Precision gene editing designed to deliver durable, curative medicines



Corporate Presentation
November 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 the timing of and our ability to make regulatory filings such as INDs, the design and timing of the INTEGR8 trial and initial clinical data, expectations regarding MGX-001 including the preclinical profile with best-in-class treatment potential, statements regarding the Company's plans to prioritize its preclinical pipeline and potential for value creation and sustainable growth, statements regarding upcoming milestones, statements concerning the potential of therapies and product candidates, statements concerning the impact of organizational restructuring, statements concerning our anticipated cash runway, and any other statements that are not historical facts. 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.

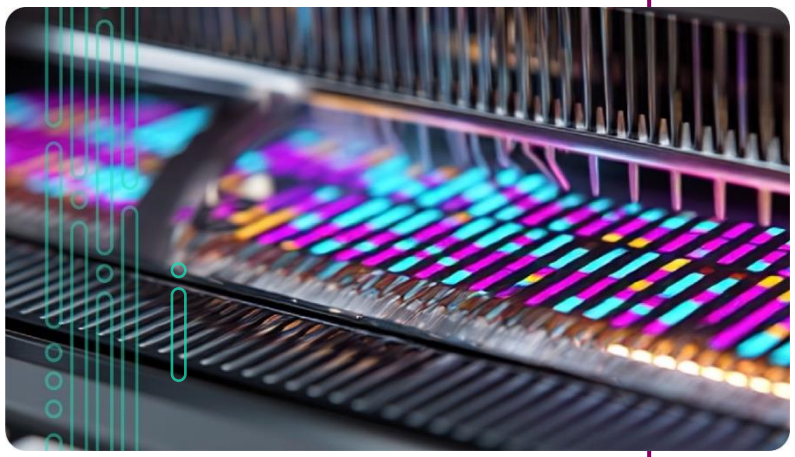
We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short- and long-term business operations and objectives, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including but not limited to 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; the risk that the FDA or other regulatory authorities may place a clinical hold on our clinical trials or that initiation of our clinical trials may be delayed; 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; the volatility of capital markets and other adverse macroeconomic factors; 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 potentially curative genetic medicines

Metagenomi THERAPEUTICS



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

Focusing on lead program **MGX-001 in hemophilia A advancing to the clinic** with clear development path and well-defined clinical endpoints

Expanding indications by leveraging **differentiated site-specific large gene integration systems and partnered assets** targeting cardiometabolic indications

$101.7 million in cash[1] at end of Q3 2026; **Runway anticipated to support operations into 2028**[2]

[1] Cash includes cash, cash equivalents and available-for-sale marketable securities
[2] As filed in the Company's Form 10-Q for Q3 2026 earnings on November 10, 2026

Differentiated and proprietary gene editing technologies

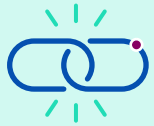
20,000 +

Suite of novel editing tools from Metagenomi's unique database



High specificity

Precise editing



Durability

Long term effectiveness



Broad targeting

Expanded genome access



Multiplexed editing

Multi-target capability

We improve editing precision and expand genome targeting and editing functionality beyond CRISPR/Cas9 to effectively address diseases with an underlying genetic cause.

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

Metagenomi Technology

Large Gene Integration
Protein replacement

Gene editing in the presence of DNA templates to allow for site-specific gene integration

Protein Knockdown
Cardiometabolic pathways

Programmable nucleases or base editors make deletions or change a single base to cause protein knockdown

Precision Corrections
Genetic disorders

Gene correction by single nucleotide changes delivered as RNA

Multiplex Editing
Cell therapy

Simultaneous multiplexed base editing for protein knockdown and site-specific transgene insertion

Knockdown & Correction
CNS & muscle

Compact nucleases and base editors delivered by AAV to extrahepatic tissues

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

Focused pipeline anchored by differentiated gene editing technologies

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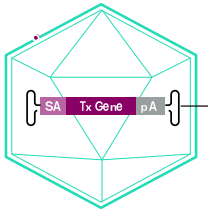
Metagenomi is exploring opportunities to pursue neuromuscular disease targets & liver disease targets such as A1AT and Wilson Disease, as well as business development to expand therapeutic applications including cell therapy.

