Precision gene editing designed to deliver durable, curative medicines

Hemophilia A lead program | IND 2026

Corporate Presentation
May 2026

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.

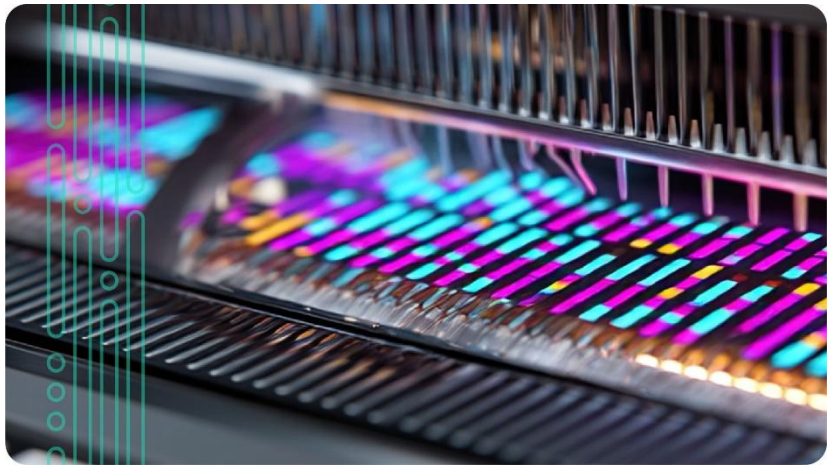
We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short- and long-term business operations and objectives, and financial needs. These forward-looking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

A differentiated *in vivo* gene editing company advancing curative genetic medicines

Metagenomi THERAPEUTICS



An *in vivo* CRISPR gene editing company capitalizing on its proprietary technologies to create curative genetic medicines

Focusing on lead program MGX-001 in hemophilia A advancing to the clinic

Expanding indications leveraging site-specific gene integration system and partnered assets targeting cardiometabolic indications

