MGX-001 Program and Business Update

November 11, 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.

New data supports MGX-001 advancing toward the clinic

Demonstrated curative Factor VIII activity with best-in-class treatment potential

- Dose-dependent efficacy of both AAV and LNP
- Therapeutically relevant FVIII activity in each animal treated in all but the lowest dose
- Data informs clinical dose regimen strategy

Builds on Previous data

- Durable FVIII activity over an approximately 19-month study
- Encouraging safety profile, with minimal steroid use at the time of dosing
- No off target editing

Potential competitive advantages of MGX-001

- Enables endogenous production of FVIII for hemostatic regulation
- Potential to effectively treat both adults and children
- One-time potentially curative therapy allowing patients a hemophilia free mindset

Strategic evolution focuses resources for advancement

Prioritizing high impact programs

- Advancing wholly-owned MGX-001 hemophilia A program toward IND/CTA by Q4'26
- Advancing additional secreted protein deficiency indications
- Focusing on cardiometabolic collaboration with Ionis

Streamlined organization

- Implemented workforce reduction of 25%
- Anticipate extension of cash runway into Q4'27

Transitioned to clinical development leadership

- **Jian Irish, Ph.D., M.B.A.** appointed CEO
- **Willard Dere, M.D.** appointed Board Chair
- **Brian Thomas, Ph.D.,** co-founder, former CEO, continues on Board

Glenn F. Pierce, MD, PhD

was born with
severe hemophilia A

was cured in 2008
via liver transplant

Career highlights:

Past:

Biogen: senior vice president of hematology, cell and gene therapie.

Ambys Medicines: co-founder and CMO (cell and gene therapy liver regeneration start-up).

Voyager Therapeutics: Interim CSO.

National Bleeding Disorders Foundation (NBDF): board of directors and president.

Present:

WFH

World Federation of Hemophilia (WFH): vice president, medical

MASAC

U.S. medical and scientific advisory council (MASAC)

Over 35 years of experience

Hemophilia A: a validated target waiting for a durable cure

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

~500,000
worldwide[2]

Hemophilia A is the most common X-linked inherited bleeding disorder, almost exclusively affecting males.

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

Current SOC:

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 breakthough bleeding
- Treatment burden, non-curative

Gene therapy

- Variable initial efficacy
- Significant 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]

One-time treatment cost[3]:
$2.9M[5]

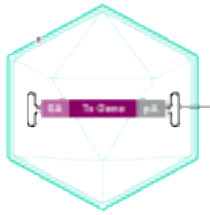
NASDAQ: **MGX**

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.
5 - Zemplenyi A et al., Pharmacoeconomics (2024) 42(3):319–328.
Hemophilia joint bleeds image: International Hemophilia Training Center.

MGX-001 mechanism leverages natural promoter

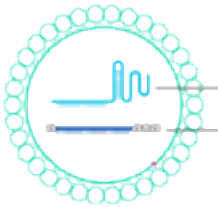
MGX-001 components:

AAV delivers FVIII gene (donor DNA):