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

MGX-001: leveraging natural promoter to drive durable Factor VIII (FVIII) production

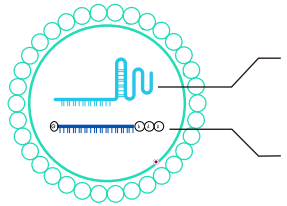
MGX-001 components:

AAV delivers donor DNA:



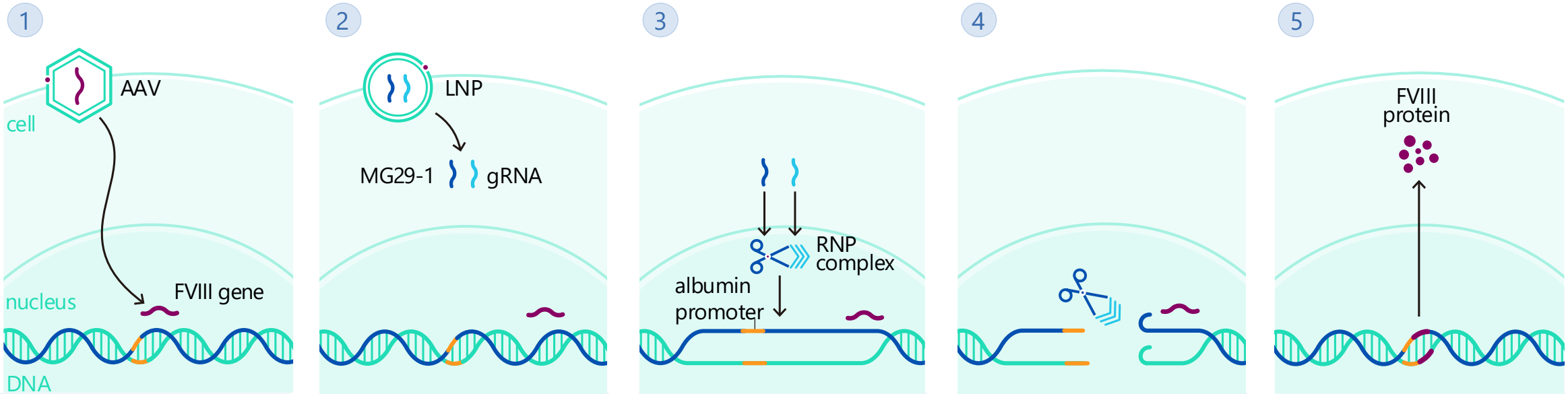
Promoterless FVIII gene

LNP delivers CRISPR nuclease mRNA & gRNA targeting albumin



Guide RNA (gRNA)

Nuclease mRNA (MG29-1)



AAV delivers FVIII gene

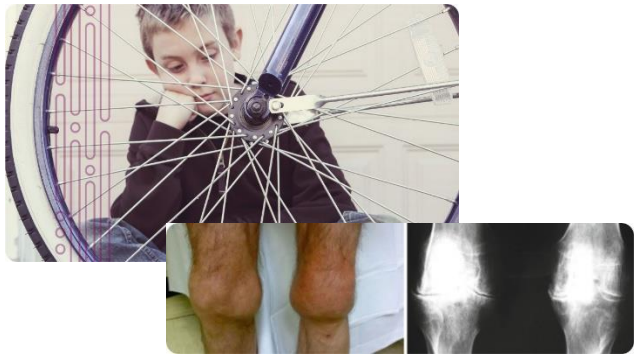
LNP delivers CRISPR cargo

CRISPR cargo forms complex

Cut at albumin locus and FVIII gene integrates

Albumin promoter drives sustained FVIII production

Hemophilia A: potentially life-threatening, blood-clotting disease with high treatment burden



Hemophilia A is caused by variety of mutations in the Factor VIII (FVIII) gene all leading to loss of functional FVIII protein.

Lack of FVIII protein disrupts normal clotting cascade and increases bleeding. Repeated bleeding episodes in joints or soft tissues lead to progressive joint damage, inflammation and pain.

~500,000

patients worldwide[1]

~25,000

patients in the U.S.[2]

(~50% of patients severe; ~30% of patients moderate[3])

- **IND cleared to initiate INTEGR8 phase 1/2 trial in adult patients with moderately severe to severe hemophilia A**
- **Plan to initiate with adult patients and expand to adolescent and pediatric patients**

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

1 - Stonebraker, J. S., et al, 2010. Haemophilia. Vol. 16, pp. 20–32
2 - CDC Surveillance 2024
3 - World Federation of Hemophilia Bleeding Disorders Registry, 2023

Hemophilia A unmet needs: high treatment burden and lack of durable cure

Current Standard of Care:



Factor VIII replacement therapy

- IV typically dosed 1 - 3 times/week, significant adherence challenges
- Frequent infusions and short half-life lead to FVIII peaks and troughs
- Ongoing risks of breakthrough and micro bleeds resulting in cumulative joint damage



Non-factor bispecific "mimetic"

