

PRECISION
BIOSCIENCES

Precision BioSciences
In Vivo Gene Editing Update

April 2024



Forward-Looking Statements

This presentation contains forward-looking statements, as may any related presentations, within the meaning of the Private Securities Litigation Reform Act of 1995. The Company intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements contained herein and in any related presentation that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the pre-clinical and clinical development, research advancement and expected safety, efficacy and benefit of our product candidates and gene editing approaches, including editing efficiency, defined outcomes, therapeutic edits, safety and differentiating aspects; the suitability of azer-cel for oncology indications and non-oncology indications including immunological diseases; the suitability of ARCUS nucleases for gene insertion, large gene deletion, and other complex gene editing approaches; the expected timing of regulatory processes; expectations about our operational initiatives and business strategy; expectations about achievement of key milestones; expectations about market trends and opportunity; expectations regarding partnership opportunities; our expected cash runway; expectations about achievement of key milestones and receipt of any milestone, royalty, or other payments; expectations regarding our liquidity and capital resources; and anticipated timing of initial clinical data. In some cases, you can identify forward-looking statements by terms such as “aim,” “anticipate,” “approach,” “believe,” “contemplate,” “could,” “designed to,” “estimate,” “expect,” “goal,” “intend,” “look,” “may,” “mission,” “plan,” “possible,” “potential,” “predict,” “project,” “promise,” “pursue,” “should,” “target,” “will,” “would,” and other similar words or expressions, or the negative of these words or similar words or expressions, are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions.

Forward-looking statements are based on management’s current expectations, beliefs and assumptions and on information currently available to us. These statements are neither promises nor guarantees, but involve number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to: our ability to become profitable; our ability to procure sufficient funding to advance our programs; risks associated with raising additional capital and requirements under our current debt instruments and effects of restrictions thereunder; our operating expenses and our ability to predict what those expenses will be; our limited operating history; the success of our programs and product candidates in which we expend our resources; our limited ability or inability to assess the safety and efficacy of our product candidates; our dependence on our ARCUS technology; the risk that other genome-editing technologies may provide significant advantages over our ARCUS technology; the initiation, cost, timing, progress, achievement of milestones and results of research and development activities, preclinical studies and clinical trials; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, and biotechnology fields; our or our collaborators’ ability to identify, develop and commercialize product candidates; potential product liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates; the U.S. and foreign regulatory landscape applicable to our and our collaborators’ development of product candidates; our or our collaborators’ or other licensees’ ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; our or our collaborators’ other licensees’ ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; potential manufacturing problems associated with the development or commercialization of any of our product candidates; delays or difficulties in our and our collaborators’ ability to enroll patients; changes in interim “top-line” and initial data that we announce or publish; if our product candidates do not work as intended or cause undesirable side effects; risks associated with applicable healthcare, data protection, privacy and security regulations and our compliance therewith; the rate and degree of market acceptance of any of our product candidates; the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements; our current and future relationships with and reliance on third parties including suppliers and manufacturers; our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates; potential litigation relating to infringement or misappropriation of intellectual property rights; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate key executives and personnel; market and economic conditions; effects of system failures and security breaches; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events; effects of sustained inflation, supply chain disruptions and major central bank policy actions; insurance expenses and exposure to uninsured liabilities; effects of tax rules; risks related to ownership of our common stock; our ability to meet the requirements of and maintain listing of our common stock on NASDAQ or other public stock exchanges and other important factors discussed under the caption “Risk Factors” in our Annual Report on Form 10-K for the annual period ended December 31, 2023, as any such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC’s website at www.sec.gov and the Investors page of our website under SEC Filings at investor.precisionbiosciences.com.

All forward-looking statements speak only as of the date of this presentation and, except as required by applicable law, we have no obligation to update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Precision consults with various presentation speakers and compensates them for their time and expertise.