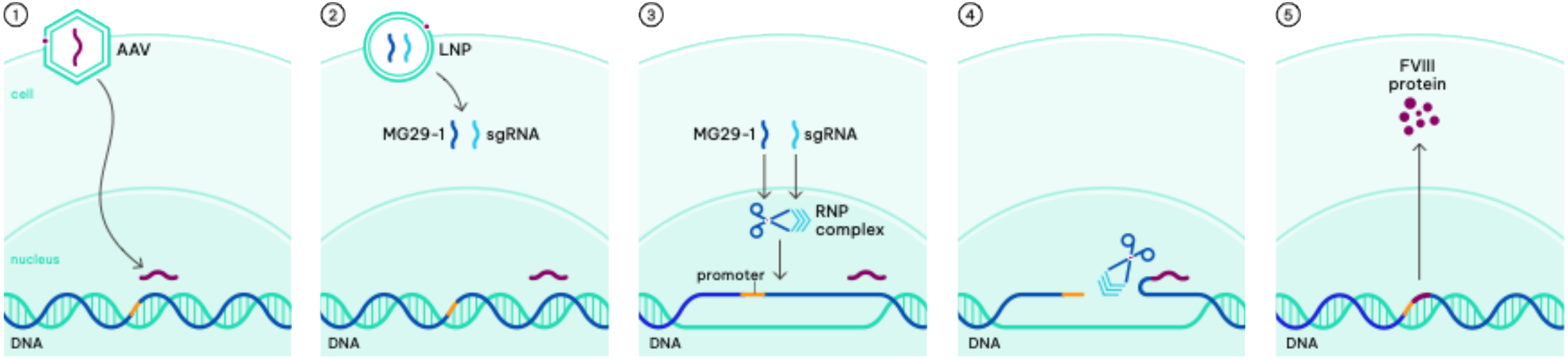
promoterless FVIII gene

LNP delivers nuclease mRNA & sgRNA targeting albumin site:



guide RNA to albumin gene (sgRNA)

nuclease mRNA (MG29-1)



AAV delivers promoterless FVIII gene. AAV enters hepatocytes and the donor FVIII cassette localizes to the nucleus.

LNP delivers MG29-1 nuclease mRNA + guide targeting albumin promoter. The mRNA is released in the cytoplasm.

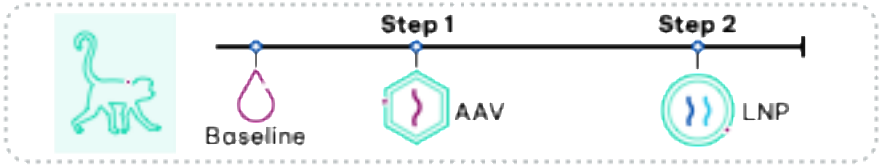
The mRNA is translated into MG29-1 nuclease, which binds the guide RNA to form a ribonucleoprotein (RNP) complex.

The guide pairs with the matching bases and MG29-1 nuclease cuts at the albumin locus.

The FVIII cassette integrates at the albumin cut site via natural end-joining.

The albumin promoter drives the expression of FVIII, which triggers the production of FVIII protein.

NHP study designs



Durability study

N=3

Study duration: **19 months**

	NHP FVIII AAV dose (vg/kg)	NHP FVIII LNP dose (mg/kg)
Animal 1001		
Animal 1002	2.0×10^{13}	1.0
Animal 1003*		

Pre-development candidate

Dose range finding study

N=24.