- SQ dosed 1, 2 or 4 weeks post loading, challenging FVIII monitoring
- Only ~10-15% FVIII-equivalent protection; require FVIII supplementation for serious injury or surgery
- Ongoing risks of breakthrough bleeds
- Risks of microbleeds and late-onset arthropathy unclear

Recently Withdrawn Gene Therapy:



- Unpredictable efficacy
- Lack of durability with declining FVIII
- Prolonged corticosteroid use
- Not suitable for pediatric patients

Annual treatment cost[1]:

~$565K - $750K

Lifetime treatment cost[2]:

~$18M - $24M

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

Genome editing offers a potentially durable, one-time treatment for hemophilia A

Hemophilia A represents clear opportunity for a curative treatment:

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

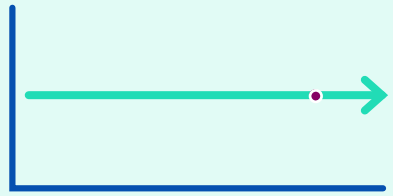
MGX-001 seeks to provide precise gene editing and direct integration into chromosome:

Technology:



Site-specific large gene integration

Durability:

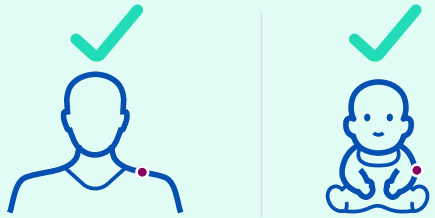


Regulatory status:



IND cleared to initiate INTEGR8 study

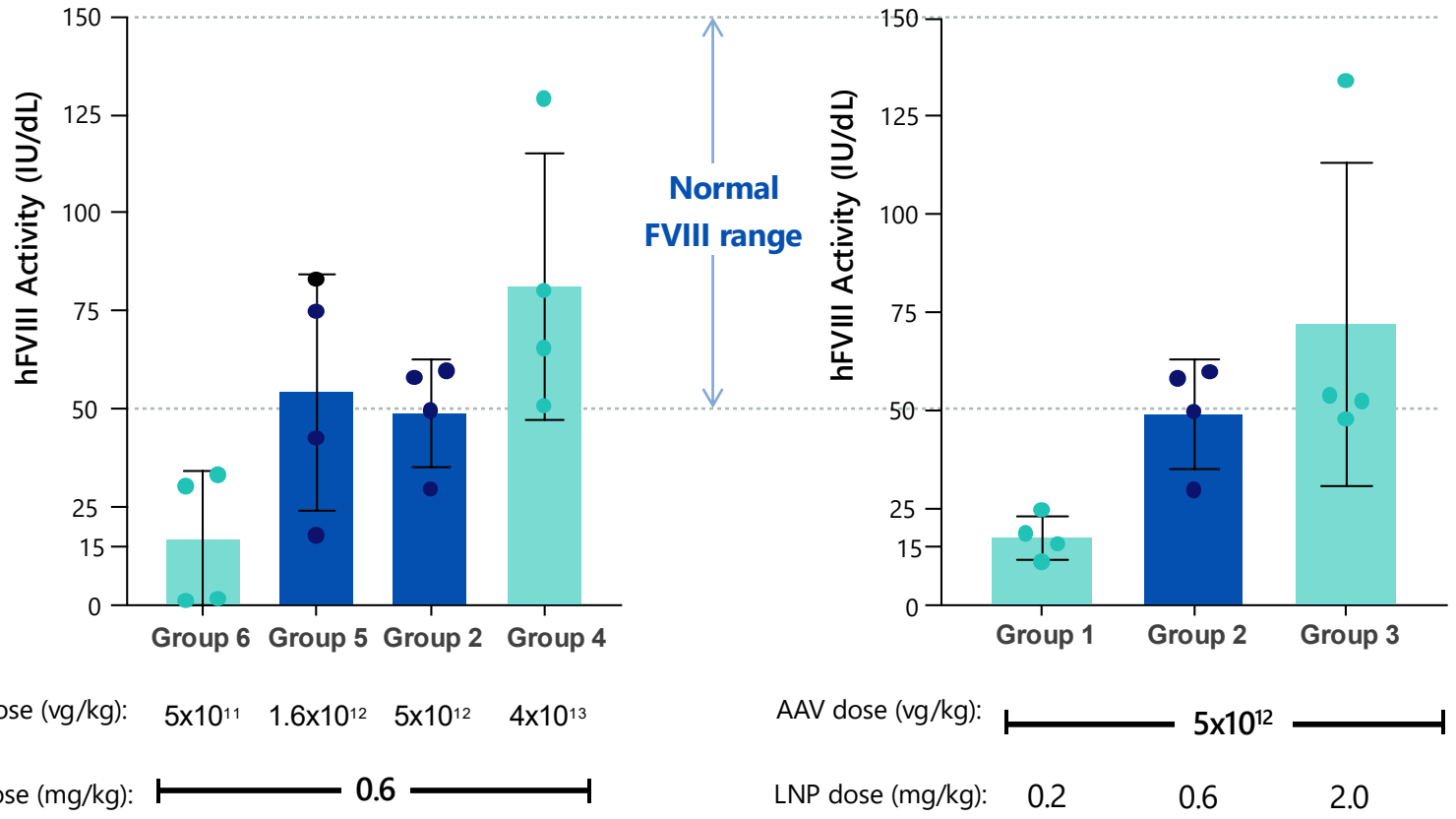
Pediatric potential:



