



Precision BioSciences & Novartis to Collaborate  
on Potentially Curative *In Vivo* Gene Editing  
Program for Hemoglobinopathies

*June 22, 2022*



PRECISION  
BIOSCIENCES

# 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. All statements contained in this 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 goal of providing a one time, potentially curative treatment for certain hemoglobinopathies, the success of the collaboration with Novartis, including the receipt of any milestone, royalty, or other payments pursuant to and the satisfaction of obligations under the Agreement, clinical and regulatory development and expected efficacy and benefit of our platform and product candidates, expectations about our operational initiatives and business strategy, expectations about achievement of key milestones, and expected cash runway. In some cases, you can identify forward-looking statements by terms such as “aim,” “anticipate,” “approach,” “believe,” “contemplate,” “could,” “estimate,” “expect,” “goal,” “intend,” “look,” “may,” “mission,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would,” or the negative thereof and similar words and expressions.

Forward-looking statements are based on management’s current expectations, beliefs and assumptions and on information currently available to us. Such statements are subject to a 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 and requirements under our current debt instruments and effects of restrictions thereunder; risks associated with raising additional capital; 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 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; pending and potential 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’ ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate; our or our collaborators’ 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; our ability to obtain an adequate supply of T cells from qualified donors; our ability to achieve our anticipated operating efficiencies at our manufacturing facility; 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 COVID-19 pandemic and variants thereof, or any pandemic, epidemic or outbreak of an infectious disease; insurance expenses and exposure to uninsured liabilities; effects of tax rules; risks related to ownership of our common stock and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2022, 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](http://www.sec.gov) and the Investors page of our website under SEC Filings at [investor.precisionbiosciences.com](http://investor.precisionbiosciences.com).

Michael Amoroso  
President & Chief Executive Officer

# Precision Biosciences is Delivering on the Promise of Therapeutic Genome Editing to Transform the Future of Medicine

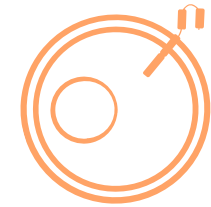


## ***In Vivo* Editing for Genetic Diseases**

*On target, potentially curative, one-time treatments*

## **ARCUS<sup>®</sup> Genome Editing Platform**

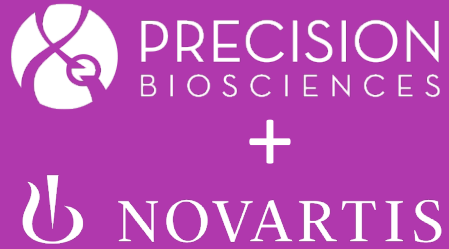
*Precision and Versatility for In Vivo and Ex Vivo Therapeutics*



## **Ex Vivo single-gene edit for Allogeneic CAR T immunotherapy**

*Single-dose, donor-derived, off-the-shelf CAR T cells*

# In Vivo Gene Insertion Collaboration with Novartis for Sickle Cell Disease



Builds on the unique gene insertion capabilities of ARCUS<sup>®</sup> and further validates ARCUS as a premium genome editing platform

**Collaboration with Novartis,** a global gene therapy leader with broad commitment to hemoglobinopathies

**Precision to develop a single ARCUS nuclease** for certain hemoglobinopathies

**Goal to design ARCUS nuclease for safe and efficient *in vivo* gene insertion**

- ✓ Precision receives \$75M upfront for a single target/single nuclease
- ✓ Eligible to receive up to an additional \$1.4B in milestones and tiered royalties on sales of licensed products
- ✓ Collaboration adds hematopoietic stem cells (HSCs) to existing *in vivo* gene editing programs targeting the liver, muscle and central nervous system
- ✓ One-time, potentially curative treatment for hard-to-treat genetic blood disorders such as sickle cell disease (SCD) and beta thalassemia
- ✓ Novartis plus \$50M equity offering extends Precision's expected cash runway to year end 2024

# Novartis, the Partner of Choice for an *In Vivo* Gene Editing Hemoglobinopathy Transformational Therapy

- Collaboration with Novartis provides validation to Precision's ARCUS platform
- Novartis brings depth of experience with gene editing approaches
- Novartis provides development and commercialization expertise in hemoglobinopathies, including sickle cell disease and beta thalassemia