Today's Speakers



Michael Amoroso
President and
Chief Executive Officer



Jeff Smith
Co-Founder, Chief
Research Officer



Alex Kelly
Chief Financial Officer



Alan List, M.D.
Chief Medical Officer



Focusing on Our Foundation—In Vivo Gene Editing

Precision—from dual to a single platform gene editing company

Ex Vivo CAR T
Accretive Event

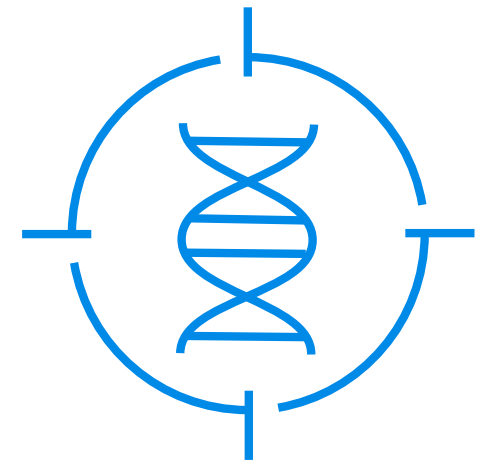
In Vivo
Gene Editing

Go-Forward Singular Focus In Vivo Gene Editing

Pivoting to Our Foundational Strength

- ARCUS - wholly owned genome editing platform
- Optimized for gene insertion, excision, and elimination
- Over 25 years of gene editing expertise and protein engineering
- Expect existing cash and cash equivalents, expected operational receipts, operational efficiencies, recent financing, availability of the ATM facility, and available credit to fund OpEx and CapEx into **second half of 2026**

Focused Execution 2024-2026



Expected cash runway now enables funding wholly owned *In Vivo* programs HBV & PMM, through Phase 1 data



Sufficient Cash Runway to Realize Multiple Near-Term Opportunities in 2024-25

Near-term clinical & regulatory validation of ARCUS

- In-Clinic* **Lead Partnered Program** with iECURE for **OTC deficiency** now in clinic with **clinical data expected in 2024 or 2025**
- On-Track* **Wholly owned PBGENE-HBV** program **IND &/or CTA filing expected in 2024** with Phase 1 **clinical data in H1 2025**
- On-Track* **Wholly owned PBGENE-PMM** program **IND &/or CTA filing expected in 2025**

- Projected Cash runway into 2H 2026** through Phase 1 clinical data read-outs
- Returning three advanced preclinical programs to pipeline**, develop on own or through partners



ARCUS Focused on Sophisticated Edits Leveraging Unique Advantages

PROGRAM	INDICATION	TISSUE	TARGET	EDIT TYPE / DELIVERY	RESEARCH	IND-ENABLING	CLINICAL	PARTNER
PBGENE-HBV	Chronic hepatitis B	Liver	HBV	Elimination/LNP				
PBGENE-PMM	m3243 primary mitochondrial myopathy	Muscle	PMM	Elimination/AAV				
PBGENE-DMD	Duchenne muscular dystrophy	Muscle	DMD	Excision/AAV			<i>Returning to Precision Under Assessment</i>	
PBGENE-LIVER	Undisclosed	Liver	—	Insertion/—				
PBGENE-CNS	Undisclosed	CNS	—	—				
iECURE-OTC*	Ornithine transcarbamylase deficiency	Liver	OTC	Insertion/AAV				
PBGENE-NVS	Sickle cell disease/ beta thalassemia	HSCs	—	Insertion/—				



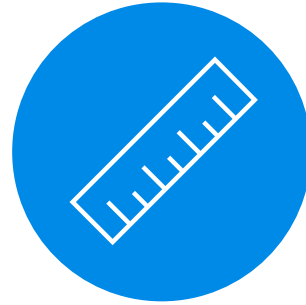
*iECURE-OTC also named ECUR-506 under investigation in the OTC-HOPE study

ARCUS is a Differentiated & Sophisticated Editing Tool



All About The Cut

- 3 Prime Overhang Cut
- Drives Homology-Directed Repair (HDR)
- Complementary overhangs drive "Perfect" Re-ligation



Size Matters

- Smallest gene editor (~1500 bp)
- Small size enables delivery of MORE payload allowing sophisticated edits
- Enables delivery both non-viral and viral, to diverse tissues in the body