MGX-001 is a potentially durable, one-time treatment for patients – the pediatric population has the most to gain

Normal physiological FVIII range achieved in preclinical model

Development candidate



Dose range finding study in NHP:

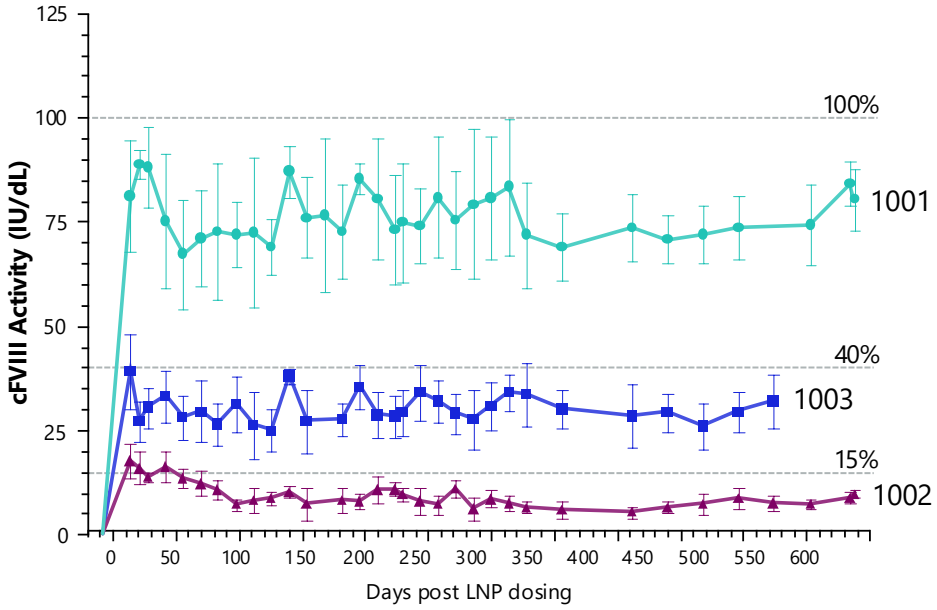
- Confirmed clear dose-response relationship
- Identified minimal / optimal doses
- Achieved FVIII activity in normal range

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

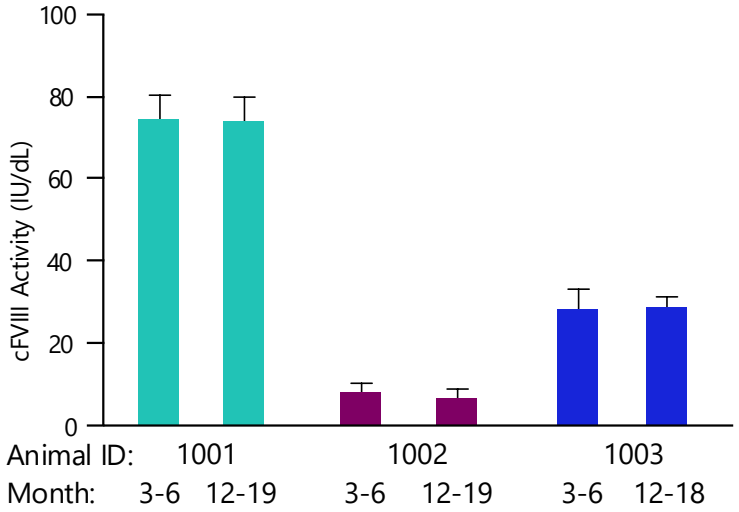
cFVIII NHP durability study: Stable expression over ~19 months

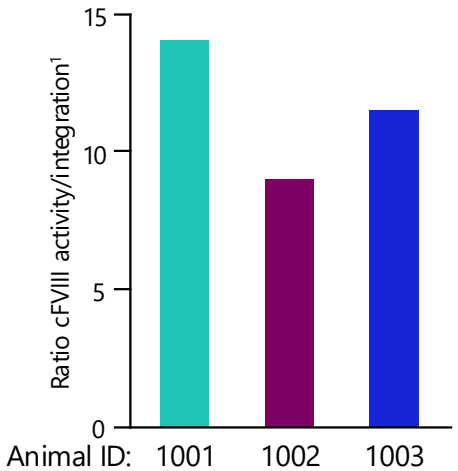


Cynomolgus FVIII (cFVIII) activity values are the mean and standard deviation of at least three independent assay runs with each sample run in at least duplicate in each assay.