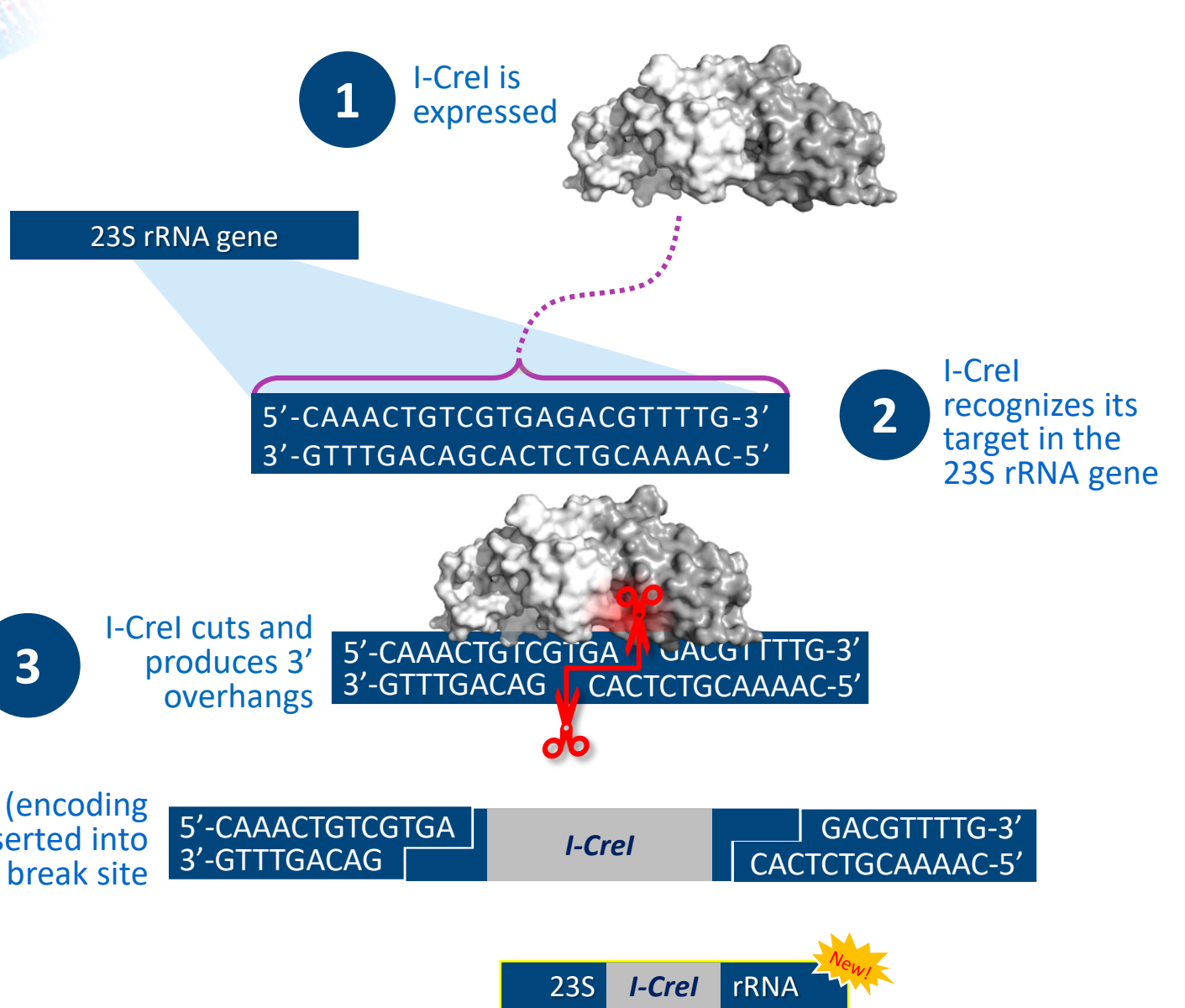
“ We identify here a collaborative opportunity to imagine a unique therapeutic option for patients with hemoglobinopathies, such as sickle cell disease and beta thalassemia – a potential one-time treatment administered directly to the patient that would overcome many of the hurdles present today with other therapeutic technologies. We look forward to working with Precision and leveraging the ARCUS technology platform, which could bring a differentiated approach to the treatment of patients with hemoglobinopathies. ”

**Jay Bradner**

President of the Novartis Institutes for Biomedical Research (NIBR), the Novartis innovation engine

Derek Jantz, Ph.D.  
Chief Scientific Officer, Co-Founder

ARCUS is derived from **I-Crel**, a homing endonuclease from algae evolved for precise genome editing.