Study duration **3 weeks.**

FVIII evaluation: **day 5, 8, 11**

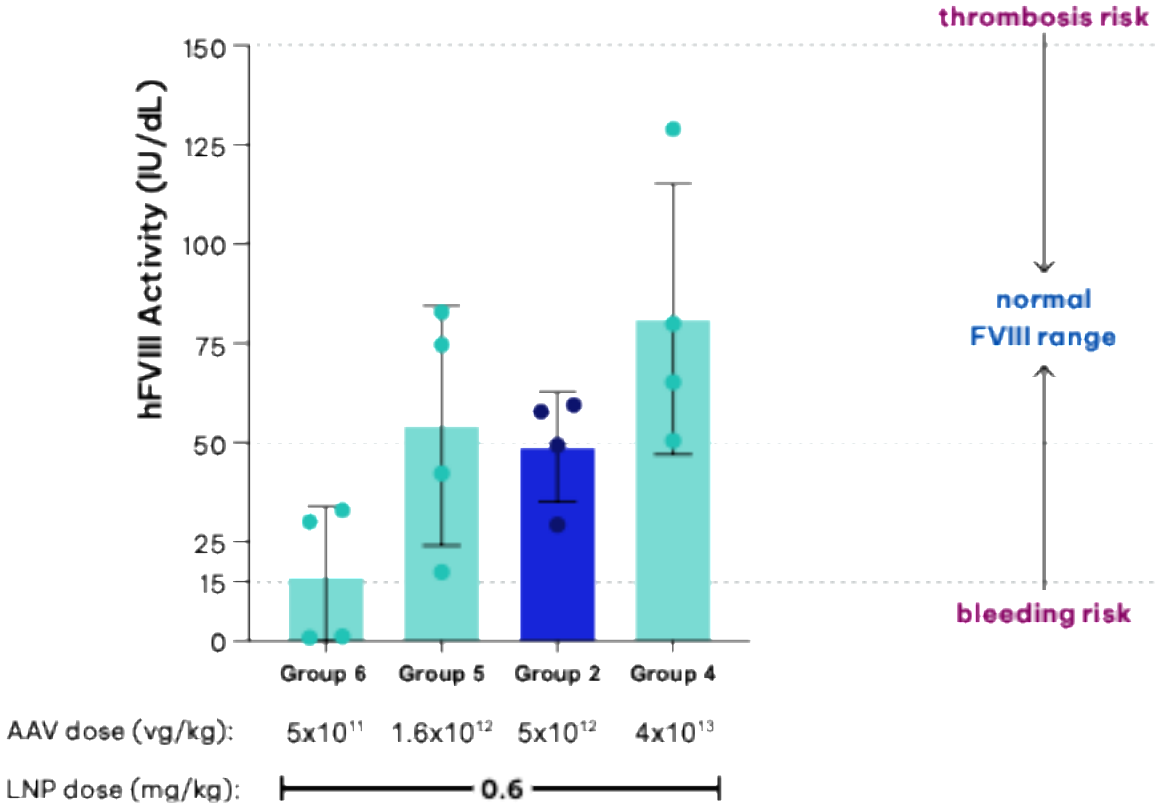
		Human FVIII AAV dose (vg/kg)	Human FVIII LNP dose (mg/kg)
Group 1:	N=4	5.0×10^{12}	0.2
Group 2:	N=4	5.0×10^{12}	0.6
Group 3:	N=4	5.0×10^{12}	2.0
Group 4:	N=4	4.0×10^{13}	0.6
Group 5:	N=4	1.6×10^{12}	0.6
Group 6:	N=4	5.0×10^{11}	0.6

Development candidate

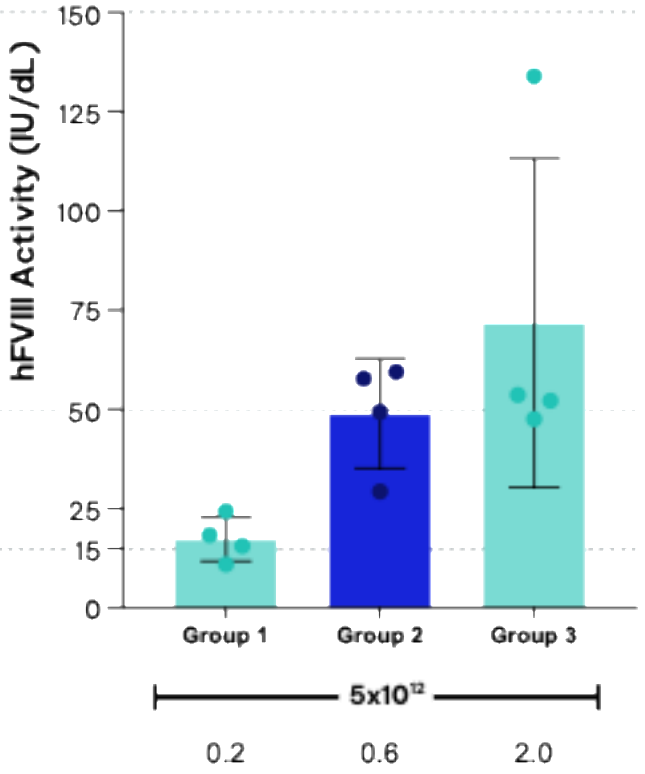
Dose dependent FVIII activity in NHP: minimally efficacious and clinically relevant doses identified

Development candidate

AAV dose response identified the optimal efficacious dose of $5x10^{12}$ vg/kg:



LNP dose response identified 0.2 mpk as the minimally efficacious dose and 0.6 mg/kg as optimal dose:



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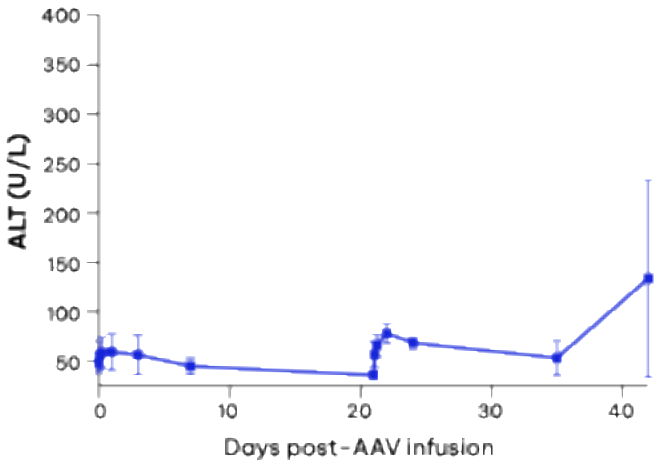
FVIII activity for each animals is the mean of values on d5, d8, d11 post LNP measured with a capture-chromogenic assay. hFVIII activity was stable from d5 to d11 post LNP. Xyntha was used for the standard curve. Means and standard deviation per group are shown.

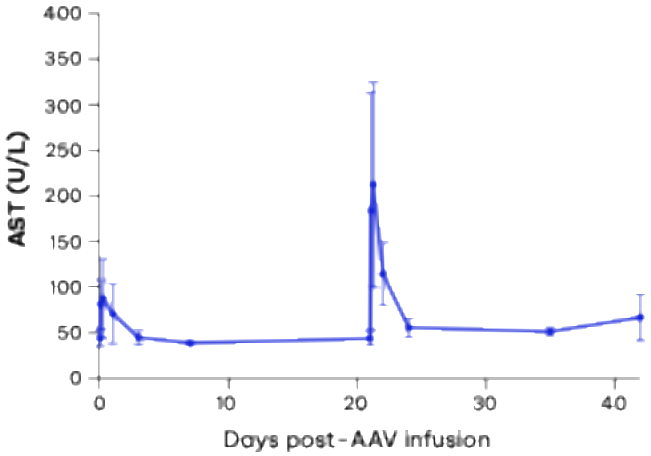
Optimal dose group demonstrated encouraging safety profile supporting curative potential

Development candidate

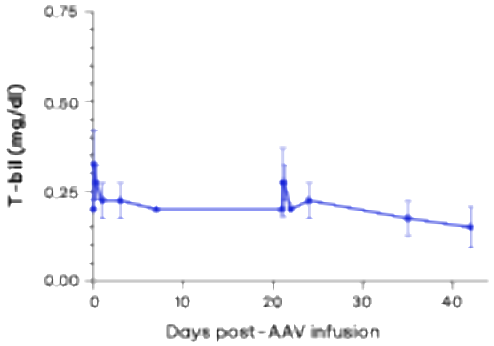
Mild and transient ALT changes:



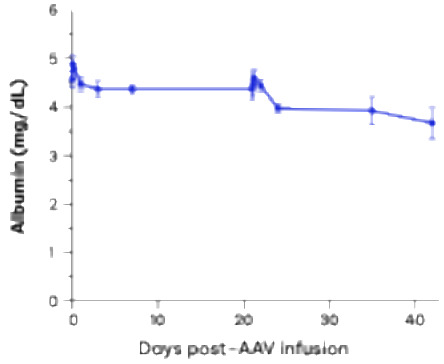
Mild and transient AST changes:



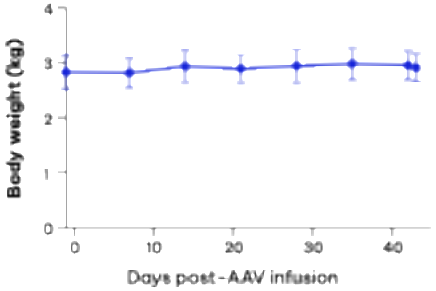
No change in bilirubin:



Albumin remained within normal physiological range:



Body weights stable:



Summary of safety findings:

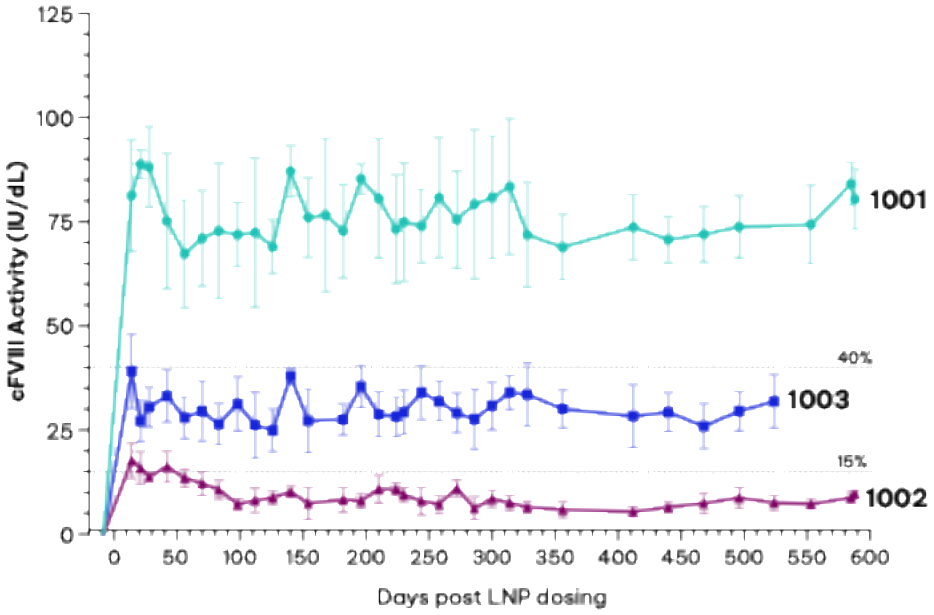
- Mild transient elevation of liver transaminases after the infusion of LNP.
- No significant change in total bilirubin.
- Circulating albumin levels remain within the normal physiological levels.
- Animals exhibited normal weight gain.

Data are the means and standard deviation for each group (n=4 / grp). LNP was dosed on day 21.

Durable, therapeutic levels of FVIII achieved in NHP

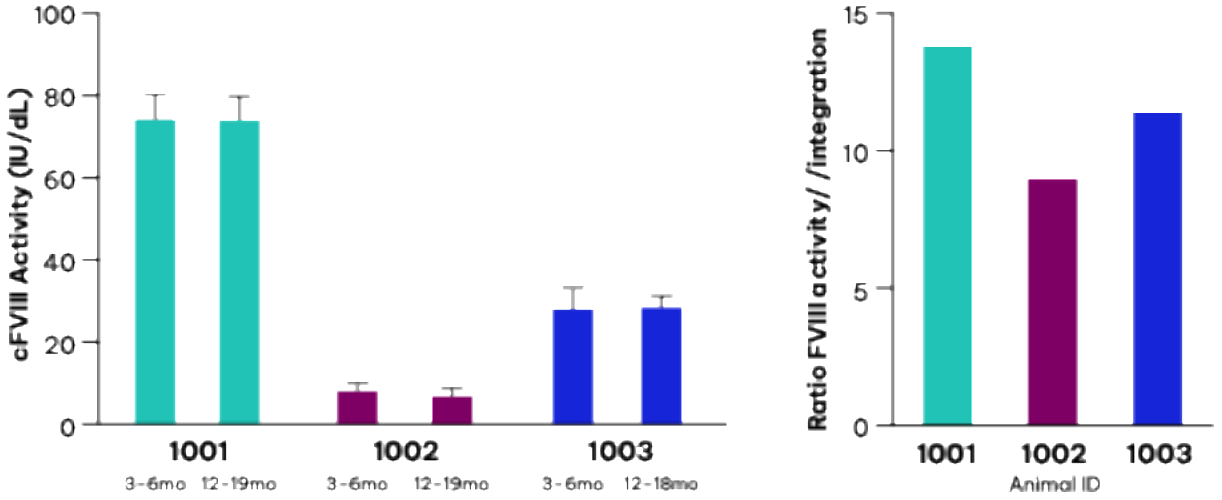
Pre-development candidate

NHP durability study:



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.