Animal 1003 died on day 540 (17.8 mo) post LNP, assessed as unrelated to the treatment.

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





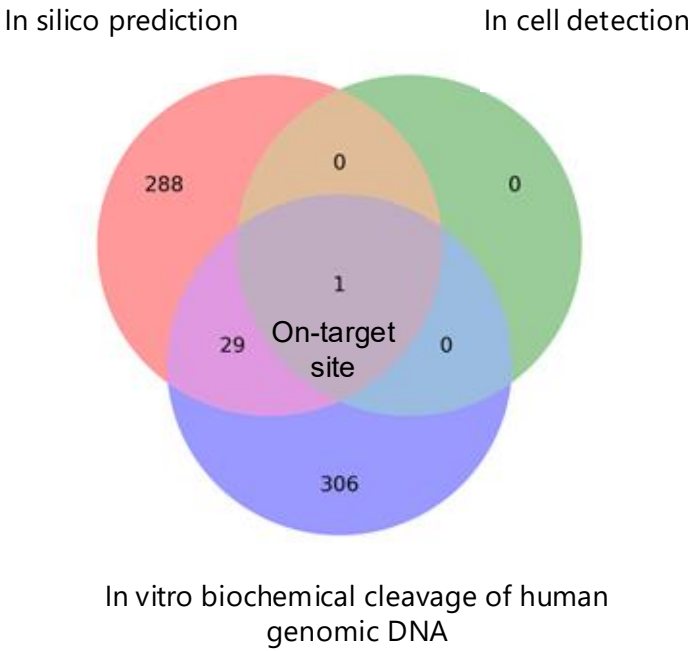
1 - Integration in forward orientation (copies per 100 haploid genomes, average of 5 liver lobes).

Off-target evaluation confirmed gene editing safety profile

Development candidate

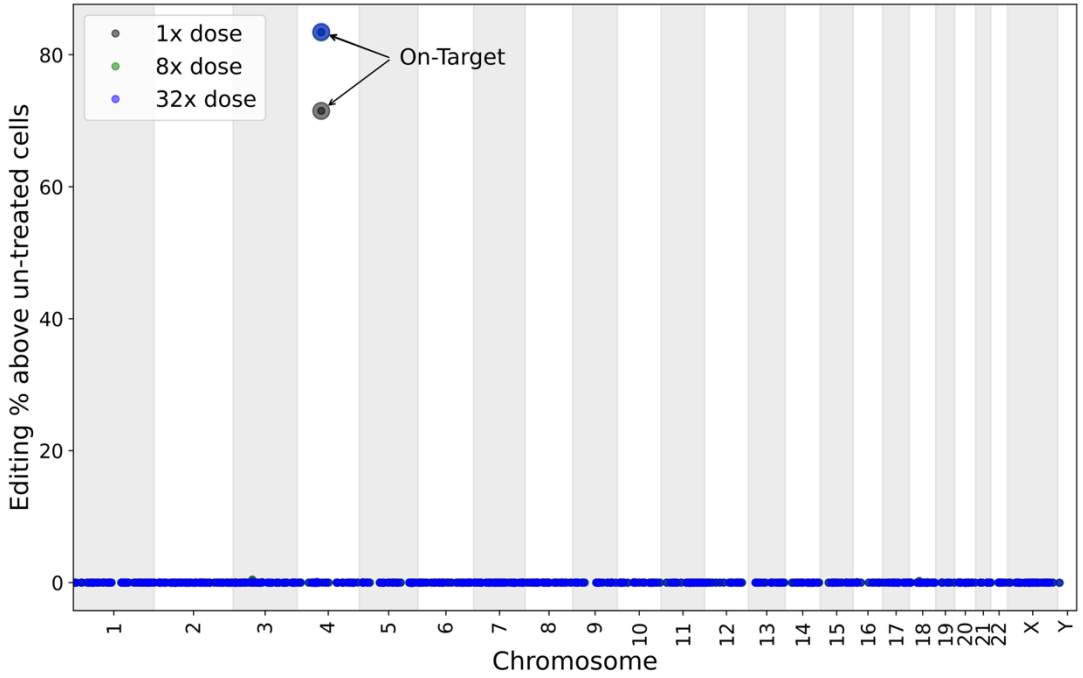
Discovery of potential off-target sites

Identified 623 potential off-target editing sites using industry standard orthogonal methods



