PRECISION BIOSCIENCES

Corporate Deck

August 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, mitochondrial gene editing, viral gene elimination 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 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 stat

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 NASDAO or other public stock exchanges and other important factors discussed under the caption "Risk Factors" in our Ouarterly Report on Form 10-Q for the guarterly period ended June 30, 2024, 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.



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Corporate Overview



Focusing on Our Foundation—In Vivo Gene Editing Through our gene editing platform ARCUS

Go-Forward Singular Focus In Vivo Gene Editing

Leveraging 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
- Cash & cash equivalents (6/30/2024) = \$124 million
- Expect existing cash and cash equivalents, expected operational receipts, operational efficiencies, availability of the ATM facility, and available credit to fund OpEx and CapEx into **second half** of **2026**

Expected cash runway now enables funding In Vivo programs through Phase 1 data

Focused Execution

2024-2026



ARCUS Focused on Sophisticated Edits Leveraging Unique Advantages

	PROGRAM	INDICATION	TISSUE	TARGET	US Patient Pool	RESEARCH	IND-ENABLING	CLINICAL	PARTNER
\bigstar	PBGENE-HBV	Chronic hepatitis B	Liver	HBV	1-2 Million				A
\bigstar	PBGENE-PMM	m3243 mitochondrial disease	Muscle	PMM	20 Thousand				
	PBGENE-DMD	Duchenne muscular dystrophy	Muscle	DMD	8 Thousand		Req	egained By Precision Under	
	PBGENE-LIVER	Undisclosed	Liver	_	-		Pr		
	PBGENE-CNS	Undisclosed	CNS	_	-		Ass	essment	
	iECURE-OTC*	Ornithine transcarbamylase deficiency	Liver	OTC	5-6 Thousand				EC⊍RE
	PBGENE-NVS	Sickle cell disease/ beta thalassemia	HSCs	_	100 Thousand				ம் novartis

Precision wholly owned organic program

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

ARCUS Potential to Capture a Significant Portion of the Genetic Medicines Market Versus Other Liver-focused Editors

The Genetic Medicines Market Opportunity is Substantial

2**5-\$35**B Gene Therapy market size by 2030 Gene Editing CAGR $+30-40\%^{1}$ 2025 2026 2027 2022 2023 2024 2028 2029 2020 2030 2021

Gene Editing Expected to Disrupt and Continue to Grow the Genetic Medicines Market

Precision's <u>first indications through</u> <u>organic and partnered programs</u> represent a US market opportunity to potentially treat

400-500k patients*



Total Estimated Sales (\$MM)

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ARCUS Technology Overview



Bringing the Dream to Reality with Creation of ARCUS

ARCUS

Our proprietary gene editing platform naturally evolved to drive high efficiency editing

- ARCUS is derived from the homing endonuclease I-CreI found in green algae
- Evolved to safely edit by inserting in genome, adding function
 - CRISPR-based editing tools engineered from enzymes evolved to knockout DNA only
- Extremely efficient at generating Defined Outcomes* due to predominant repair using Homology Directed Repair (HDR) or "Perfect Religation" versus Non-Homologous End Joining (NHEJ)
- DNA recognition and cutting **fully integrated** into a single protein component for high specificity and efficiency – no guide RNA
- Iterative protein engineering to optimize for safety
- > **65 patents issued** covering ARCUS and in vivo gene editing

ARCUS for the More Sophisticated Gene Edit

Designed by nature for a multitude of applications versus other gene editing modalities









The ARCUS Cut is Uniquely Designed to Drive Defined Outcomes

ARCUS cut leads to HDR or "Perfect" Re-ligation









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Genotoxic effects of base and prime editing in human hematopoietic stem cells; Nature Biotechnology, 2023, Fiumara, M.

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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"

Gene Insertion to a "Safe Harbor" Locus in Hematopoietic Stem Cells



ARCUS will be used to add an antisickling gene to hematopoietic stem cells (HSCs)

Permanent integration of an antisickling gene into a "safe harbor" locus in HSCs is expected to prevent the sickle cell phenotype in mature erythrocytes.







Size Matters for <u>Where</u> You Can Deliver

ARCUS can use different delivery vehicles to target diverse tissue types







Size Matters for **What** You Can Deliver:

Small ARCUS Size Allows Two Nucleases in One AAV for **Gene Excision** in DMD



ARCUS Nucleases Excise Mutations and Restore Function in DMD



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









Simplicity: ARCUS is the Only Single Protein Component Editor





> Easy to deliver

> High efficiency

 \rangle Low dose improves safety



Simplicity: Simultaneous Delivery of Multiple Components in Separate Delivery Vehicles Results in Lower Efficiency





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PBGENE-HBV

Viral Elimination



Target CTA/IND 2024

> 300 million cHBV infections globally



> 1,000,000 cHBV infections in the US

PBGENE-HBV Designed For Broad Patient Applicability

Only modality in development designed to <u>eliminate cccDNA</u> and <u>inactivate integrated</u> <u>HBV DNA</u> -> essential for functional cure (undetectable HBV DNA and HBsAg)