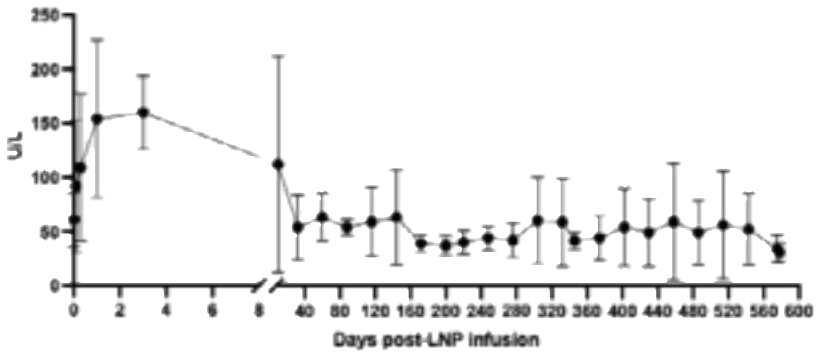
Plasma FVIII activity levels unchanged between 3-6 months and 12-19 months and correlate to integration:



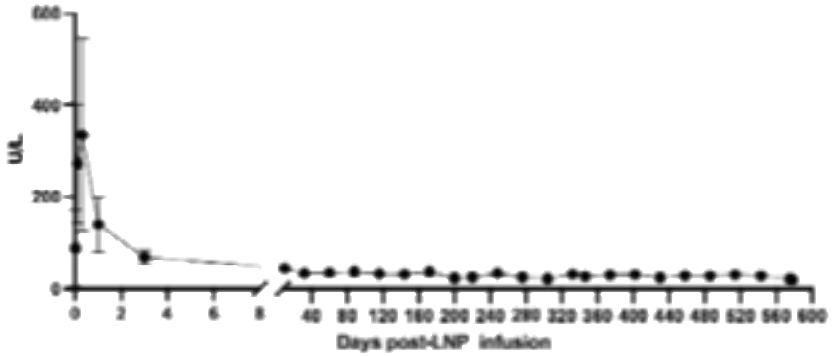
1 - Integration in forward orientation (copies per 100 haploid genomes, average of 5 liver lobes).

Treatment well tolerated over 19 month duration of the study

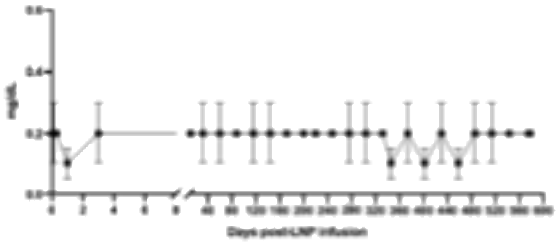
Alanine transaminase (ALT) levels post LNP infusion:



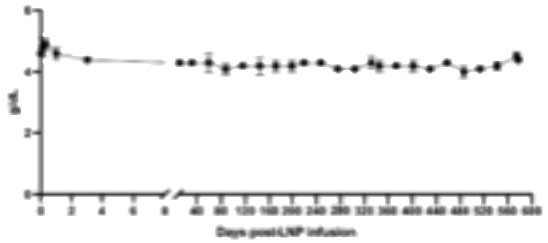
Aspartate transaminase (AST) levels post LNP infusion:



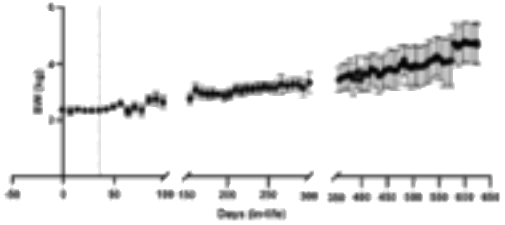
Total bilirubin levels post LNP infusion:



Albumin levels post LNP infusion:



Body weights:



Pre-development candidate

Summary of safety findings:

- Transient elevation of liver transaminases after the infusion of LNP.
- No significant change in total bilirubin.
- Circulating albumin levels remain within the normal physiological levels.
- Animals exhibited normal weight gain.