Evaluation of potential off-target sites

Tested 623 potential sites in PHH from 3 human donors edited with 3 doses (1x, 8x, 32x) of MGX-001



No off-target edits identified in PHH at any dose, including super-saturating doses far exceeding the therapeutic dose

Abbreviations:
PHH = Primary Human Hepatocytes
1 x dose = dose that results in 90% of maximal on-target editing (EC90)
32 x dose = 32 x EC90

Compelling preclinical profile achieved across efficacy, durability, and safety

Novel mechanism of action integrates gene directly into chromosome

- FVIII integration leveraging albumin promoter to achieve **rapid onset of normal FVIII activity level**
- Lower dose of promoterless AAV designed to deliver **safety advantage over traditional gene therapy**
- Precise FVIII integration facilitated by **proprietary CRISPR gene edit**

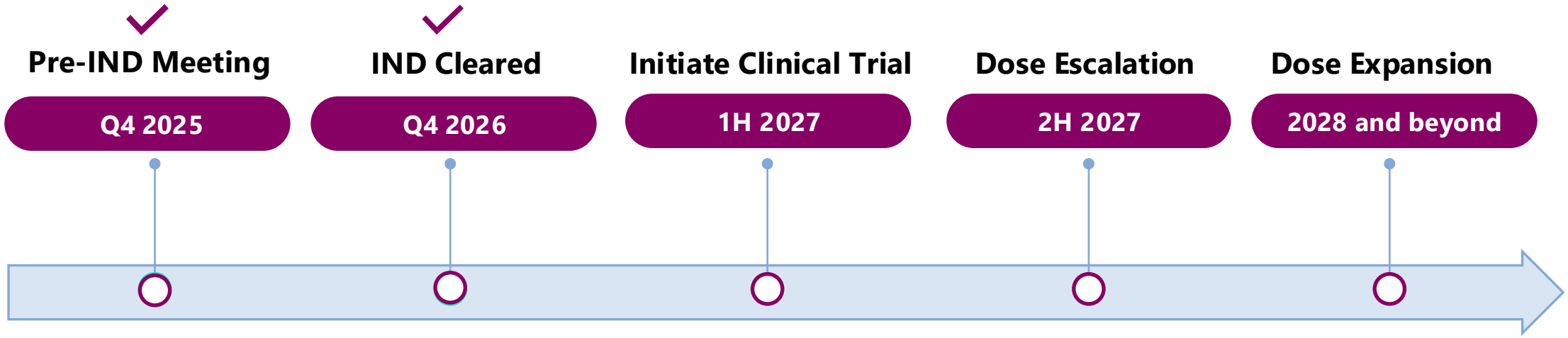
Extensive and supportive preclinical data set in NHPs

- FVIII activity achieved in **normal physiologic range with clear dose response**
- **Durable FVIII activity** over approximately 19-month study
- **Encouraging safety profile** with minimal corticosteroids and no genotoxicity observed

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**
- **IND cleared for initiation of INTEGR8 trial**

MGX-001: INTEGR8 Phase 1/2 study timeline



Dec 2025 FDA meeting — collaborative, favorable outcome

IND clearance for INTEGR8, first-in-human Phase 1/2 trial

Initiation of CTA submissions ex-US

Initiate INTEGR8 global multi-center, single-arm, open label Phase 1/2 trial

CTAs approval ex-US

Initial clinical data including safety, tolerability and FVIII functional activity

Cohort expansion at dose achieving target FVIII activity level in normal physiologic range

Expansion to adolescent and pediatric patients

Goal: To develop a one-time durable therapy for adults and children with hemophilia A