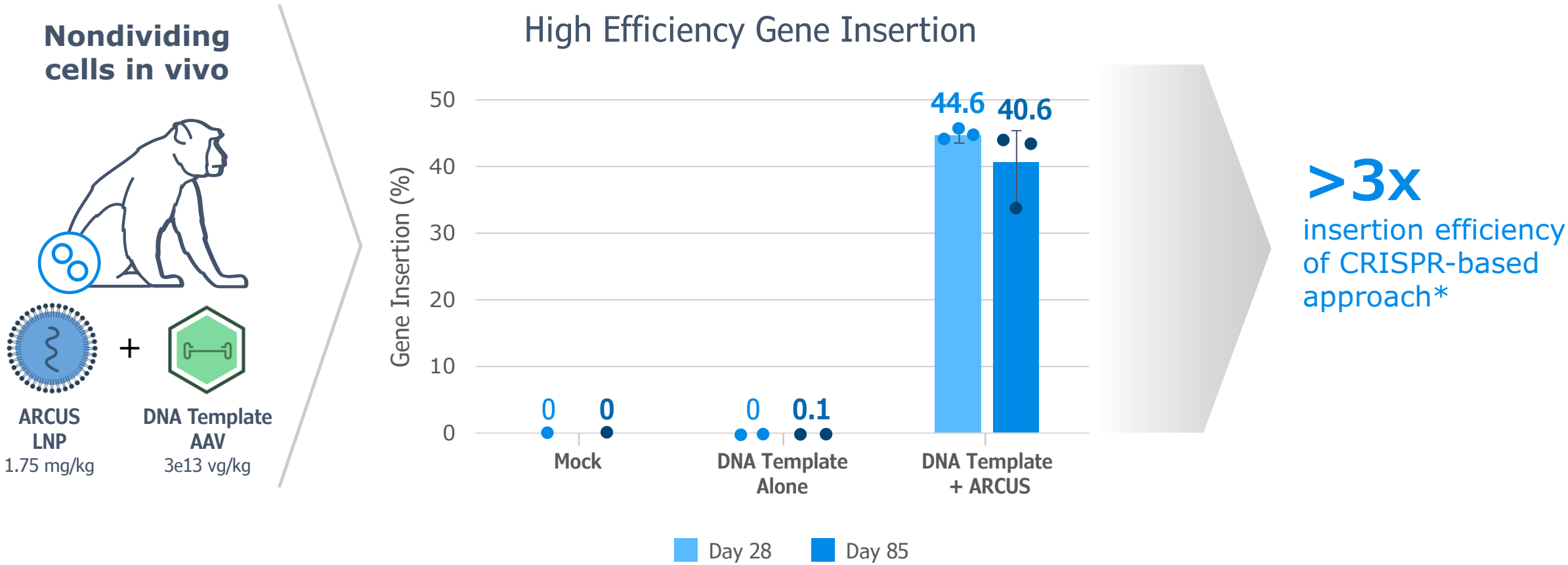
Keep It Simple

- Only single component editor that recognizes and cuts DNA
- Single component streamlines delivery and results in highest efficiency
- Single component editor requires lower dose of delivery vehicle

***In Vivo* Programs Based on ARCUS' Unique Advantages**



The Cut: ARCUS Inserts with High Efficiency in Adult Nonhuman Primates, Example Previously Thought to be Unachievable