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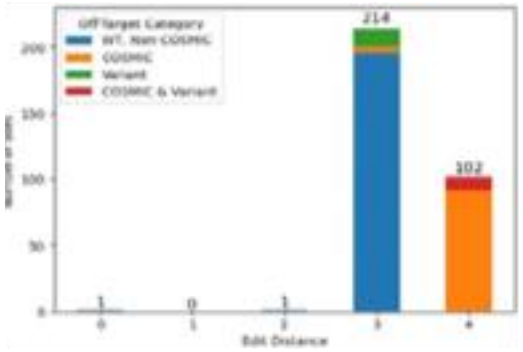
All graphs are mean and standard deviation for N=3 NHP's.
Animal 1003 died on day 540 (17.8 mo) post LNP, assessed as unrelated to the treatment.

No genotoxicity observed with MGX-001

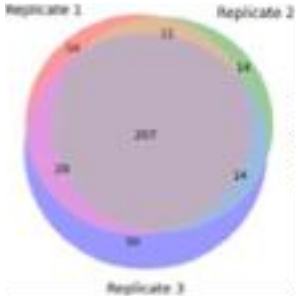
Development candidate

Discovery of potential off-target sites

1. In silico off-target



2. Biochemical off-target discovery:

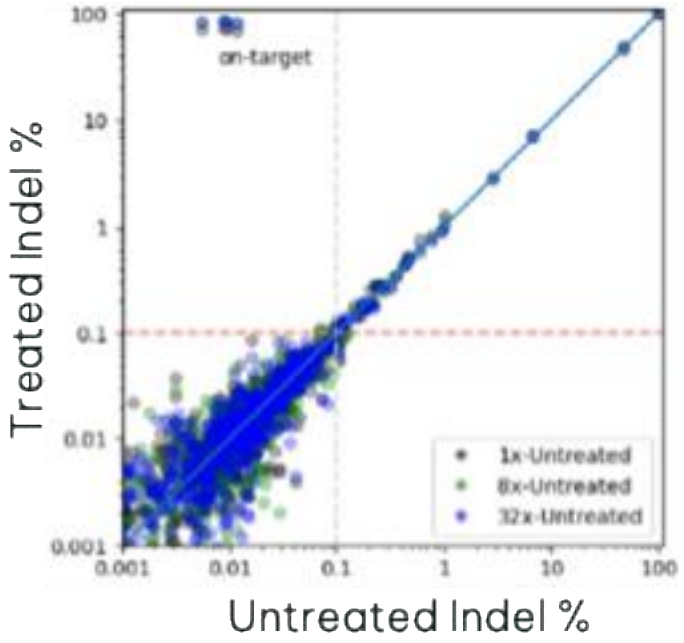


No potential off-targets were discovered in cell-based assays.

3. In cell off-target discovery:
No potential off-targets were found.

No validated off target sites observed

3 independent primary human hepatocyte donors:



No validated off-target editing observed

High genome integrity maintained as observed in off-target editing, and AAV integration assays.