> Precision Advancing Next Steps:

- Final PBGENE-HBV clinical candidate ready
- On-going discussions with global regulatory authorities in first wave markets
- Final step: pre-CTA/IND toxicology studies on-going
- FIH study site-selection and feasibility in process
- CTA/IND expected filing in 2024

Only ARCUS designed to eliminate cccDNA and inactivate HBV DNA



Size & Simplicity Optimal to Target cccDNA and Integrated HBV DNA



Efficacy: Non-Human Primate (NHP) Study Demonstrates Up to 99% Viral Engagement, Suggestive of Strong Potential Efficacy Profile of PBGENE-HBV



Final clinical candidate expected to eliminate majority of cccDNA, this unique mechanism of action is critical to drive durable functional cures

Notes:



1.Final optimized candidate nuclease derived from prior optimized nuclease - only one amino acid difference with similar efficacy 2.NHP study- 2 doses of PBGENE-HBV 42 days apart; viral engagement (elimination + inactivation through indels) measured at D90 3.Prior nuclease data presented at R&D Day in Sep '23 - substantial improvement from prior NHP study showing 66% elimination and 15% indels

Efficacy–New Model: PBGENE-HBV Significantly and Sustainably Reduces HBV DNA as a Monotherapy in New Transgenic Mouse Model





Even after stopping NUC, PBGENE-HBV durably reduces HBV DNA as seen in combination cohort. Supports potential for stopping NUC and functional cures in future FIH study



2. HBV DNA levels measured in plasma

Safety: PBGENE-HBV Final Clinical Candidate Demonstrates Robust Safety Package Supporting Advancement Towards Clinical Trials

- PBGENE-HBV specifically cuts HBV DNA leading to elimination of cccDNA and inactivation of integrated HBV DNA without impacting any genes in the human genome
 - No increased risk of translocations or integrations
- PBGENE-HBV was well tolerated in non-human primates over multiple administrations
 - Rapidly cleared after each dose administration
 - Transient transaminase elevations and non-adverse changes in blood parameters
- Preclinical safety data supports the advancement of PBGENE-HBV to clinical trials as a potentially curative, finite treatment for HBV



PBGENE-HBV Phase 1 Clinical Considerations





PBGENE-HBV Program Accomplishments



- Final Clinical Candidate Nominated
- FDA Pre-IND Meeting in January 2024
 - Clinical Trial Material Manufactured
 - Clinical Trial Sites Identified

on-track

Submit IND/CTA in 2024

site-selection underway



Initiate First-in-Human (FIH) Clinical Studies



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PBGENE-PMM

Mutant Mitochondrial DNA Elimination



m.3243 Mitochondrial Disease Currently Lacks a Curative Treatment ~20K m.3243 PMM patients in the US alone

Patients today lack curative

treatments and

receive supportive

care only through

"mito cocktails"1

m.3243-associated mitochondrial diseases often lead to defects in energy production affecting high energy-demand tissues (e.g. skeletal muscle)







Sources:

https://www.ninds.nih.gov/health-information/disorders/mitochondrial-myopathies; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6938233/

2. Calculated based disease epidemiology studies and secondary literature

Multi-Copy Mitochondrial DNA (mtDNA) is Critical for Mitochondrial Function





PBGENE-PMM Distinguishes a Single Base Difference at m.3243

m.3243A>G

Mutation Prevalence of 1/500¹

 ~36% of Mitochondrial Diseases are driven by m.3243A>G² m.3243 associated mitochondrial disease estimated at ~20k patients in the US alone

Mutant mtDNA sequence

5'-CAGGGCCCGGTAATCGCATAAA-3'

5'-CAG A GCCCGGTAATCGCATAAA-3'

Wild-type (healthy) mtDNA sequence



1.Manwaring et al 2006 Population prevalence of the MELAS A3243G mutation. Mitochondrion 2.Schon et al., 2023, National Mitochondrial Disease Registry in England... Euromit2023 Conference, Bologna, Italy, June 13, 2023;

mitoARCUS Therapeutic Approach to Shift Heteroplasmy



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



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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

Received: 18 May 2023	Wendy K. Shoop @12, Janel Lape', Megan Trum', Alea Powell', Emma Sevign					
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Published online: 30 November 2023						

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

mtDNA Mutations Are Commonly Heteroplasmic

Situation where two or more mtDNA variants exist in same mitochondria







PBGENE-PMM Improved Mitochondrial Function



mtDNA, mitochondrial DNA; WT, wild-type; experiments in cybrid cells.

PBGENE-PMM Program Accomplishments





Precision BioSciences Offering Meaningful Catalysts in Next 6-18 Months

Ample cash runway to fund multiple potential regulatory submissions and clinical data readouts



Sources: 6/30/24 10-Q; \$50M includes upfront payment and near-term milestones