I-Crel evolved to insert DNA into a defined location in a large genome



# Safety

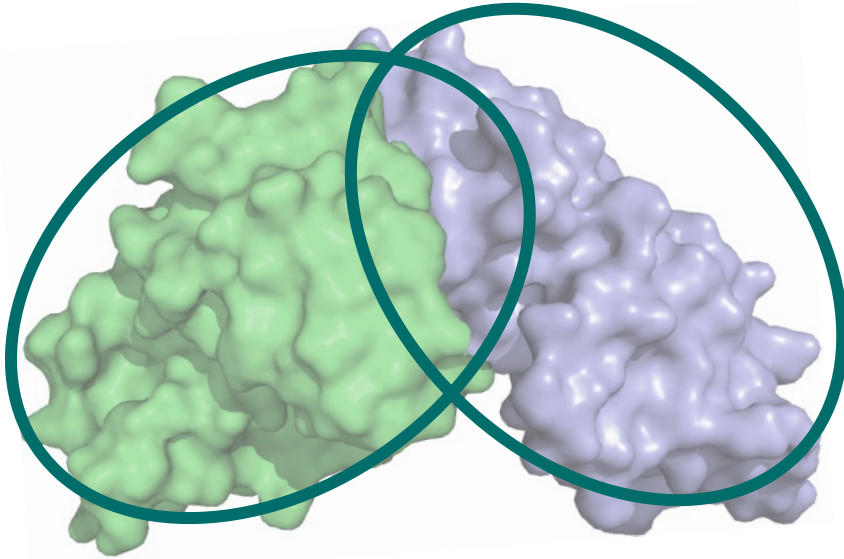
ARCUS is inactive until it binds to its target DNA site

This allows ARCUS to be expressed for extended periods of time from an adeno-associated virus (AAV) vector without accumulating off-target gene edits.

➤ 16 ARCUS nucleases have been evaluated in non-human primates representing, collectively, >80 years of event-free in life safety testing.

