



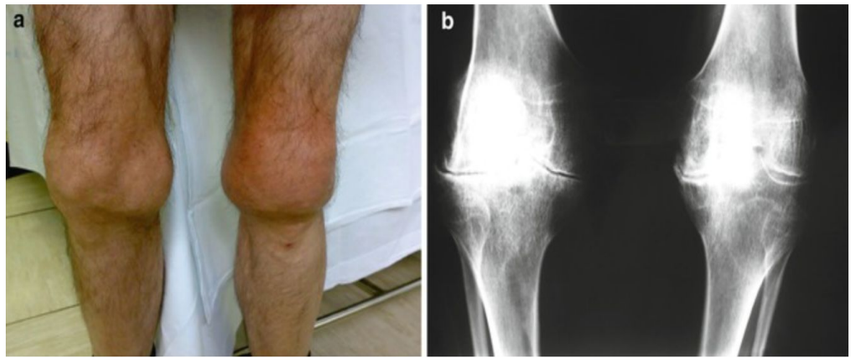
MGX-001 approach presents opportunity to accelerate development into similar secreted protein disorders

Hemophilia A
MGX-001

Life-altering bleeding disorder



Adapted from Den Uijl et al, Haemophilia 2011



https://www.ihtc.org/hemophilia-joint-bleeds

DISEASE BACKGROUND

Most common X-linked inherited bleeding disorder; vast majority of patients are male

Caused by large variety of mutations in the 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;*

More than **500,000** patients globally**

*Soucie, John Michael, et al. “Occurrence…” *Haemophilia*, vol. 26, no. 3, pp. 487–493
**Stonebraker, J. S., et. al. "A study…" *Haemophilia* 16, 20–32

Hemophilia A
MGX-001

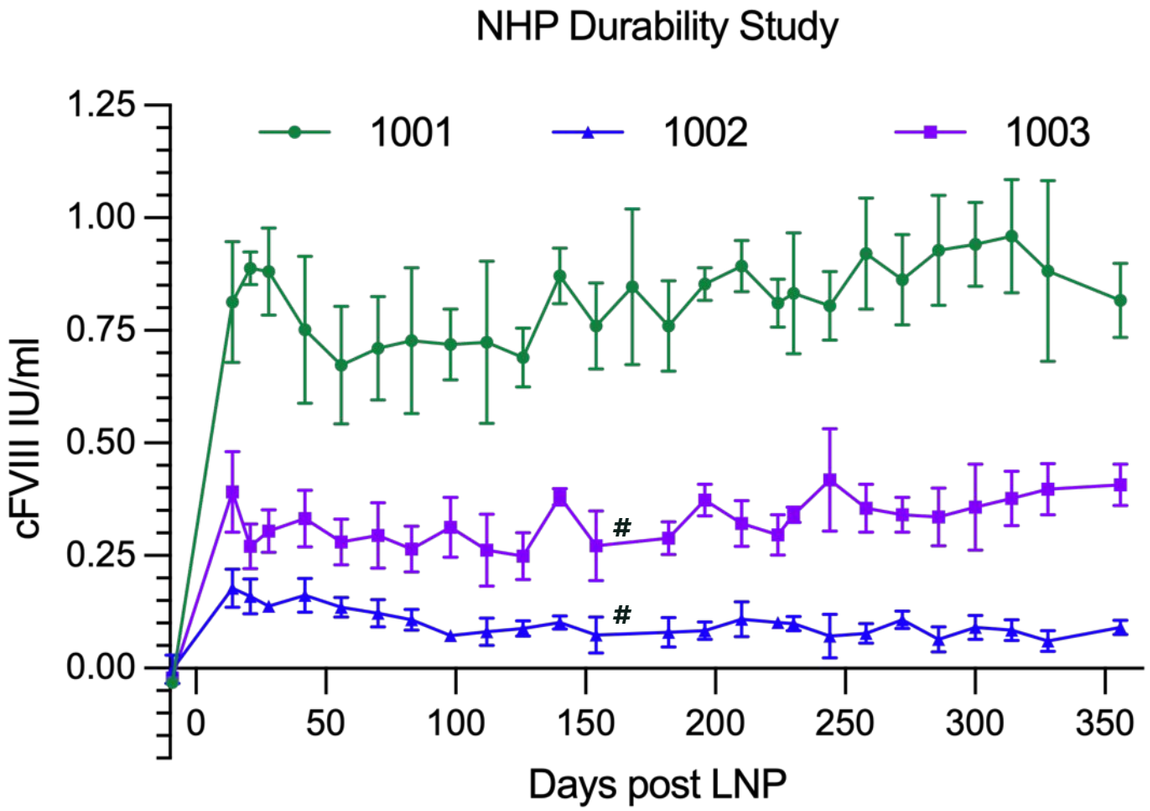
FVIII activity levels sustained for 12 months in this NHP study