Differentiated gene editing beyond CRISPR/Cas9

20,000 +

Signature editing systems from Metagenomi's database

Proprietary CRISPR genome editing

High specificity

Precise editing

Durable integration

Large gene insertion

Broad targeting

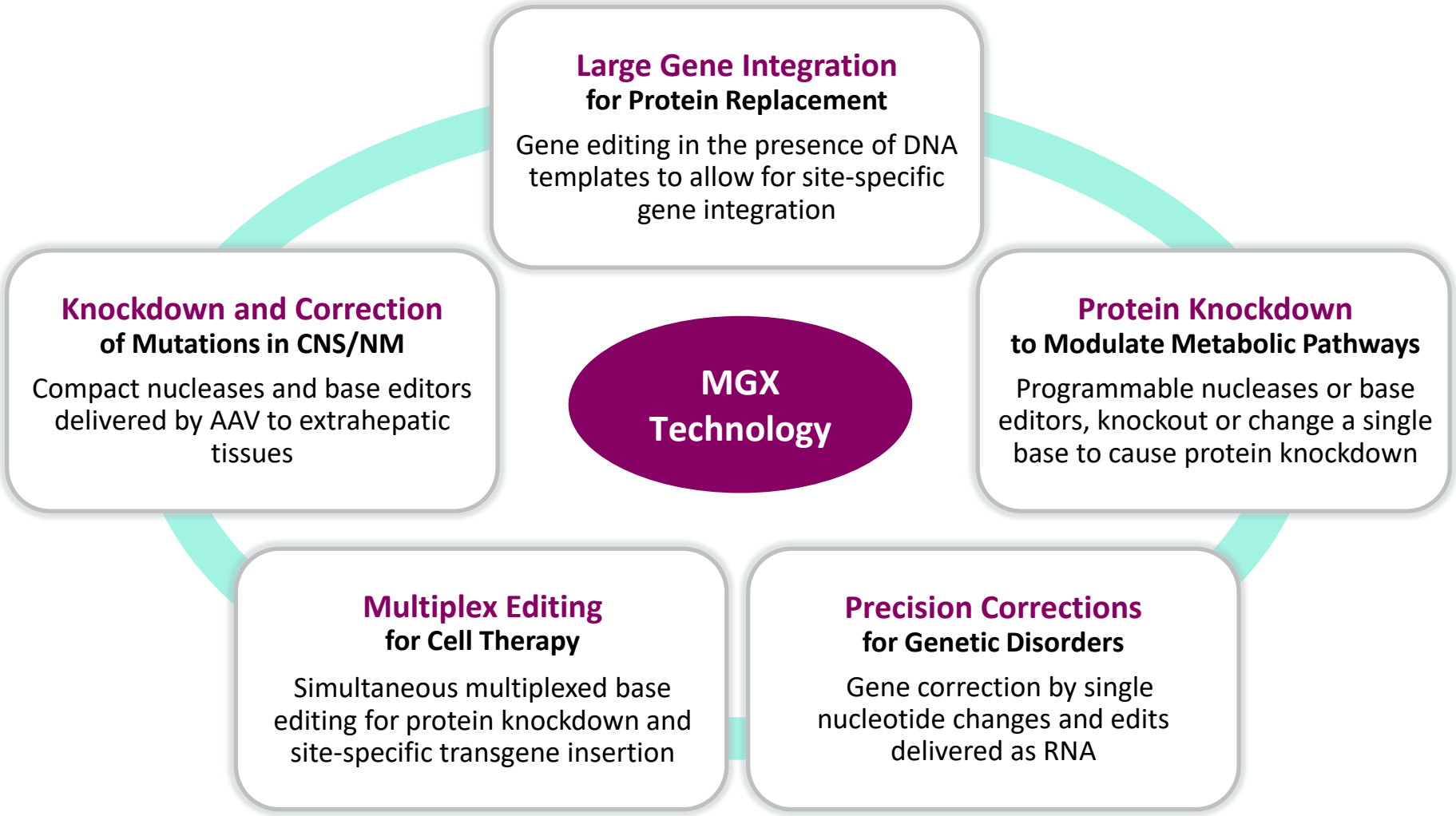
Expanded genome access

Multiplexed editing

Multi-gene capability

We improve editing precision and expand genome targeting and editing functionality beyond CRISPR/Cas9 to effectively address genetically-driven diseases.

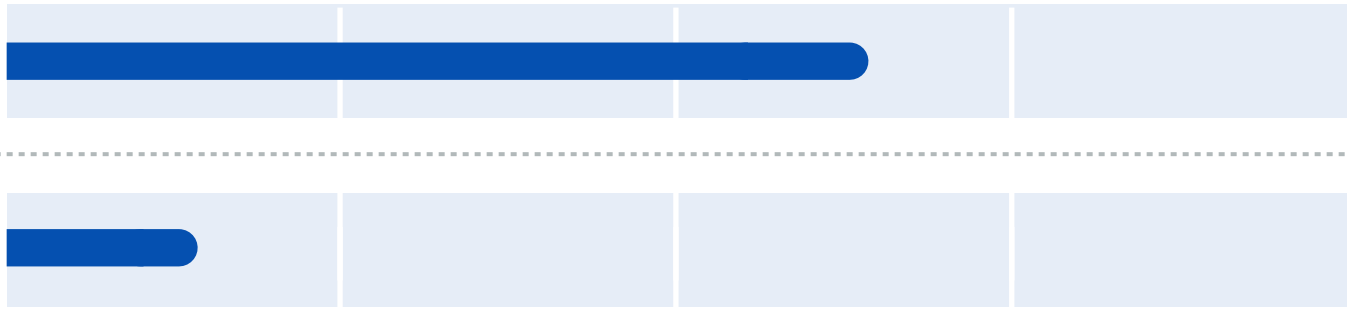
A versatile platform designed to address a wide range of genetic diseases



Potentially capable of correcting any type of genetic mutation found anywhere in the human genome

Focused pipeline anchored by differentiated lead program

Editing platform:	Indication:	Editing target:	Discovery	Lead optimization	IND-enabling	Clinical
Protein replacement via gene insertion	MGX-001 Hemophilia A	ALB				
	Undisclosed	Undisclosed				
Protein reduction via gene knockout	Cardiometabolic Diseases	TTR AGT APOC3 Undisclosed				



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Metagenomi is exploring opportunities to pursue neuromuscular disease targets & liver disease targets such as A1AT and Wilson Disease, as well as business development to expand therapeutic applications including cell therapy.

MGX-001 development roadmap to clinic

NOW

Pre-IND Interaction Complete

Dec 2025 FDA meeting — collaborative, favorable outcome

Q4 2026

IND Submission

Submit IND for first-in-human Phase 1/2 study

2027

First Patient Dosed

Global single-arm study; observe initial safety and efficacy within weeks of dosing

2027 and beyond

Dose Escalation

Identify target dose; expand to pediatric patients

Goal: Enable a new standard of care for hemophilia A – a one-time cure freeing patients from lifelong treatment burden and bleeding risk

$140.2 million in cash, cash equivalents, and available-for-sale marketable securities at end of Q1 2026
Runway anticipated to support operations through Q4 2027

MGX-001 - designed to deliver a durable, one-time treatment for Hemophilia A

Hemophilia A: large, validated market still lacking a durable cure

~26,500
patients in the U.S.[1]

~500,000
worldwide[2]

Hemophilia A is the most common X-linked inherited and de novo bleeding disorder, largely affecting males.

Caused by variety of mutations in the Factor VIII (FVIII) gene leading to loss of functional FVIII protein.