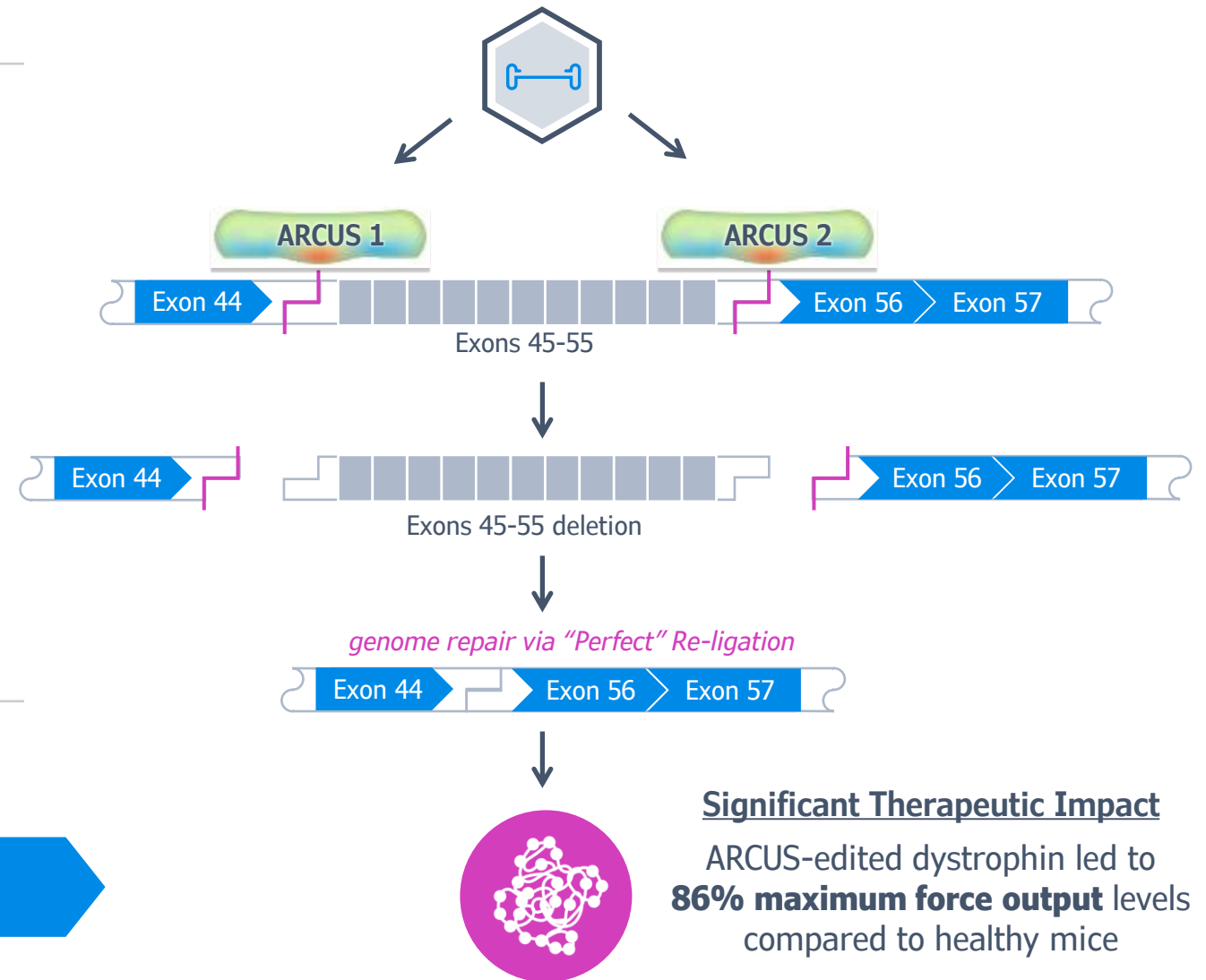


*45% gene insertion calculated for total liver tissue, much higher if only calculating insertion into hepatocytes

*ASGCT 2023, poster 926, Regeneron/Intellia, "Targeted Gene Insertion of *Factor 9* as a Potential Durable Treatment for Hemophilia B"