Proof of concept for durable and therapeutically relevant FVIII levels achieved in nonhuman primates

- FVIII activity levels do not decrease over time
- FVIII activity levels at 12 month time point are:
  - 1001: 0.81 IU/ml (81.7% normal FVIII values)
  - 1002: 0.09 IU/ml (9.1% normal FVIII values)
  - 1003: 0.41 IU/mL (41% normal FVIII values)
- FVIII activity levels correlate with gene integration frequency from biopsy samples (0.7 – 2.9%)

FVIII levels (IU/ml) over specific time periods

	3-6 months post LNP (d83-d182)		9-12 months post LNP (d272-d356)	
Animal	**Mean**	Stdev	**Mean**	Stdev
1001	**0.762**	0.064	**0.898**	0.054
1002	**0.086**	0.014	**0.083**	0.018
1003	**0.290**	0.045	**0.369**	0.029



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

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

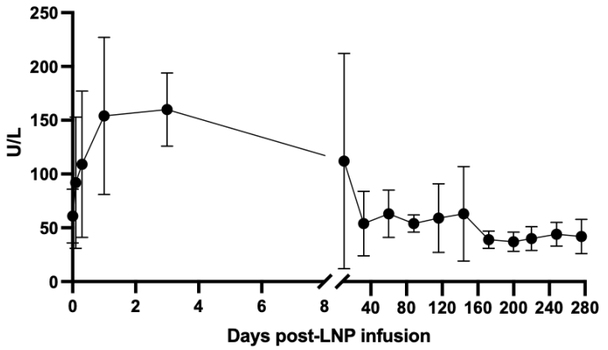
Cyno FVIII gene sequence used to avoid immune response, detection of transgene derived cFVIII achieved by incorporating a single amino acid change that blocks binding of a monoclonal antibody

Summary of safety findings in this NHP study

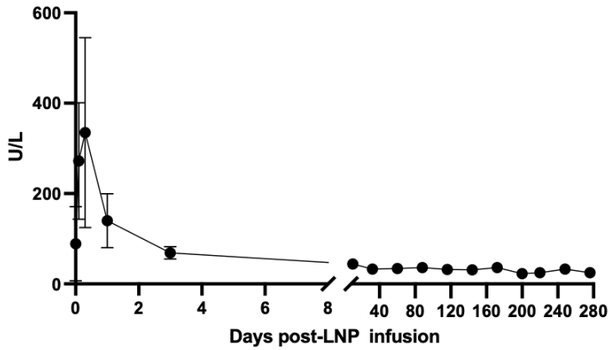
SUMMARY OF SAFETY FINDINGS:

- Transient elevation of liver function tests after the infusion of AAV and LNP
- No significant change in total bilirubin post AAV and LNP
- Integration of the FVIII gene at the albumin locus had no impact on circulating albumin levels
- Animals are healthy and exhibit normal weight gain

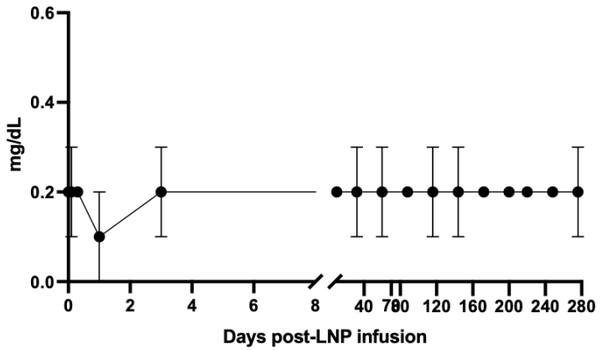
Alanine transaminase (ALT) levels post LNP infusion