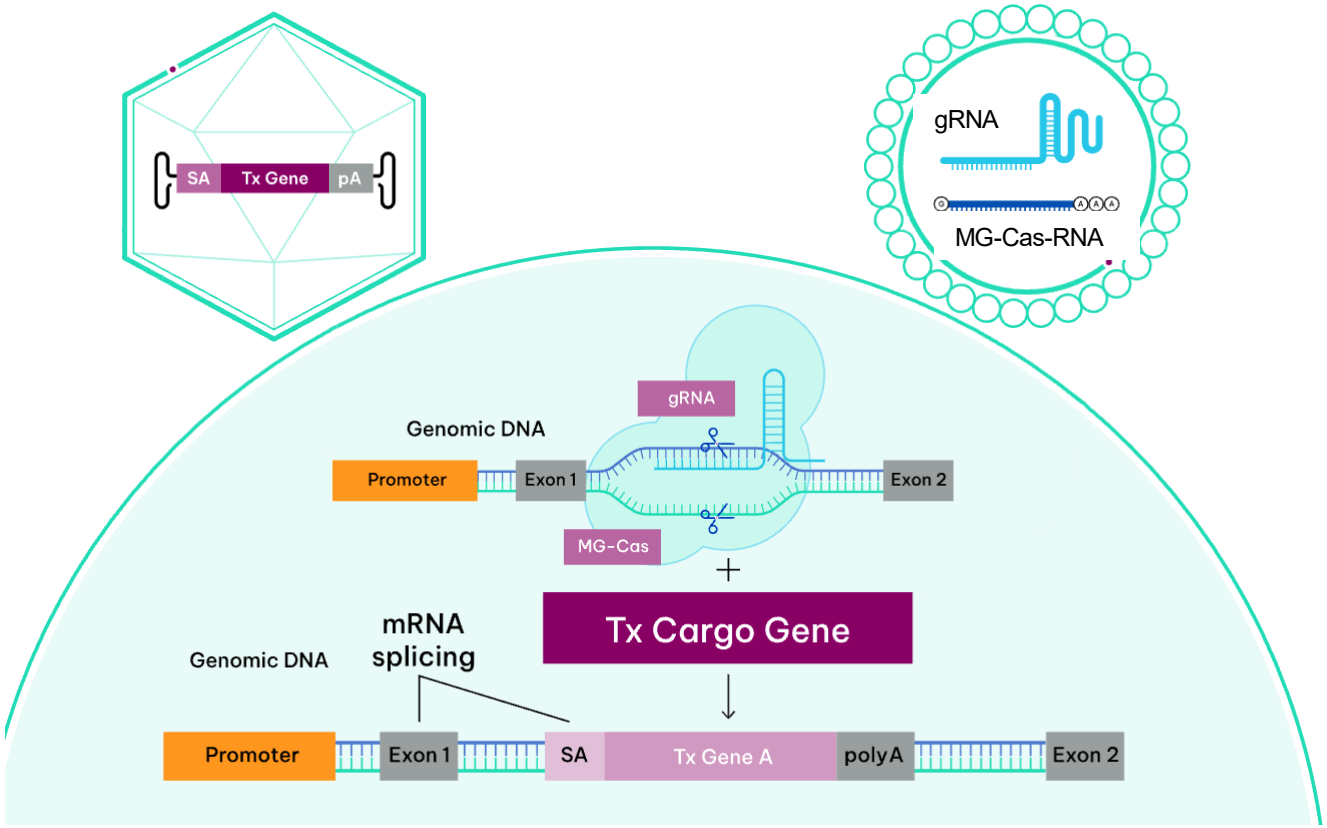
Broadening therapeutic potential with transformative gene editing

Leverage site-specific large gene integration across additional indications

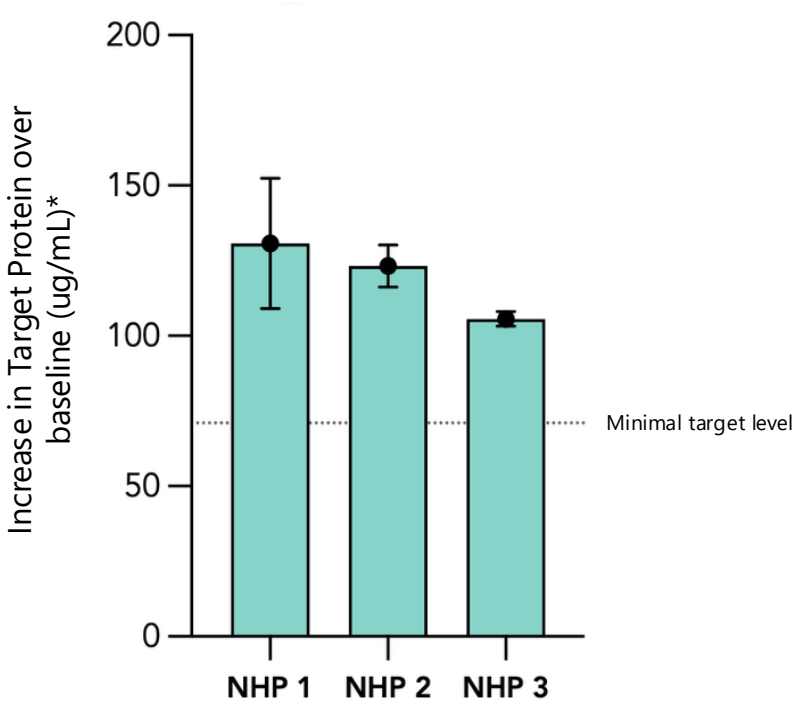
Potential to substitute therapeutic transgene delivered by site-specific large gene integration to address additional diseases