NASDAQ: **MGX**

Current Standard of Care:

Factor VIII replacement therapy

- IV typically dosed 1 - 3 times/week
- Significant adherence challenges
- Risk of breakthrough bleeding
- Chronic treatment, non-curative

Bi-specific antibody "mimetic"

- SQ dosed 1, 2 or 4 weeks post loading
- Risk of breakthrough bleeding
- Treatment burden, non-curative

Recent Curative Gene Therapy Attempted:

- Variable initial efficacy
- Decline in FVIII levels over time
- High risk of prolonged corticosteroid use
- Not suitable for pediatric patients

Annual treatment cost[3]:

~$565K - $750K

Lifetime treatment cost:

~$18M - $24M[4]

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.
3 - ICER. Gene Therapy for Hemophilia B and A: Final Evidence Report. Dec 22, 2022.
4 - Curtis R et al. Poster presented at: 65th ASH Annual Meeting & Exposition; December 11, 2023; San Diego, CA.

Genome editing offers a potentially ideal curative approach for Hemophilia A

Hemophilia A is an ideal indication for genome editing approach:

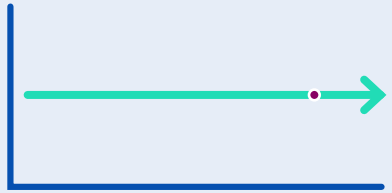
- Monogenic and well-characterized biology with clear biomarker
- Clearly defined target threshold of curative FVIII level & wide safety range
- Robust preclinical models and regulatory familiarity
- Strong advocacy and infrastructure
- Clear opportunity for a durable cure

MGX-001 is uniquely suited for patients of all ages:

Technology:

proprietary Type V nuclease

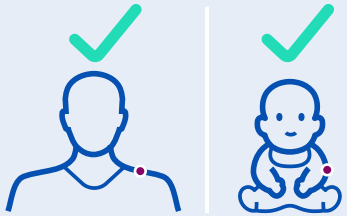
Durability:



Regulatory status:

IND-enabling stage

Pediatric potential:



MGX-001 is a potentially durable, curative approach for adults and children – the population with the most to gain

Compelling preclinical profile achieved across efficacy, durability, and safety

Extensive and supportive preclinical data set

- FVIII activity achieved in **curative range** with clear dose response in NHPs
- **Durable** FVIII activity over approximately 19-month study in NHPs
- **Encouraging safety profile** with single doses of steroids, and no genotoxicity observed

Novel mechanism of action

- FVIII integration leveraging **albumin promoter** to achieve normalized activity level
- **Promoterless FVIII gene** delivered by AAV effective at **lower dose** than approved gene therapies
- Precise FVIII integration facilitated by proprietary CRISPR nuclease MG29-1 achieving **no detectable off-target** editing