The Size: ARCUS Nucleases Excise Mutations and Restore Function in DMD

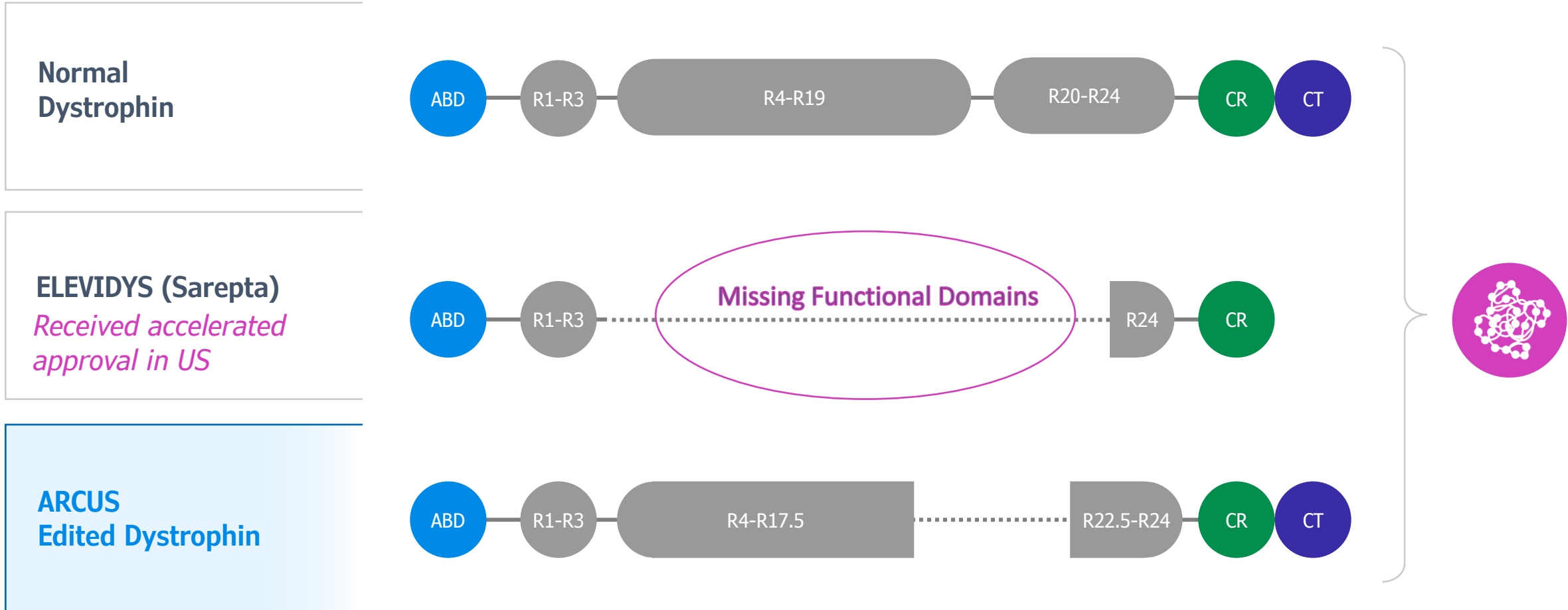
Two complementary ARCUS nucleases delivered in a single AAV are used to excise a mutation “hot spot” in Exons 45-55 responsible for ~50% of DMD cases