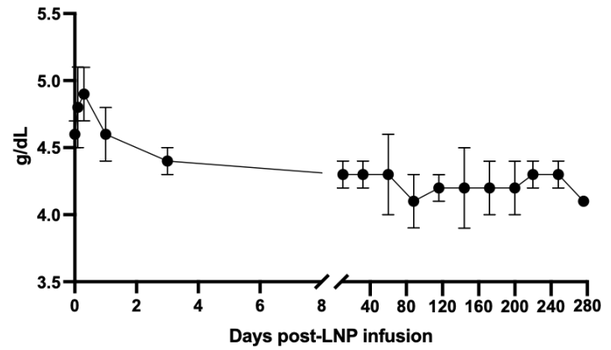
Aspartate transaminase (AST) levels post LNP infusion



Total bilirubin levels post LNP infusion



Albumin levels post LNP infusion



Transthyretin Amyloidosis (TTR)

A single treatment to knockdown gene expression

Partnered with IONIS

THERAPEUTIC CHALLENGES

Despite available approaches, disease still associated with significant morbidity and mortality

Currently lifelong course of treatment

OUR APPROACH

Use our programmable nucleases to knock down wild type or mutated versions of TTR

POTENTIAL BENEFIT

Single-dose treatment for lifelong, stable knockdown of TTR

DISEASE BACKGROUND

Caused by misfolded and aggregated transthyretin (TTR) protein

Potential for organ dysfunction, primarily in the heart and / or peripheral nerves

Potential for progressive heart failure and death within 3 - 5 years of disease onset

PREVALENCE

Up to **40,000** patients worldwide with hereditary ATTR*

300,000–500,000 patients worldwide with wild-type ATTR**

*Hawkins, P. N., et al. “Evolving…” *Annals of Medicine*, 47(8), 625–638.
**Mohamed-Salem L, et al. “Prevalence…” *Int J Cardiol*. 270:192-196.

Refractory hypertension

Leveraging the angiotensinogen (AGT) pathway to treat significant unmet need

Partnered with IONIS

THERAPEUTIC CHALLENGES

Many patients do not reach their blood pressure goals despite multiple approved classes of drugs

Significant issues of adherence to taking large number of daily oral pills

OUR APPROACH

Use our programmable nucleases to knock down AGT

AGT is a novel target which inhibits a pathway known to be associated with multiple diseases

POTENTIAL BENEFIT

Single-dose treatment for lifelong, stable knockdown of AGT

Reliably and consistently control blood pressure throughout the day

Reduce risk of cardiac and other adverse events

DISEASE BACKGROUND

Uncontrolled high blood pressure despite use of at least five antihypertensive agents without achieving goal BP

Potential for heart attack, stroke, vision and kidney damage

PREVALENCE

900,000 patients in the US with refractory hypertension*

*Yoon, Minjae, et al. “Prevalence…” *Hypertension Research*, vol. 45, no. 8, pp. 1353–1362

Targeting disease with small gene corrections and large gene insertions

	Alpha-1-antitrypsin (A1AT deficiency): Protein deficiencies impacting lung & liver	**Wilson's Disease:** Serious disease of copper metabolism
THERAPEUTIC CHALLENGES	• Protein augmentation therapy has limited longer term protection of lung function • Approach is costly and not available for many patients • Infusions sometimes associated with adverse events • Organ transplantation may be required	• Copper chelators have many side effects that can lead to discontinuation • Discontinuation can lead to hepatic decompensation potentially requiring liver transplant • Fatal if left untreated
OUR APPROACH	• Use RIGS for gene correction and to avoid bystander edits • Alternative: Use base editor for gene correction of PiZ mutation in SERPINA1 gene	• Use of RIGS to insert a section of the ATP7B gene encoding the majority of disease causing mutations
POTENTIAL BENEFITS	• Single-dose treatment provides lifelong, stable A1AT protein expression	• Single dose treatment eliminates need for life-long therapy • Eliminate risk of adverse events • Approach provides potential to treat majority of patients irrespective of specific mutations