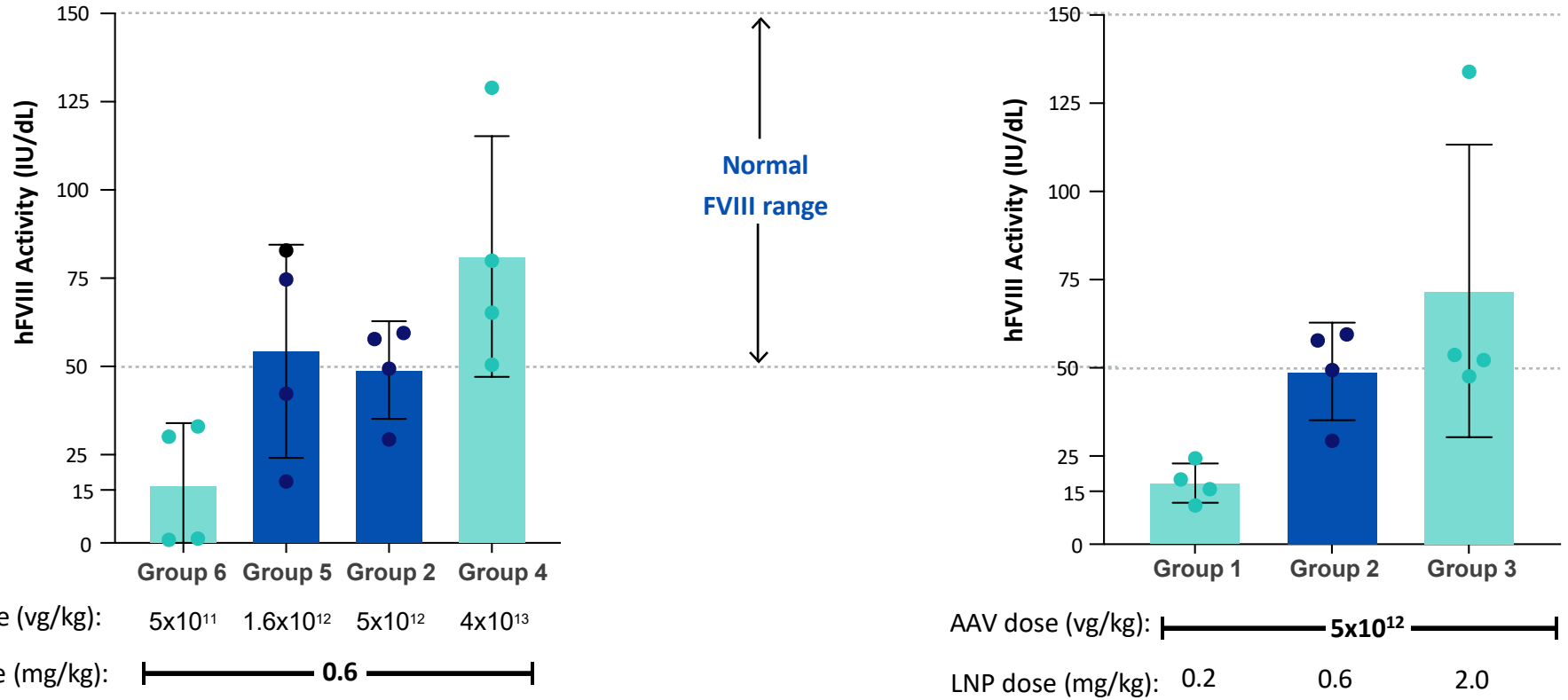
Compelling potential clinical profile

- Enables **endogenous production** of FVIII supporting hemostatic regulation
- Potential to normalize FVIII levels and deliver meaningful clinical benefit for both **adults and pediatric** patients
- Goal to be one-time durable cure allowing patients the freedom of a **hemophilia free mind**

Curative FVIII range achieved

Development candidate

Dose range finding study in NHP identified minimum and optimal efficacious doses

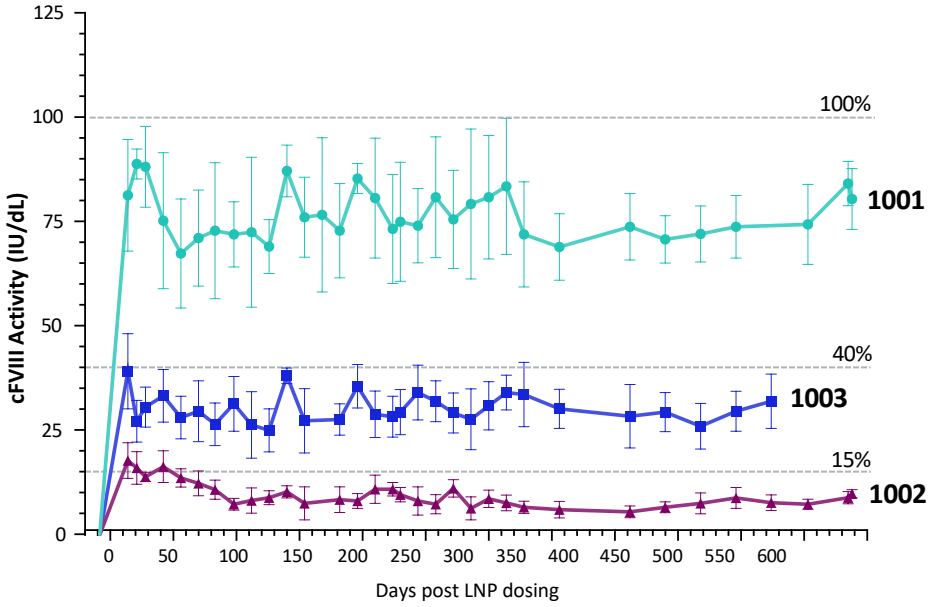


FVIII activity for each animals is the mean of values on d5, d8, d11 post LNP dosing measured with a capture-chromogenic assay. hFVIII activity was stable from d5 to d11 post LNP. Xyntha was used for the standard curve.

Durable FVIII expression demonstrated ~19 months

Pre-development candidate

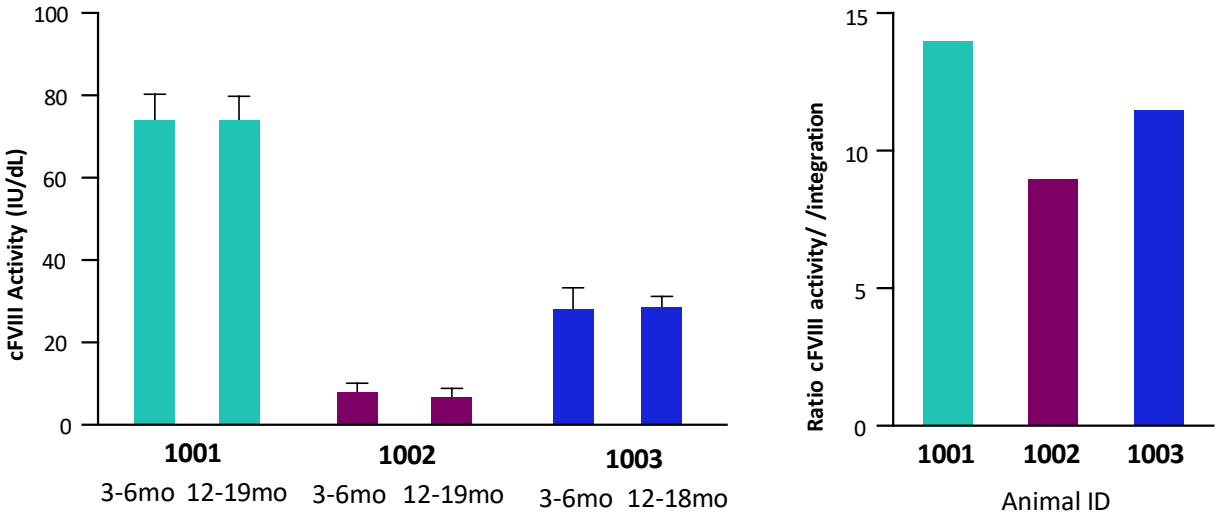
NHP durability study: Stable expression over ~19 months



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 on day 540 (17.8 mo) post LNP, assessed as unrelated to the treatment.