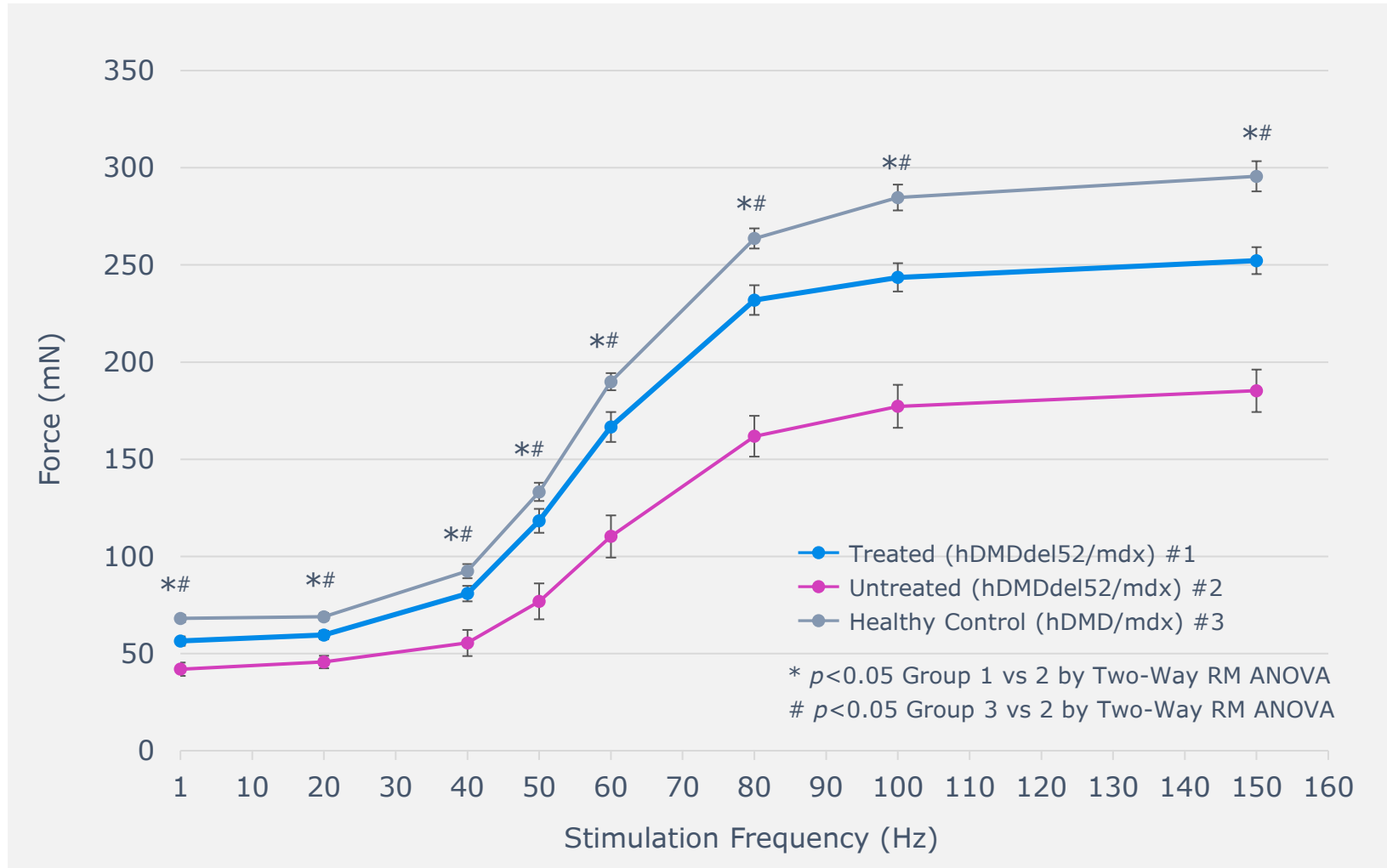
GOAL: Restore dystrophin expression



The Size: ARCUS-Edited Dystrophin Preserves Majority of Protein Domains With the Goal of Improving Function



Maximum Force Output in ARCUS-Treated Mice was Significantly Improved



ARCUS-treated mice achieved:

Editing in heart, diaphragm,
and skeletal muscle

Evidence of edited dystrophin
in muscle satellite cells








Leading to:

86% Maximum Force
Output Levels

compared to non-diseased,
control mice in the calf



ARCUS Focused on Sophisticated Edits Leveraging Unique Advantages

PROGRAM	INDICATION	TISSUE	TARGET	EDIT TYPE / DELIVERY	RESEARCH	IND-ENABLING	CLINICAL	PARTNER
PBGENE-HBV	Chronic hepatitis B	Liver	HBV	Elimination/LNP	▶			
PBGENE-PMM	m3243 primary mitochondrial myopathy	Muscle	PMM	Elimination/AAV	▶			
PBGENE-DMD	Duchenne muscular dystrophy	Muscle	DMD	Excision/AAV	▶			
PBGENE-LIVER	Undisclosed	Liver	—	Insertion/—	▶			
PBGENE-CNS	Undisclosed	CNS	—	—	▶	<i>Returning to Precision Under Assessment</i>		
iECURE-OTC*	Ornithine transcarbamylase deficiency	Liver	OTC	Insertion/AAV	▶			
PBGENE-NVS	Sickle cell disease/ beta thalassemia	HSCs	—	Insertion/—	▶			



*iECURE-OTC also named ECUR-506 under investigation in the OTC-HOPE study

Ornithine Transcarbamylase (OTC) Program is First ARCUS *In Vivo* Gene Editing Program to Progress into the Clinic

ARCUS *in vivo* gene editing now clinical stage following December 2023 approval:

- › iECURE received approval from the Australian TGA, U.K. MHRA and U.S. FDA regulatory bodies for the initiation of OTC-HOPE, a first-in-human Phase 1/2 trial evaluating ECUR-506, incorporating an ARCUS nuclease for the treatment of OTC deficiency in neonatal male patients.
- › Additional approvals expected in 2024. iECURE is preparing sites and **anticipates initiating the global clinical trial in 2024.**

CTA acceptance is important milestone for ARCUS

“The acceptance of iECURE’s CTA marks an important milestone for patients with OTC deficiency. This is the first ARCUS *in vivo* gene editing program to progress into the clinic. We look forward to supporting iECURE's continued progress with this program.” – *Michael Amoroso*

28% Of liver cells in NHPs demonstrated durable expression of the human OTC gene at the 1-year time point **following administration of ECUR-506**

*Note: therapeutic benefit expected at 5%+ editing³

~10,000 
People WW with OTCD

- › Disease prevalence is between 1 in 60,000 and 1 in 72,000
- › **Neonatal onset has been associated with mortality rates as high as 74%**

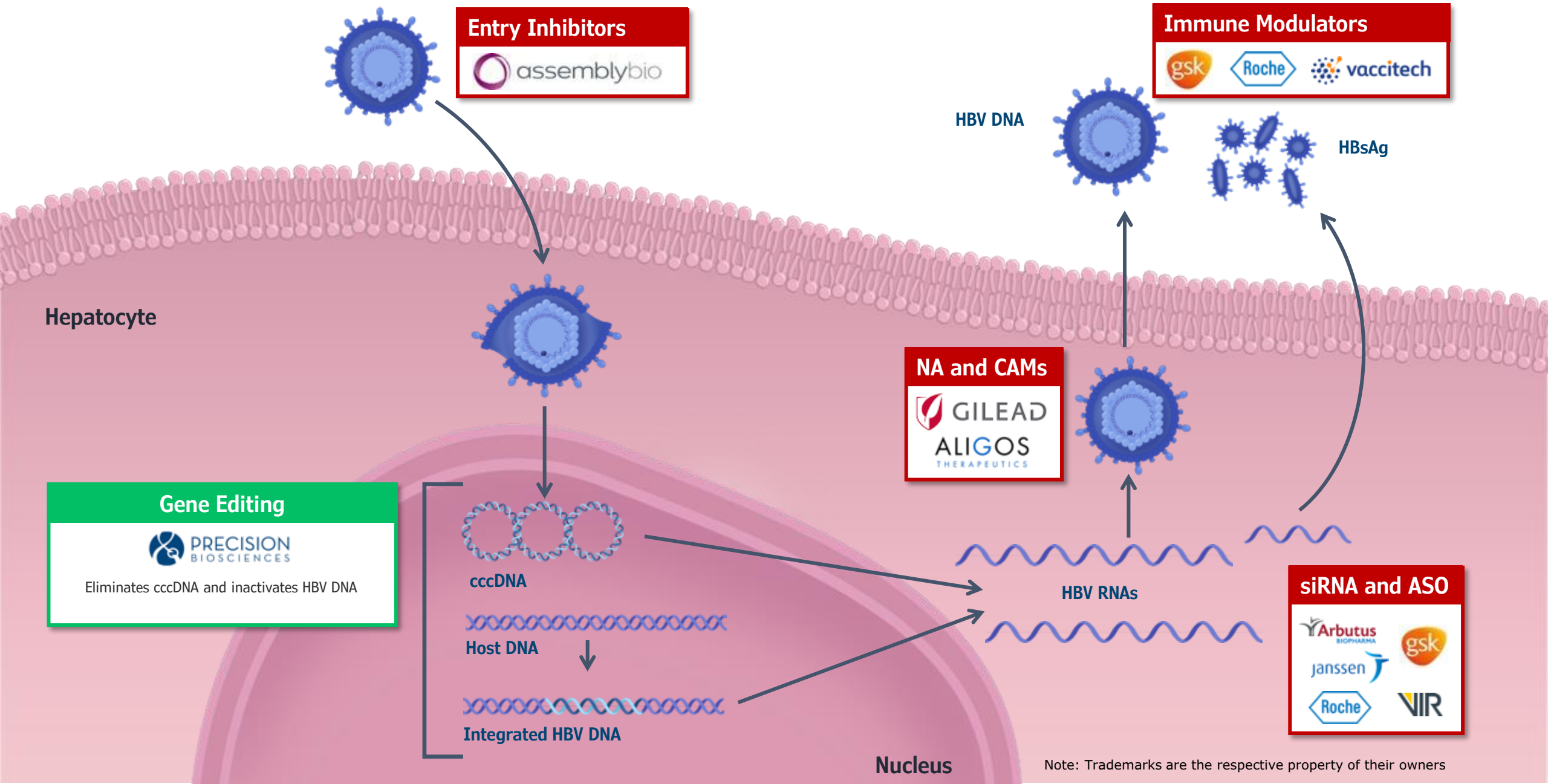
¹ Complete removal of OTC activity results in severe neonatal disease, while decreased OTC results in late-onset.