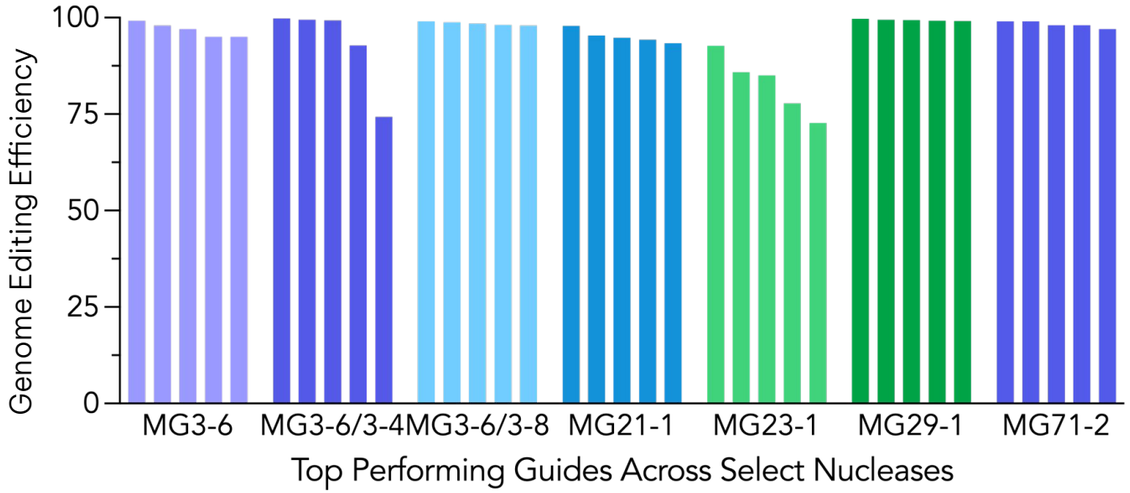
Metagenomi

Technology Platform

Highly efficient nucleases designed for any target in the human genome

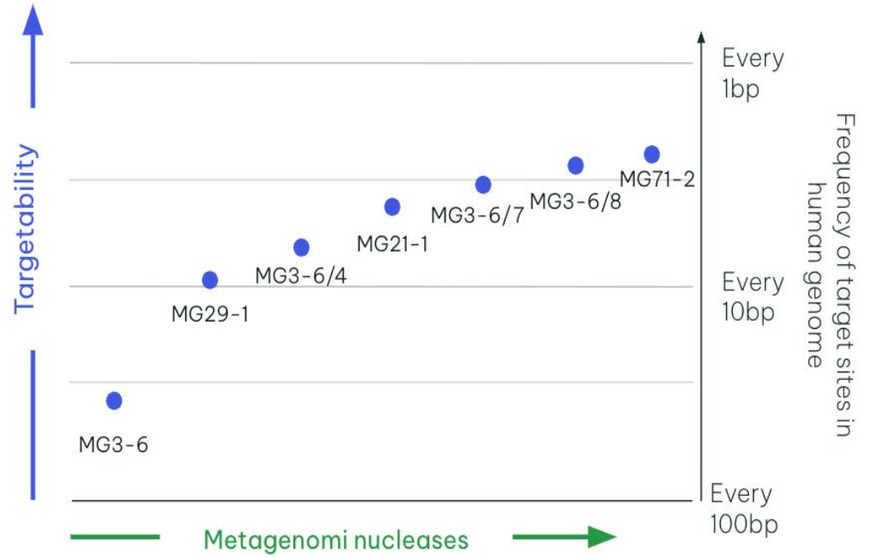
Our nucleases, selected for their native high-efficiency, expand targeting options within genes of interest

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

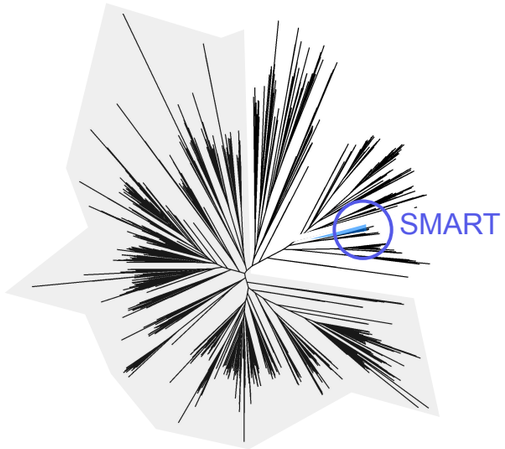
Search our metagenomics database for novel compact nucleases