Plasma FVIII activity levels unchanged between 3-6 months and 12-19 months and correlate to integration:



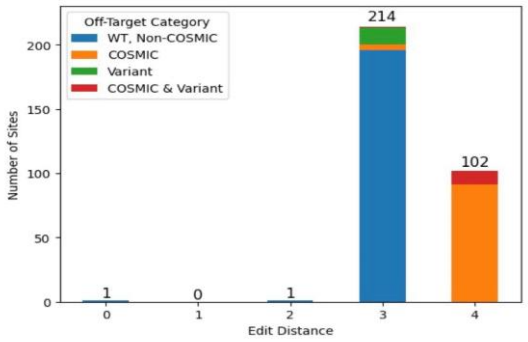
1 - Integration in forward orientation (copies per 100 haploid genomes, average of 5 liver lobes).

No genotoxicity observed

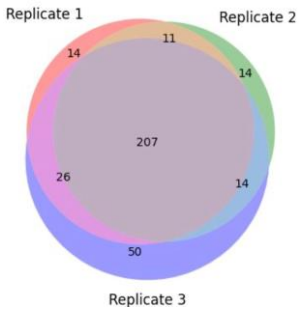
Development candidate

Discovery of potential off-target sites

1. In silico off-target discovery:



2. Biochemical off-target discovery:

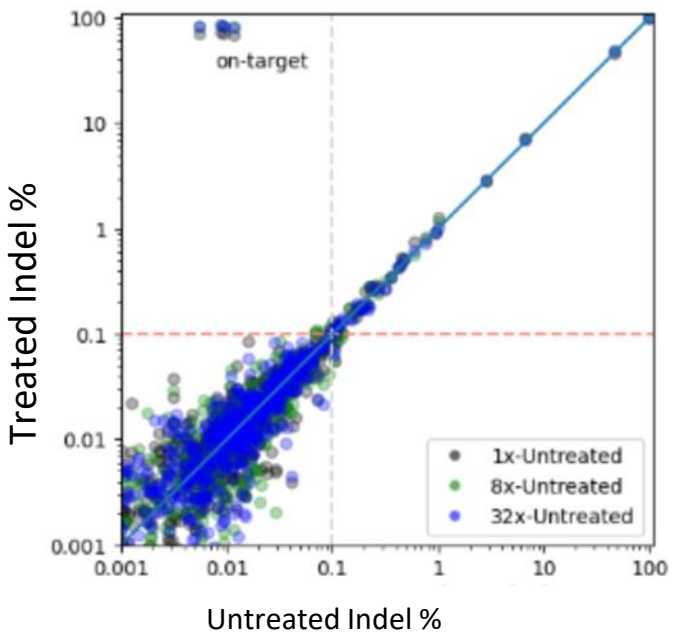


3. In cell off-target discovery:

No potential off-targets were discovered in cell-based assays.

No validated off-target sites observed

Three independent primary human hepatocyte donors:

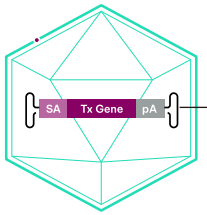


Genome integrity maintained as observed via off-target editing and AAV integration assays.

MGX-001: leveraging natural promoter through FVIII gene integration

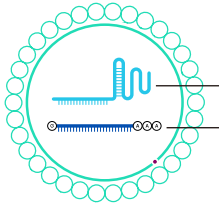
MGX-001 components:

AAV delivers FVIII gene (donor DNA):