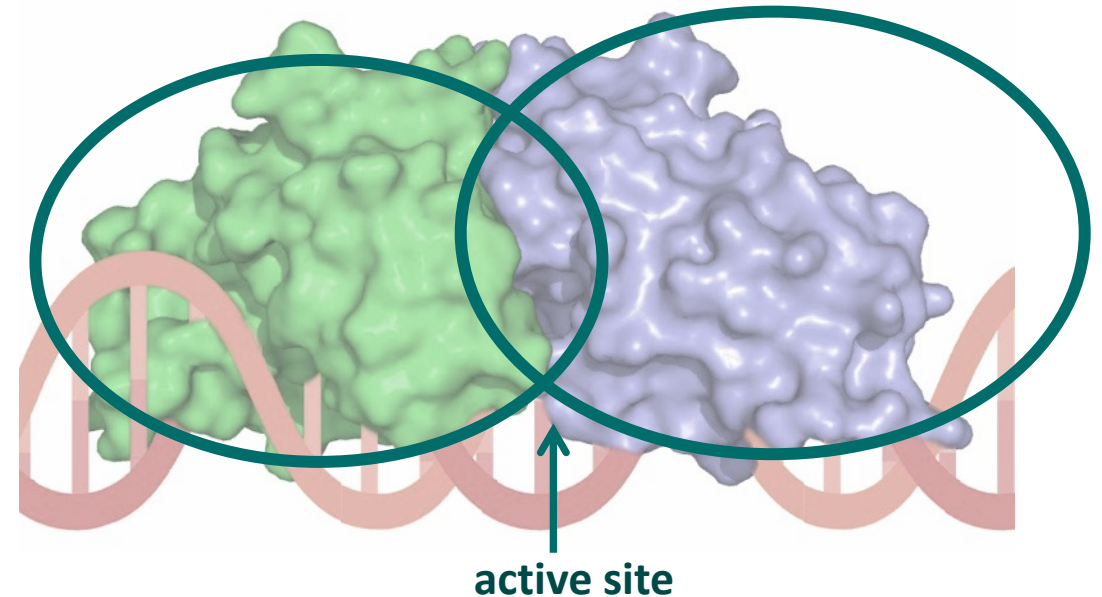
## Inactive Form of ARCUS

closed configuration buries the active site inside the protein



## Active Form of ARCUS

open configuration allows the active site to access DNA

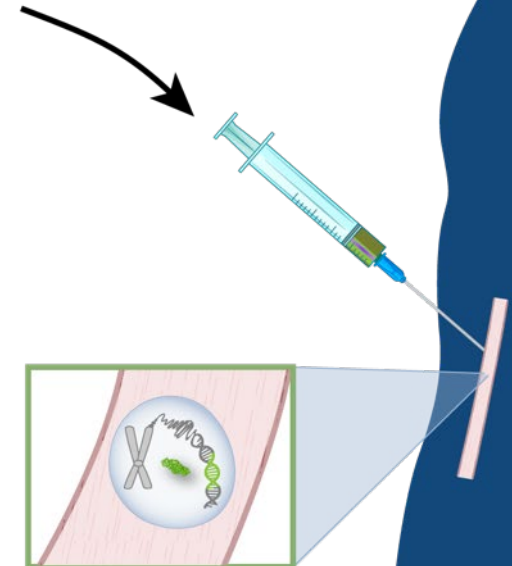
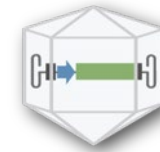
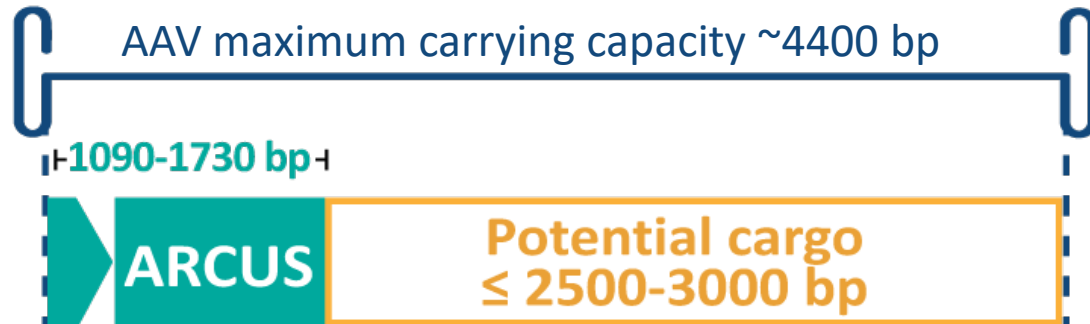


# Delivery

ARCUS  
is small

ARCUS is 364 amino acids. This enables delivery to tissues and cells using a variety of viral and non-viral delivery technologies including AAV.

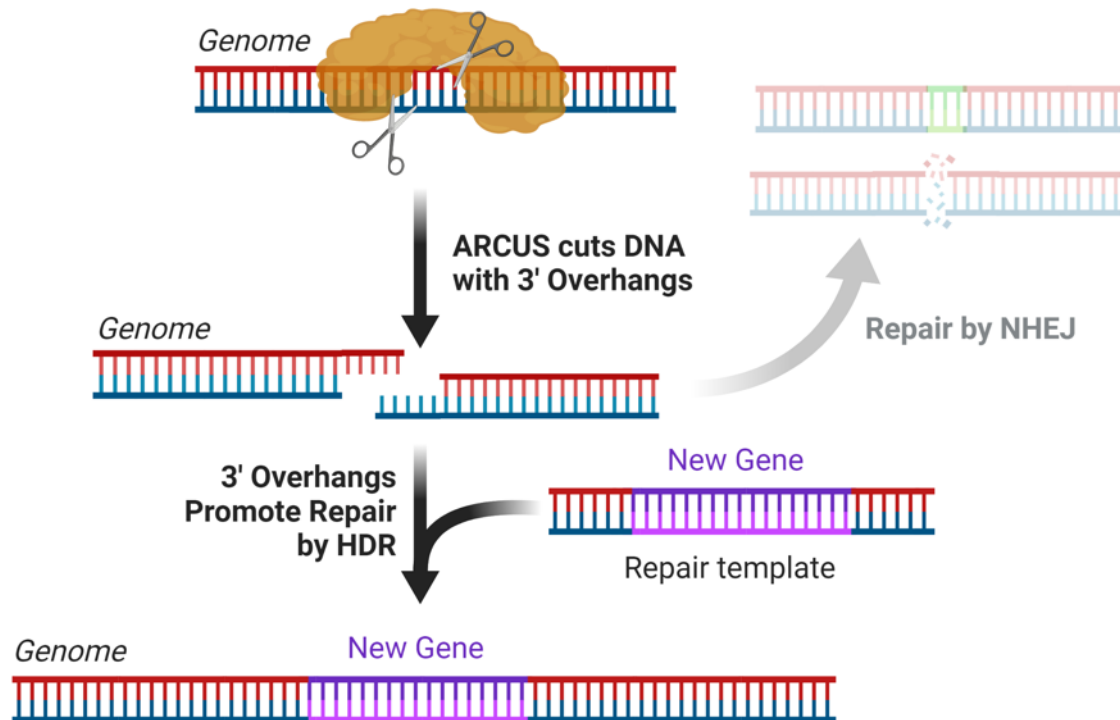
An ARCUS gene requires only a fraction of the carrying capacity of an AAV vector. This leaves the majority of the vector capacity available for other “cargo.”