Characterize small CRISPR-associated nucleases (SMall ARginine-rich sysTems: "SMART")

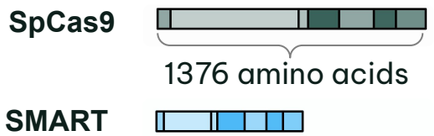
Design SMART nucleases with generative AI and ancestral sequence reconstruction (ASR)

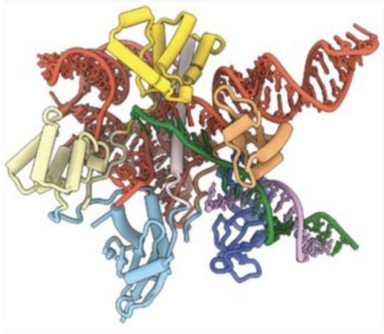
Optimize SMART nucleases with fine-tuned AI models and protein structure

Protein sequence comparisons highlight novelty of SMART CRISPR systems



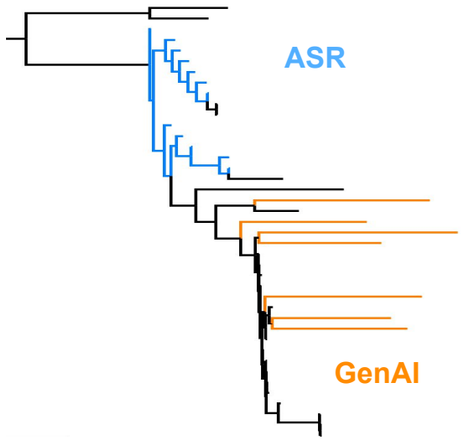
*Phylogenetic tree comparing CRISPR nucleases
*Gray shaded area indicates previously known nucleases including SpCas9





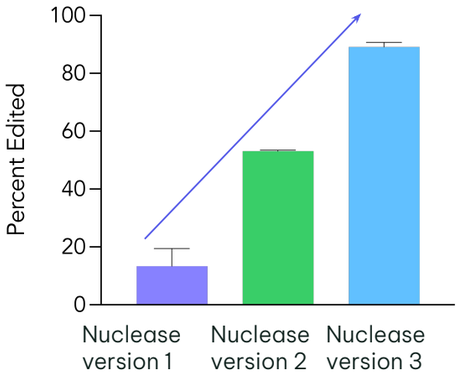
*Protein structure defined in collaboration with David Taylor, UT Austin

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

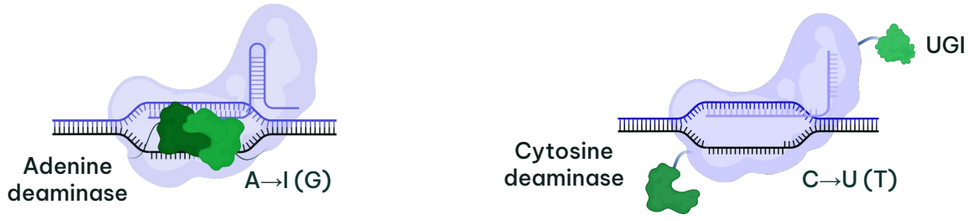
Editing efficiency improved to >90% with engineered SMART nucleases <750aa



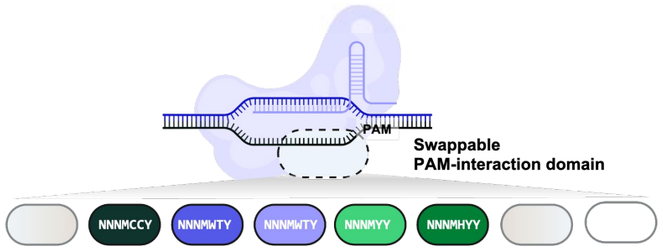
*Gene editing in human cells with engineered SMART nucleases measured by NGS
*Compact size enables all-in-one AAV delivery

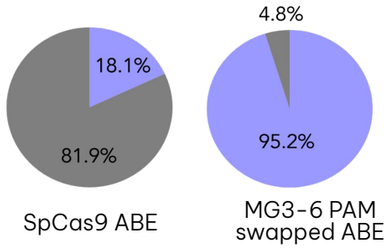
Base editing platform with broad targetability achieves efficient multiplex editing for cell engineering