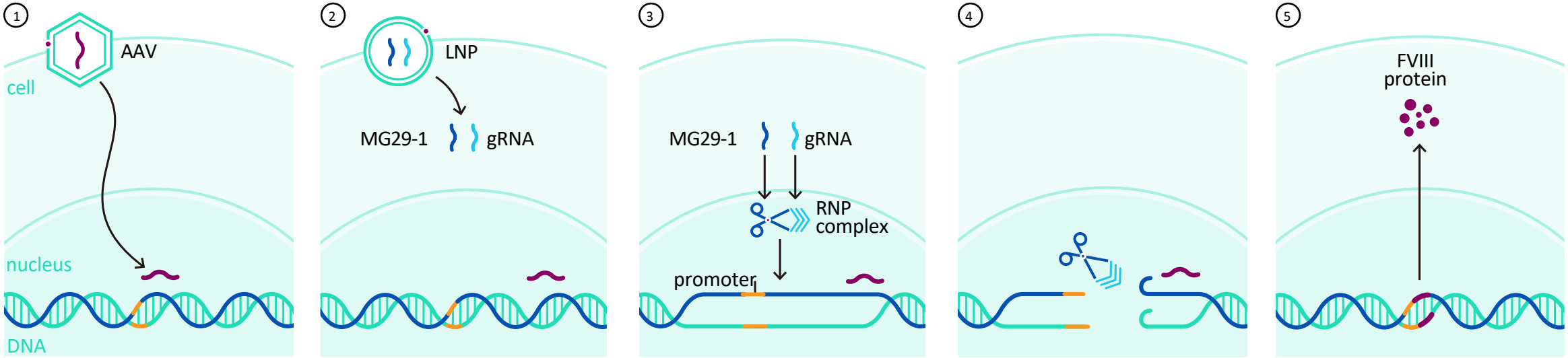
Promoterless FVIII gene

LNP delivers CRISPR nuclease mRNA & gRNA targeting albumin:



Guide RNA (gRNA)

Nuclease mRNA (MG29-1)



AAV delivers FVIII gene

LNP delivers CRISPR cargo

CRISPR cargo forms complex

Cut at albumin locus and FVIII gene integrates

Albumin promoter drives sustained FVIII production

Potential to deliver a durable cure for both adult and pediatric patients with hemophilia A

Designed to enable endogenous FVIII expression for hemostatic regulation

Compelling pre-clinical data

- Curative FVIII activity
- Durable FVIII expression

Encouraging safety profile

- Minimal steroid use
- Promoterless AAV application
- No off-target editing observed

Established regulatory framework and defined clinical endpoints

- pre-IND interaction completed
- IND submission on track for Q4 2026
- First-in human in 2027

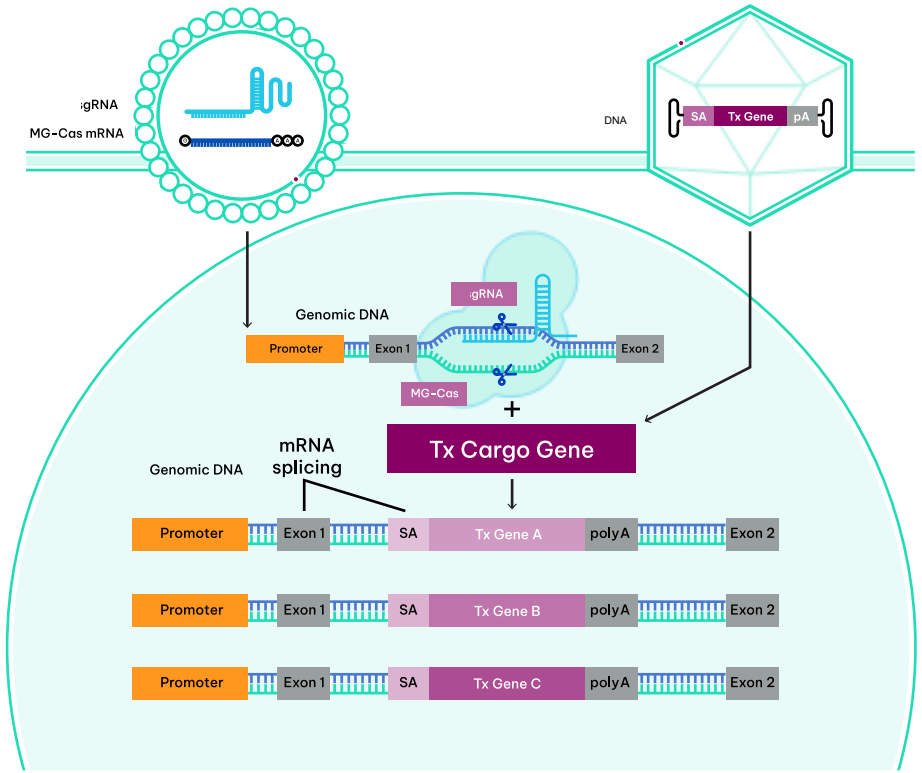
Our goal: To enable a new standard of care for hemophilia A