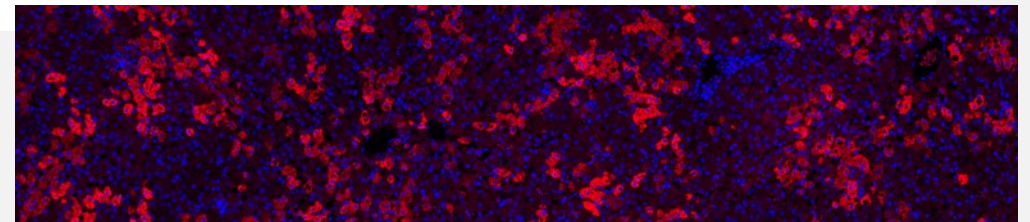
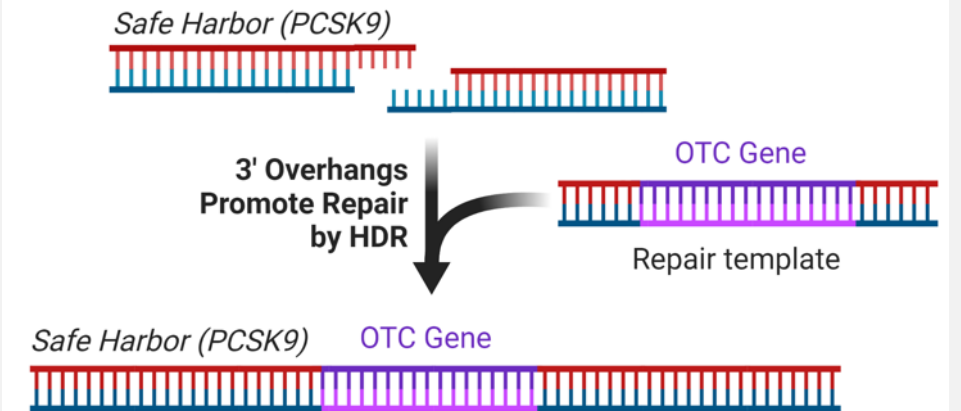
# Versatility

ARCUS can efficiently insert DNA into the genome

The 3' overhangs produced by ARCUS potently stimulate DNA repair by homology-directed repair (HDR). This enables transgenes to be inserted into the genome.



## Real world example: Targeted Insertion of an OTC Transgene in NHP Liver



■ DAPI ■ OTC

Wang, et al. ASGCT 2022

# Hemoglobinopathies are a Major World Health Problem

## Sickle Cell Disease (SCD)

Affects the structure/function of hemoglobin, reducing the ability of red blood cells to transport oxygen

- Acute sickle cell pain crises and life-threatening complications

## Beta Thalassemia

One of the most common genetic diseases caused by a disruption of normal hemoglobin production

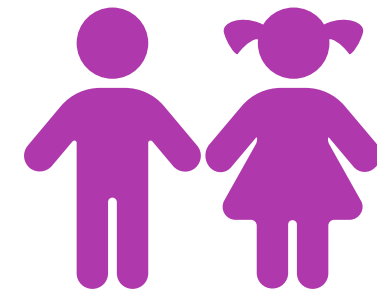
- Complications: Overproduction of red blood cells inside and outside of the bone marrow, heart disease, chronic liver hepatitis, defects of the reproductive system, diabetes, and rare skin disorders

Sickle Cell Disease Affects

**>300,000**  
newborns  
annually



**~1,000** children  
in Africa are born with SCD  
**every day** and **>50%** will not  
reach their 5<sup>th</sup> birthday



**~68,000**  
children born with  
thalassemia each year

# We are Pursuing an *In Vivo* Approach to SCD

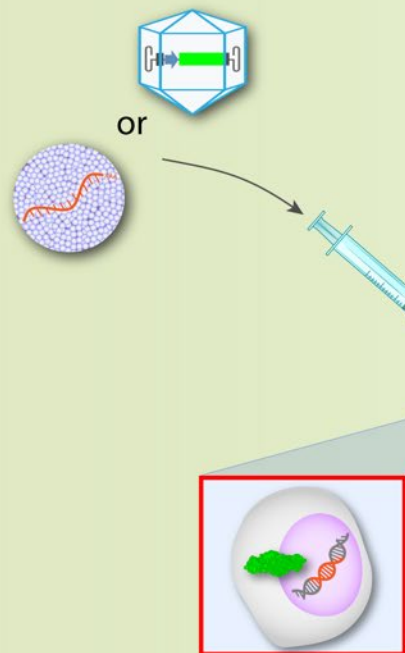
Our goal is a one-time, IV administration of drug

If successful, an *in vivo* therapy for SCD might be administered in regions that do not have transplant centers.