De-risked and clear opportunity for genome editing in Hemophilia A

Hemophilia A is an ideal entry indication for genome editing approach:

- Monogenic and well-characterized biology
- Clear biomarker–disease link
- A well defined target threshold of curative FVIII level & wide safety range
- Robust preclinical models and regulatory familiarity
- Strong advocacy and infrastructure

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

Technology:

proprietary Type V nuclease

Durability:

Regulatory status:

IND-enabling stage

Pediatric potential:

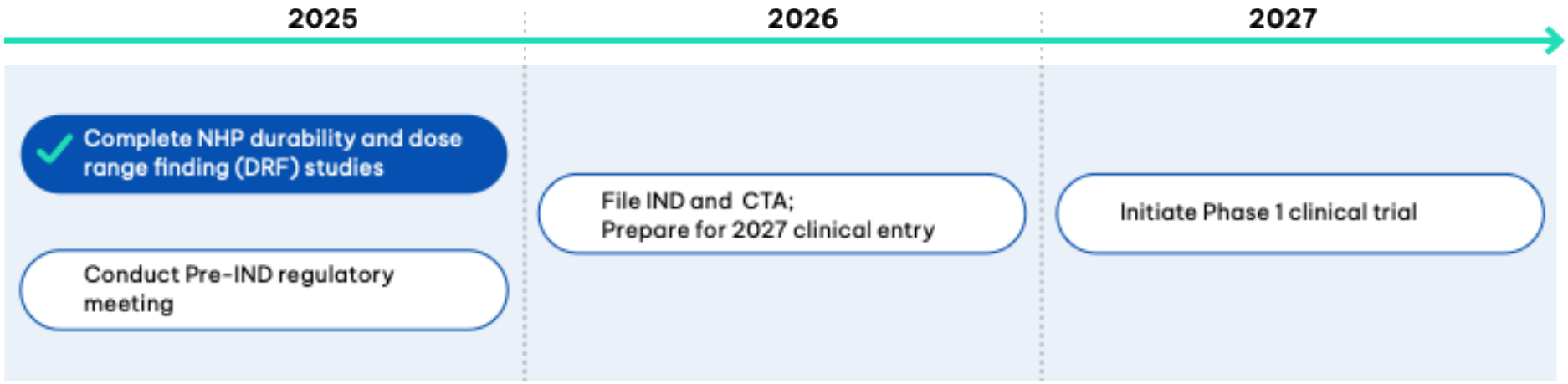
MGX-001 is a potentially durable, curative approach for adults and children – the population with the most to gain.

Focused on generating clinical data in 2027

Demonstrated curative FVIII activity in NHPs

Built upon approximately 19 month durability study data

MGX-001
Hemophilia A

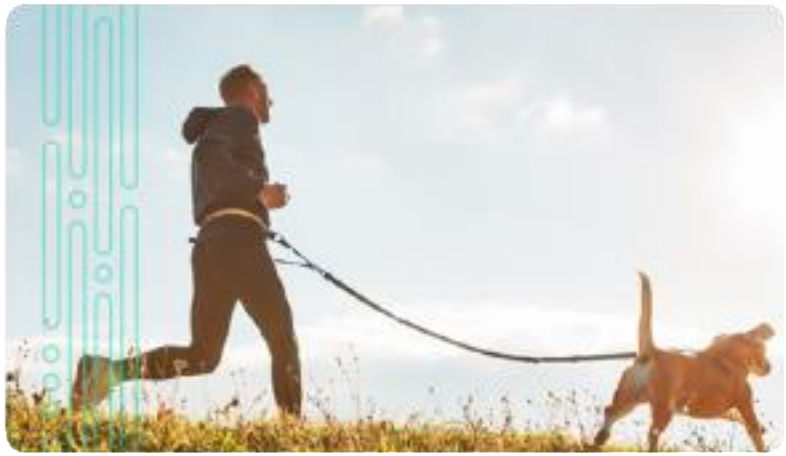


Informs clinical dose regimen strategy with best-in-class treatment potential

From novel genome editing systems to curative therapies

Metagenomi

Metagenomi is an in vivo genome editing company capitalizing on its proprietary technologies to precisely correct a wide range of genetic mutations across the human genome. The company is focused on wholly owned programs in Hemophilia A and secreted protein disorders, and partnered assets targeting cardiometabolic indications



2018

Discovering novel genome editing systems

2023

NASDAQ: MGX

2025

Developing a pipeline of in vivo therapies

Q&A

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