Expanding applications of site-specific large gene integration system

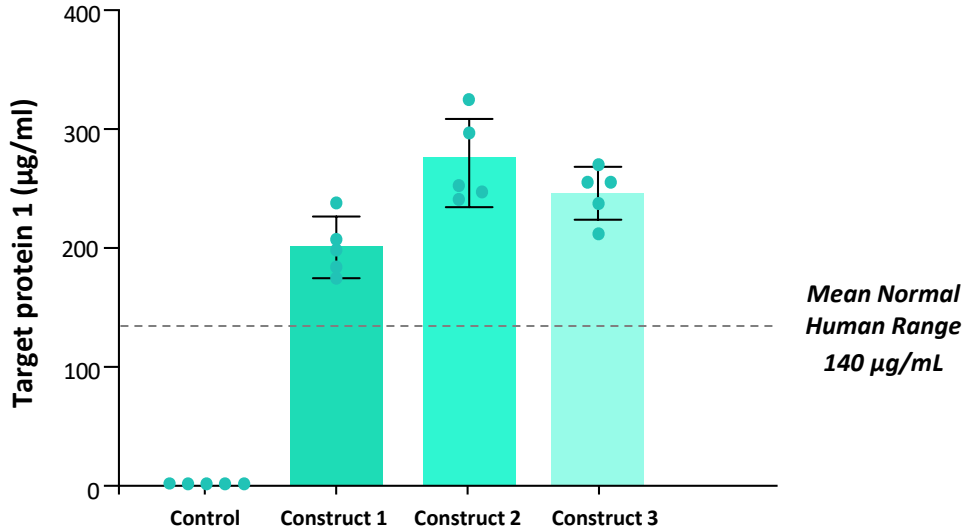
Leverage site-specific large gene integration across additional indications

Expanding MGX-001 site-specific gene integration system into additional therapeutic targets

- LNP delivers nuclease mRNA and guide targeting albumin site
- AAV delivers Transgene (donor DNA)

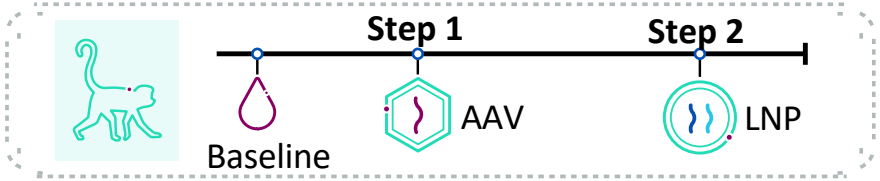


Normal circulating levels of target protein achieved in secreted protein disorder mice with multiple construct designs



- Above 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

Proof-of-concept demonstrated in additional disease models



N=3

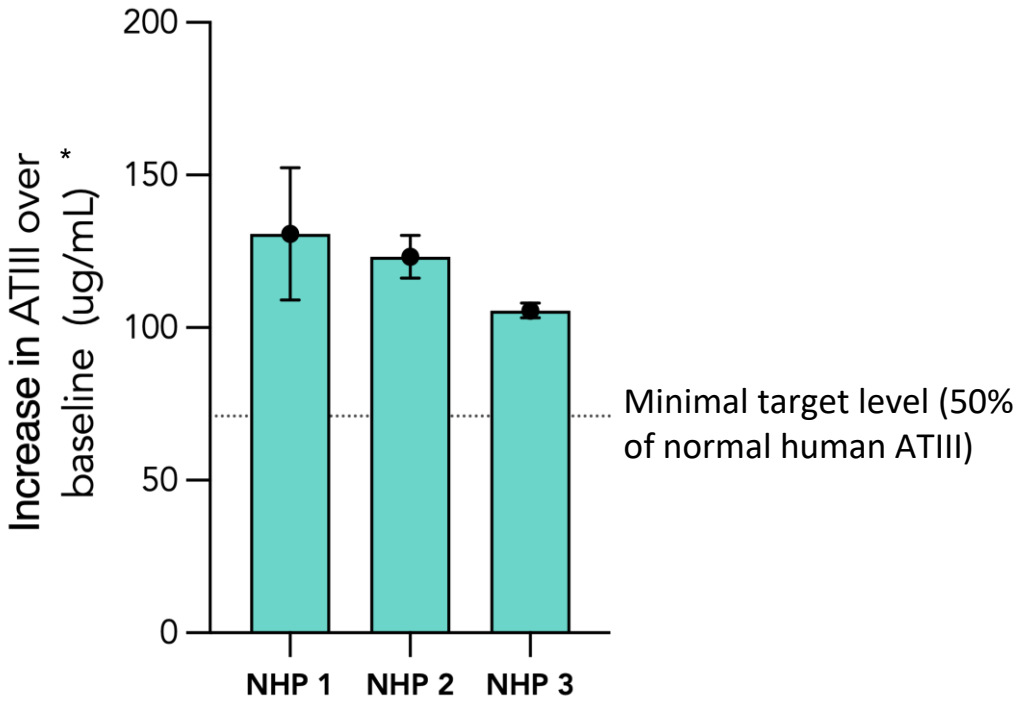
In-life, study

Ongoing at 46 days

	AAV dose (vg/kg)	LNP dose (mg/kg)
Animal 1001		
Animal 1002	1.0×10^{13}	1.0
Animal 1003		

- Severe antithrombin (AT-III) deficiency increases risk of venous thromboembolism (VTE)
- On average patients with severe disease have 50% of the normal amount of AT-III in their blood (70 ug/ml) [1,2]
- Replacing the missing AT-III with at least 50% of normal is expected to be a functional cure

Achieved circulating AT-III protein exceeding curative target of 50% of normal human levels