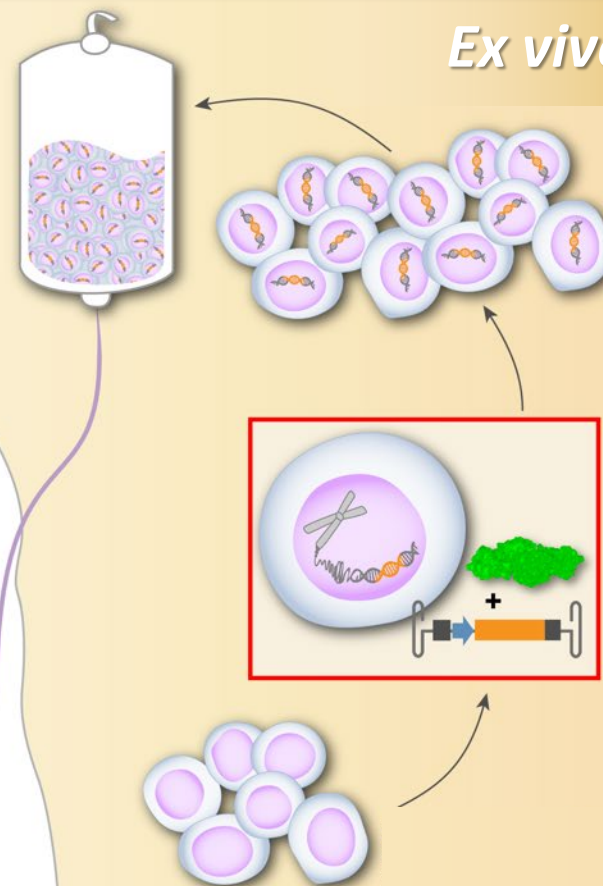
## *In vivo* gene editing



+



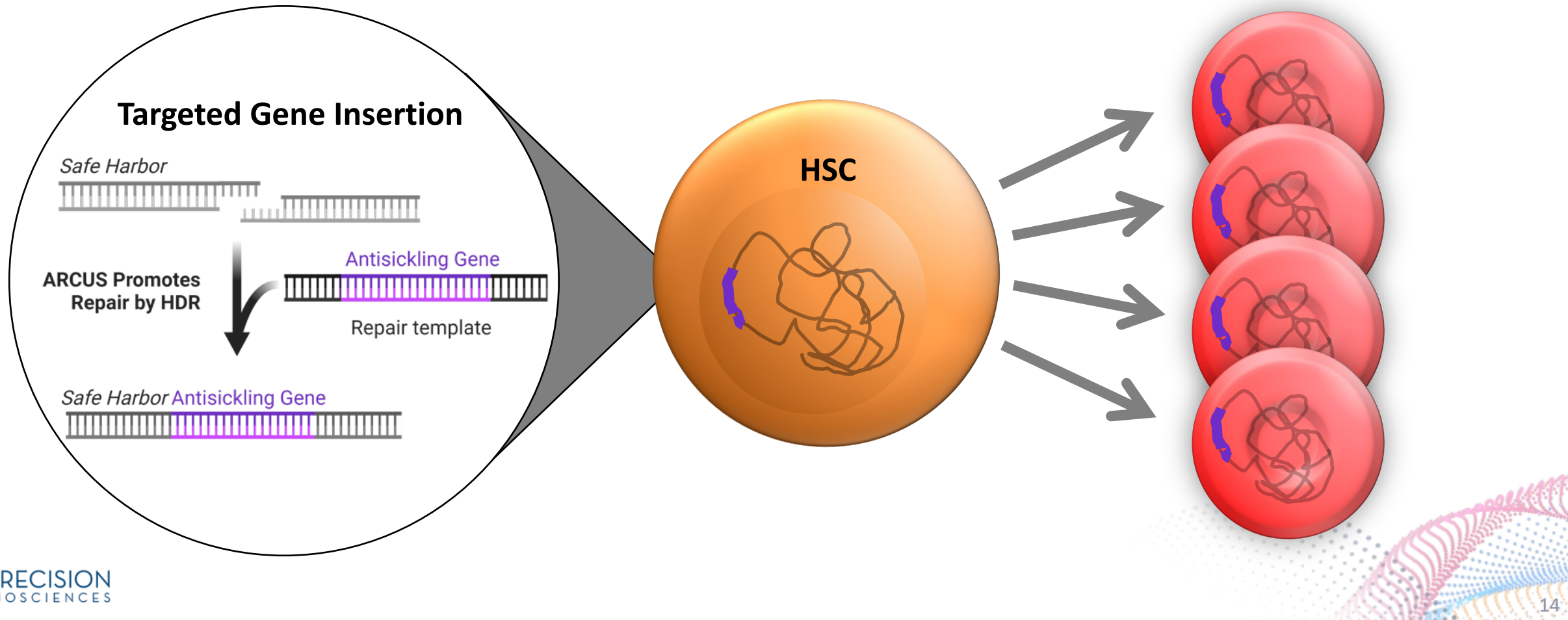
## *Ex vivo* gene editing