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



Reprogrammed chassis increases genome targetability of Base Editors

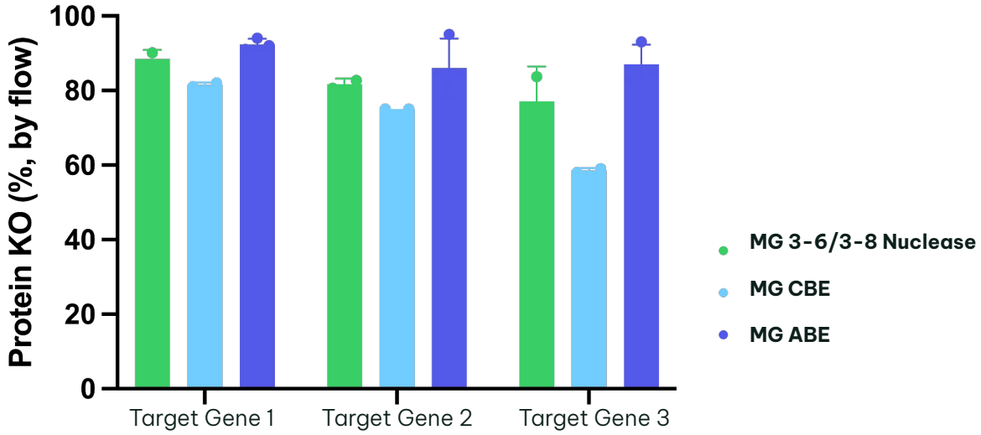




ABE: SpCas9 = 18% and MG3-6 = 95% targetability
CBE (not shown): SpCas9 = 5% and MG3-6 = 53%
*SpCas9 analysis with NGG PAM

Targetable
Nontargetable

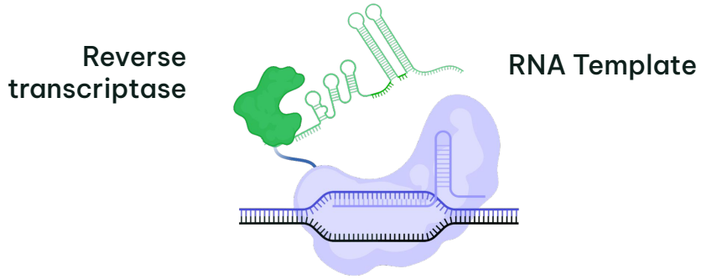
ABE, CBE and nuclease are efficient for multiplexed knockout in primary T cells



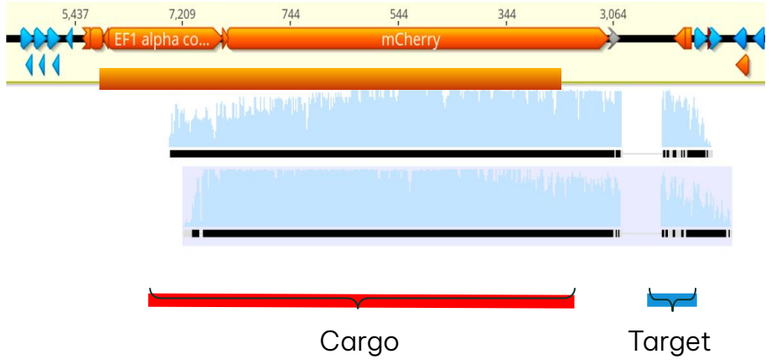
1. Top guides for three cell therapy knockout targets were tested in a multiplexed fashion
2. Edits durable over 10 days and do not impact cell viability or expansion (not shown)

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

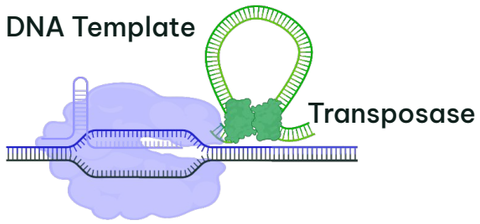
RIGS (RNA-Mediated Integration Systems)