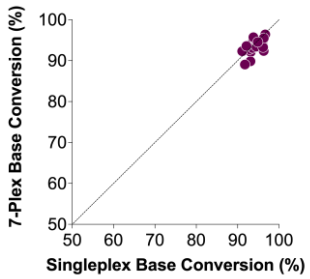


*Data are the mean of day 8 and 11 post-dosing minus the mean of days 0, 4 and 7 pre-dose

1. Lane DA, Bayston T, Olds RJ et al. Antithrombin mutation database: 2nd (1997) update. For the Plasma Coagulation Inhibitors Subcommittee of the Scientific and Standardization Committee of the International
2. Conard et al (1983). Molar antithrombin concentration in normal human plasma. Haemostasis.13:363–8

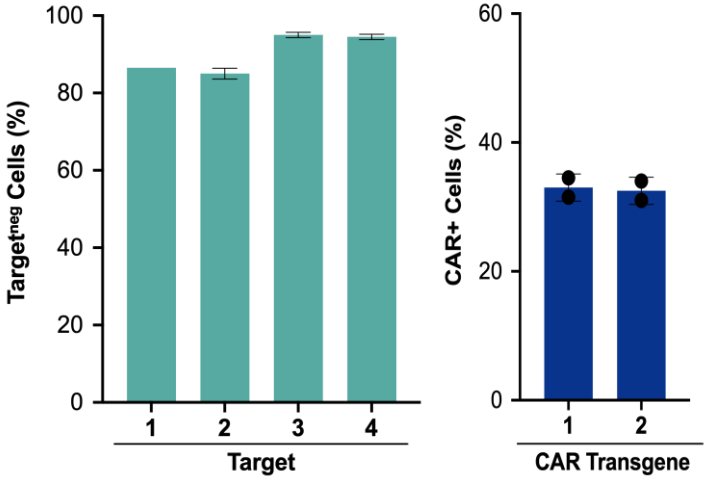
Broaden therapeutic potential with transformative gene editing

Multiplex editing and compact editors enable next-generation therapies

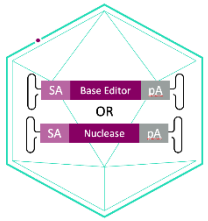


Multiplex editing in T-cells achieved across seven unique gene targets at as high efficiency as single plex editing

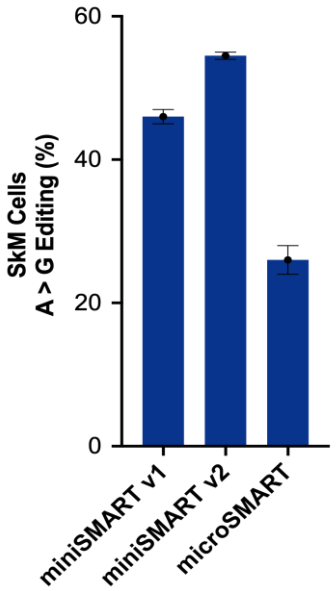
Combined protein knockdown and CAR knock-in in a single-step for cell therapy applications



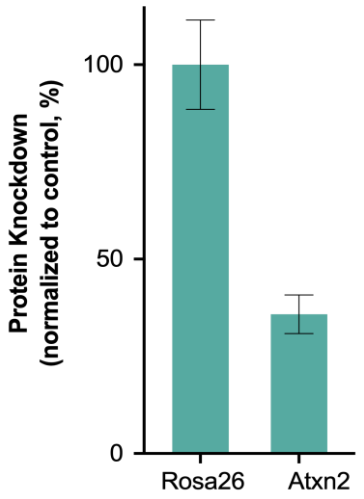
Four-plex knockdown and dual CAR knock-in in T cell with MGABE100 + 5 gRNA + DNA CAR template[1]



Compact nucleases and base editors demonstrated high editing efficiency and compatibility with AAV delivery[2,3]



Multiple compact base editors[2] demonstrated effective neuromuscular targeting



Compact nuclease MG119-28 achieved 64% knockdown of Atxn2 protein in mice[4]

NASDAQ: **MGX**

1. van Overbeek, M., et al, Presentation at 10th Annual CAR TCR Summit, 2025
2. Rallapalli, R., et al, Submitted, 2026
3. Guan, K., et al, Nature Structural and Molecular Biology, 2026
4. Senger, K., et al, Poster presented at ASGCT Annual Meeting, 2025

Strategic partnership expands reach into large cardiometabolic markets

Current indications:

- **TTR**
- **AGT**
- **APOC3**
- **Undisclosed**

IONIS

- MGX's in vivo genome editing complements Ionis leadership in cardiometabolic space
- 4 targets: two co-development and co-commercialization options
- Multibillion dollar TAM

Building a leading gene editing company focused on cures

- Broad and differentiated library of **proprietary gene editing** technologies representing a significant long-term value driver
- Advancing **MGX-001 for hemophilia A** with clear development path and well-defined clinical and regulatory endpoints
- Extending **beyond hemophilia A**, large gene integration system opens potential to address other protein deficiencies
- Pairing our gene-editing capabilities with complementary expertise to **accelerate development through collaboration**

Thank you

Metagenomi
THERAPEUTICS