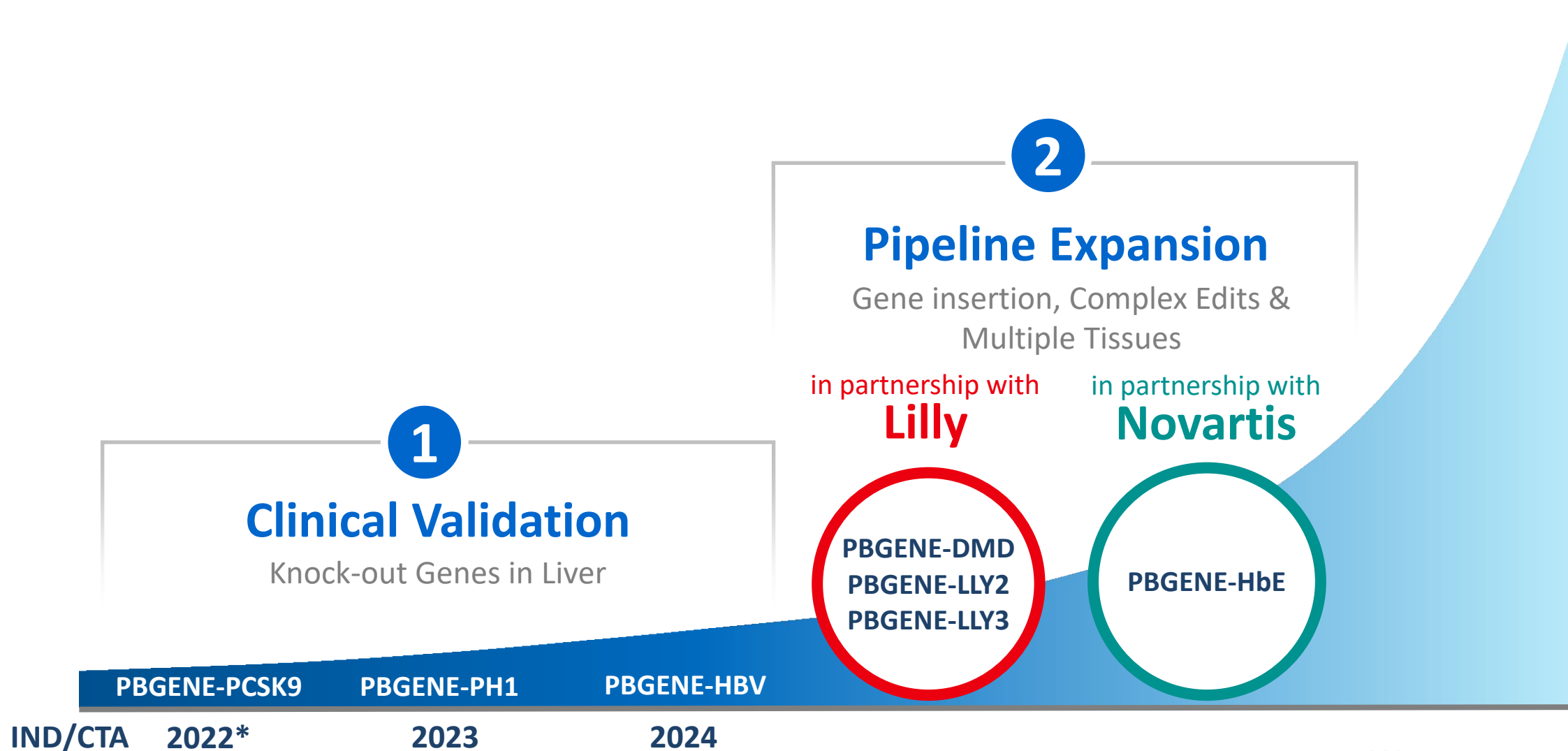
# Gene Insertion to a “Safe Harbor” Locus in Hematopoietic Stem Cells


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.