AAV delivers transgene (promoterless donor DNA)

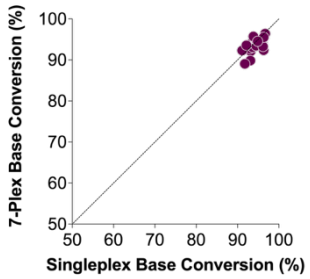
LNP delivers nuclease mRNA and guide targeting albumin site



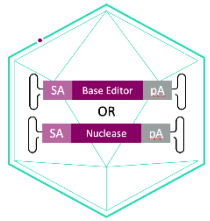
Achieved normal circulating levels of target protein in an additional disease



Multiplex editing and compact editors enable next-generation therapies

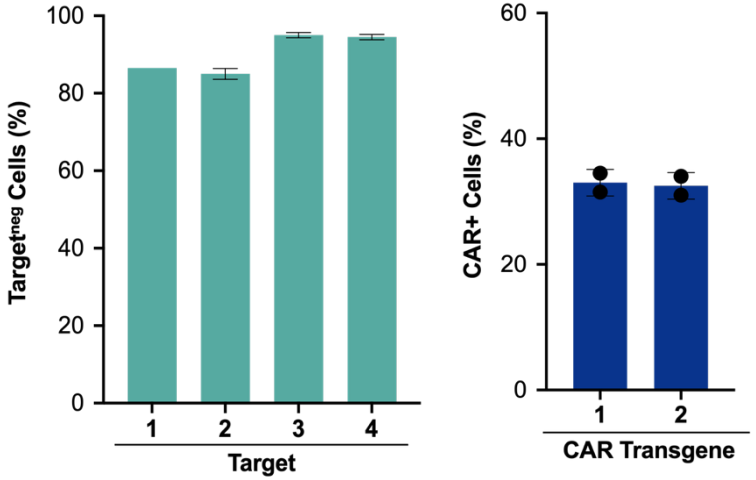


Multiplex editing in T-cells achieved across seven unique gene targets with high efficiency comparable to single plex editing

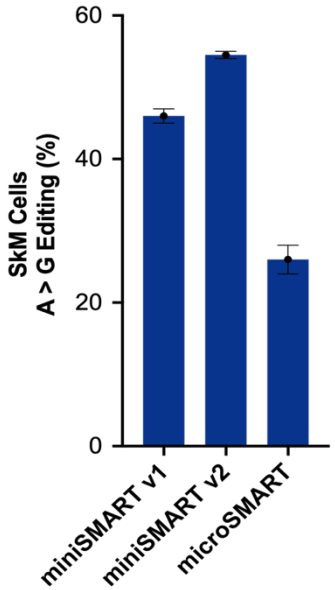


Compact nucleases and base editors demonstrated high editing efficiency and compatibility with AAV for extrahepatic delivery[2,3]

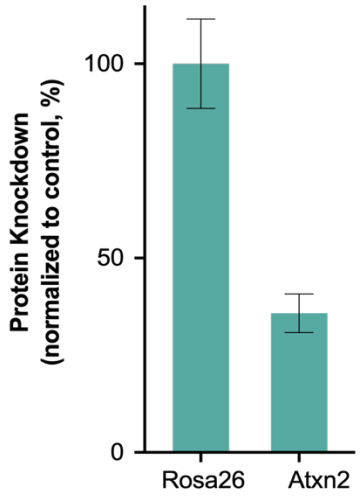
Combined protein knockdown and CAR knock-in in a single-step for cell therapy applications



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



Multiple compact base editors[2] demonstrated effective neuromuscular targeting



Compact nuclease MG119-28 achieved 64% knockdown of ATXN2 protein in mouse brain[4]

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 for protein knockdown programs 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[1]

1. TAM = Total Addressable Marked

Metagenomi pipeline and expected updates

Editing platform:	Indication:	Editing target:	Discovery	Lead optimization	IND-enabling	Clinical
Protein replacement via gene insertion	MGX-001 Hemophilia A	ALB				**INTEGR8 trial in 2027**
	Undisclosed	Undisclosed				
Protein reduction via gene knockout	Cardiometabolic Diseases	TTR AGT APOC3 Undisclosed				

IONIS

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.

Thank you

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THERAPEUTICS