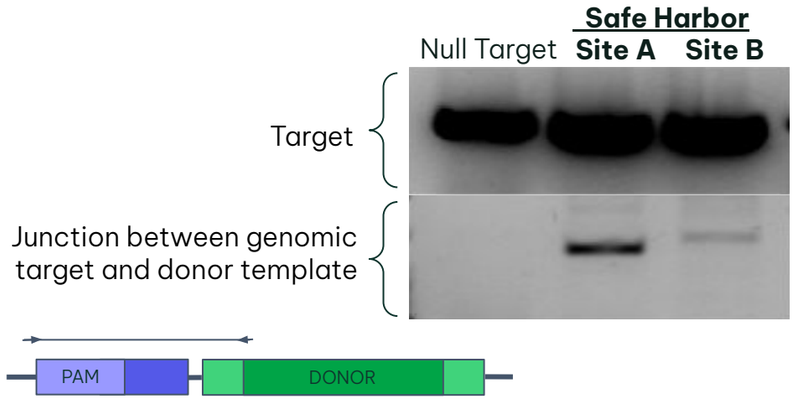
First-ever report of targeted integration of >900 bp with all-RNA delivery



CAST (DNA-Mediated Integration Systems)



Demonstrated large targeted genome integration using compact CAST in human cells



Metagenomi

Corporate Highlights

Recent and upcoming milestones drive towards the clinic

	Recent milestones achieved	2H' 2024	2025
Hemophilia A Program	✓ Generated robust proof-of-concept data in multiple NHP studies ✓ Engaged with FDA for regulatory advice ✓ Nominated Development Candidate	• Confirm 12-month durable expression of Factor VIII in NHP study • Initiate GMP manufacturing and related IND enabling activities	• Continue IND enabling activities to support an IND filing in 2026
Cardiometabolic Programs	✓ Advanced all four targets in wave one of Ionis collaboration in lead optimization	• Demonstrate *in vivo* proof-of-concept supporting Development Candidate nominations	• Nominate one to two Development Candidates
Other Therapeutic Programs	✓ Established GMP genome editing reagents for cell therapy and regulatory filing to support Affini-T IND	• Present multiplex base editing data at scientific meeting for cell therapy applications	• Continue to advance early-stage pipeline for multiple future IND filings

Cash runway into 2027

Technology innovations continue…

Technology milestones achieved

2021-2022

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

2023

- ✓ 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**

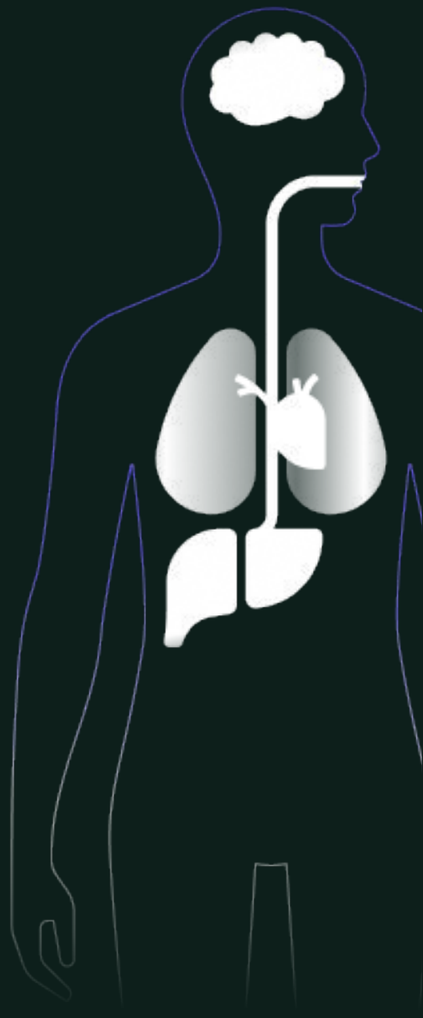
2024

- ✓ **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 (presentation pending)
- ✓ **CAST:** *in vitro* PoC for large gene integration (publication submitted)

Future Technology Milestones

2025 and beyond

- **RIGS or Base Editing:** *In vivo* PoC for small gene correction
  Example disease: A1AT deficiency
- **RIGS:** *in vivo* PoC for site-specific large gene integration with non-viral, single vector delivery
  Example disease: Wilson's
- **RIGS + CAST:** *in vivo* PoC for large gene integration
  Example diseases: Cystic Fibrosis, Duchenne Muscular Dystrophy



Thank you

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