# Gene Editing Pipeline Validation and Expansion Creates Value





**Cindy Atwell**  
Senior Vice President, Business Development



# Novartis Deal Meets all Precision Business Development Principles: Systematic and Disciplined Approach to Funding Business & Acquiring Capabilities

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## Business Development Rules of Engagement for *In Vivo* Gene Editing

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**Maximize upfront and near-term payments** to complement financing



**Garner “premium” deals that differentiate** the ARCUS gene editing platform



**Out-licensing of an area on a limited, target-by-target basis** over the next 2-3 years

- **Execute *in vivo* deals in areas outside of Precision’s organic development** (e.g., HSCs)



**Leverage ARCUS unique capabilities** (e.g., gene insertion)



Deal structure reflects **minimal distraction to internal programs**



**World renowned drug development partner**



# Deal Structure Leverages Precision Expertise for ARCUS Nuclease Creation



- Design and optimize a single, custom ARCUS nuclease for “safe harbor” target site
- ARCUS nuclease to be used for insertion of specified payloads for certain hemoglobinopathies
- Conduct *in vitro* characterization of the nuclease

*Focus on core capability creates minimal distraction to Precision internal programs*



- Novartis to develop as a potential *in vivo* treatment for sickle cell disease and beta thalassemia
- Responsible for all subsequent research (including *in vivo* pre-clinical and toxicology), development, manufacturing and commercialization

# Summary of Deal Economics: \$75M Upfront for Single Target

Upfront Payment	<b>\$75M</b> <ul style="list-style-type: none"><li>• \$50M cash</li><li>• \$25M equity at 20% premium to 10-day VWAP* ending 06/13/2022</li></ul>
Aggregate Milestones & Fees	<b>\$1.4B milestones + research funding</b>
Royalties on Commercialized Products	<b>Mid-single digit to low-double digits</b>
Shares Purchased	<b>~12.4M</b>

# Novartis Collaboration is Complementary to Precision's Existing *In Vivo* Gene Editing Partnership with Lilly

Research collaboration and license agreement aimed at treating challenging genetic diseases



+

*Lilly*

Pre-IND R&D

IND to Commercial

- 3** Initial collaboration for three targets, including Duchenne muscular dystrophy and two other undisclosed programs targeting the liver and CNS
- +**
- 3** Lilly retains right to select up to three additional gene targets

- ✓ Upfront payment of \$135M including \$35M equity
- ✓ Up to \$420M per target in development and commercialization milestones
- ✓ Mid-single digit to low-teens tiered royalties

Michael Amoroso  
President & Chief Executive Officer

# Broad and Deep *In Vivo* Gene Editing Pipeline Demonstrates Unique Attributes of ARCUS

PROGRAM	INDICATION	TISSUE	TARGET	EDIT TYPE / DELIVERY	RESEARCH	CANDIDATE SELECTION	IND-ENABLING	EXPECTED IND/CTA	PARTNER
<b>WHOLLY OWNED</b>									
<b>PBGENE-PCSK9</b>	Familial hypercholesterolemia	Liver	<i>PCSK9</i>	Deletion/AAV				2022*	
<b>PBGENE-PH1</b>	Primary hyperoxaluria type 1	Liver	<i>HAO1</i>	Deletion/LNP				2023	
<b>PBGENE-HBV</b>	Chronic hepatitis B	Liver	<i>HBV</i>	Deletion/LNP				2024	
<b>PARTNERED</b>									
<b>PBGENE-HbE</b>	Sickle cell disease/ beta thalassemia	HSCs	—	Insertion/—				—	
<b>PBGENE-DMD</b>	Duchenne muscular dystrophy	Muscle	<i>DMD</i>	Excision/AAV				—	
<b>PBGENE-LLY2</b>	Undisclosed	Liver	—	—				—	
<b>PBGENE-LLY3</b>	Undisclosed	CNS	—	—				—	
<b>iECURE-OTC</b>	Ornithine transcarbamylase deficiency	Liver	<i>OTC</i>	Insertion/AAV				—	
<b>iECURE-PKU</b>	Phenylketonuria	Liver	<i>PAH</i>	Insertion/AAV				—	

\*iECURE plans to develop PBGENE-PCSK9 through Phase 1 clinical trial; a CTA filing is expected as early as the end of 2022; Precision retains rights to future development and commercialization of PBGENE-PCSK9

**Building the leading therapeutic gene editing company** focused on high unmet needs in oncology and genetic diseases

**Technology:** ARCUS, a premier genome editing platform

**People:** Fortified Senior Leadership Team with 15+ years perfecting ARCUS protein engineering

**Focus & Discipline:**

- 3 INDs in 3 years for *in vivo* pipeline
- Lead allogeneic CAR T candidate deep in clinic
- Fiscal resources support 2.5 year cash runway to year end 2024

# Q&A