² Onset may occur at any age though is more common in infancy. HAC: Hyperammonemic Crisis, defined as plasma ammonia levels $\geq 150 \mu\text{mol/L}$ together with clinical symptoms probably related to hyperammonemia. OTC: Ornithine Transcarbamylase. Source: UpToDate; Orphanet; Hasegawa et. Al. J Pediatr Surg. 1995. Ah et. Al. GeneReviews. 2017. NORD; Lamb et. Al. BJM. 2016. Brassier et. Al. Orphanet Journal of Rare Disease 2015.; Unsinn et. Al. Orphanet Journal of Rare Diseases. 2016; Summar et al. NIH. 2008; Buerger et. Al. J. Inherit. Metab. Dis. 2013; ClearView Analysis.

³ 5-10% or greater editing or periportal hepatocytes expected to yield therapeutic benefit per KOL feedback; 5% threshold supported by Annals of Clinical and Translational Neurology



Only ARCUS designed to eliminate cccDNA and inactivate HBV DNA



Note: Trademarks are the respective property of their owners

PBGENE-HBV Program Accomplishments

Finalized mRNA optimization of payload and LNP formulation leading to 8x improvement in protein expression

FDA INTERACT Meeting in July 2023

Final Clinical Candidate Nominated

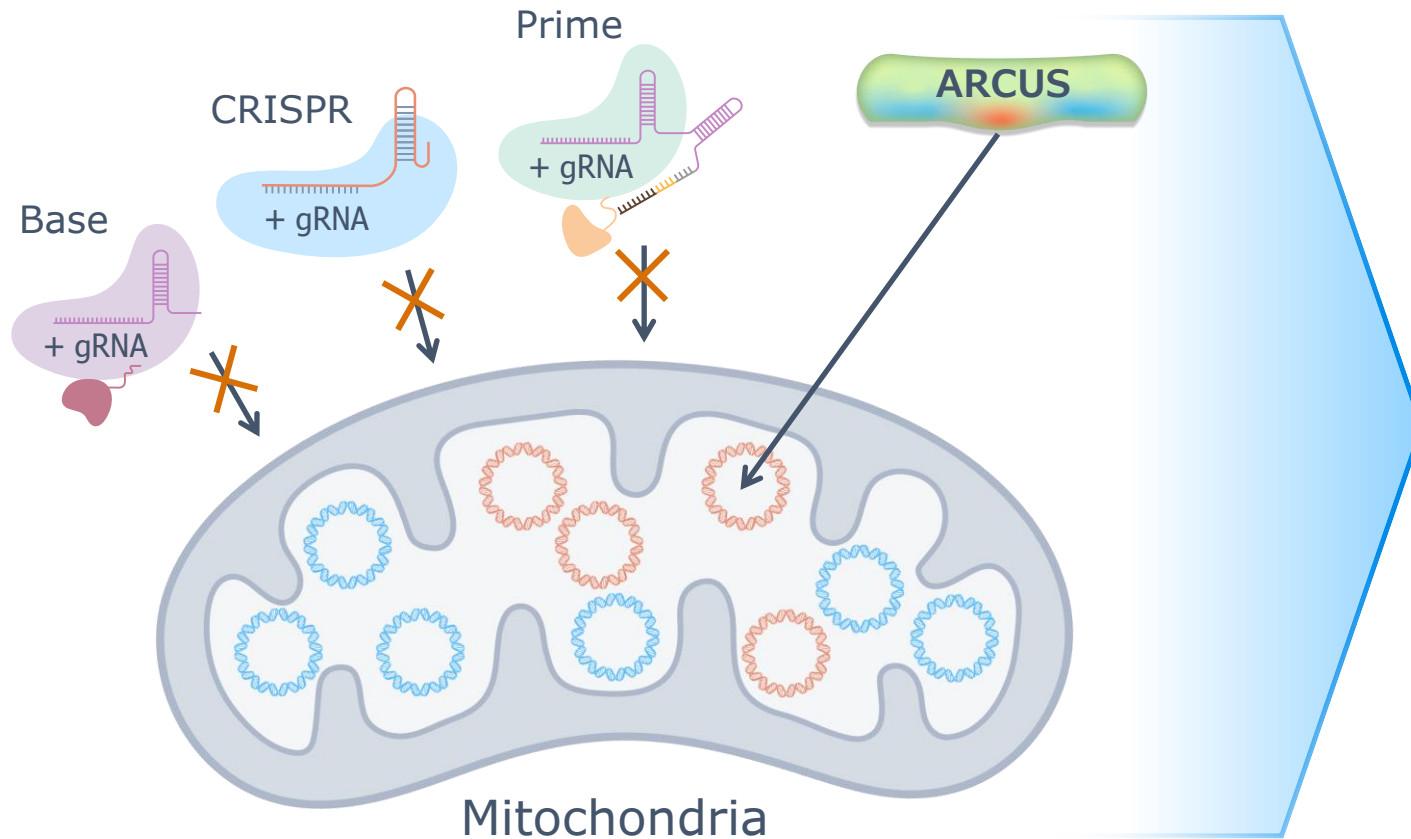
FDA Pre-IND Meeting in January 2024

on-track Submit IND/CTA in 2024

site-selection underway Initiate First-in-Human (FIH) Clinical Studies



Simplicity: ARCUS Can Go Where Few Other Gene Editors Can Follow



nature metabolism



Article

<https://doi.org/10.1038/s42255-023-00932-6>

Efficient elimination of MELAS-associated m.3243G mutant mitochondrial DNA by an engineered mitoARCUS nuclease

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PBGENE-PMM Program Highlights

- › Single component nature of ARCUS allows specific editing of mutant mtDNA with no off-target editing
- › ARCUS-induced heteroplasmy shift resulting in improved mitochondrial and respiratory function in edited cells
- › No evidence of mitoARCUS editing nuclear DNA



Reasons to Believe in Precision's Approach to Treat PMM



Simplicity of ARCUS **single component editor** enables targeting mutant mitochondrial DNA whereas other **guide RNA-based editors cannot**



Opportunity for a **one-time, potentially curative treatment** for adult patients who today are only treated with supportive care "mito-cocktails"; **15,000-25,000 patients in the US alone** who may be eligible for PBGENE-PMM



Current ARCUS nuclease can accurately discriminate a single nucleotide change **shifting heteroplasmy in favor of wild type** and improving mitochondrial function; **no evidence of mitoARCUS editing nuclear DNA**



Potentially first-in-class opportunity for m.3243 associated PMM targeting CTA and/or IND in 2025; ARCUS can be further developed to target other mitochondrial mutations



Sufficient Cash Runway to Realize Multiple Near-Term Milestones in 2024-2025

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On-Track **Wholly owned PBGENE-PMM** program **IND &/or CTA expected filing in 2025**

Projected cash runway into 2H 2026
through Phase I clinical data read-outs (OTC, HBV and PMM)
– 3 cell tx business development deals generating up to ~\$50 million in upfront & potential near-term cash
– Completion of \$40 million public offering
– Quarter ending March 31st cash balance: \$137 million sufficient to fund 3 wholly owned internal programs

Returning three advanced preclinical programs to pipeline, develop on own or through partners



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Q&A

