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 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; and expectations regarding our liquidity and capital resources. 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; pending and 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 ability to obtain orphan drug designation or fast track designation for our product candidates or to realize the expected benefits of these designations; 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; 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; 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 and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 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.

PRECISION
BIOSCIENCES

Welcome To Our R&D Day 2023

September 12, 2023

Today's Overview

- Precision 2.0 New Identity
- ARCUS In Vivo Differentiation & Supporting Preclinical Data
- Precision's Updated Development Plan

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

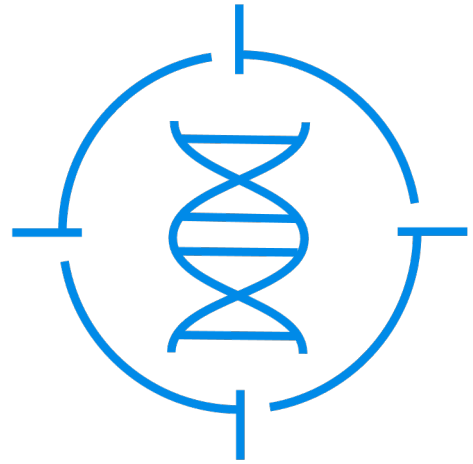
Go-Forward Singular Focus

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
- > 65 patents issued covering ARCUS and in vivo gene editing

Focused Execution
2023-2025

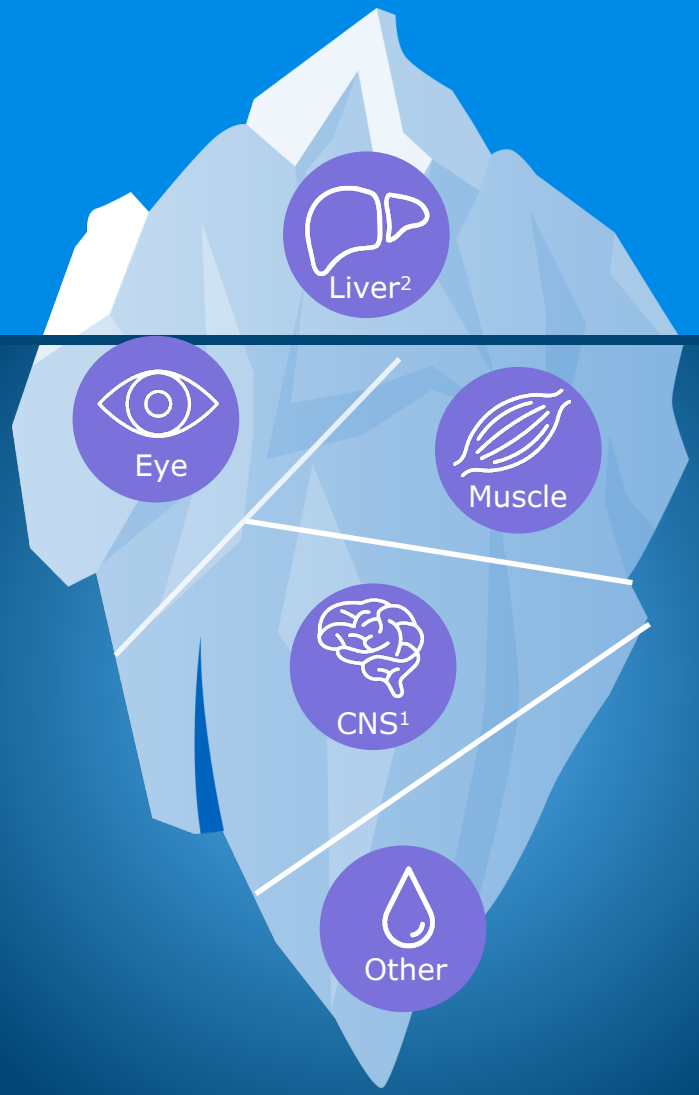


Expected cash runway now enables funding *In Vivo* into Phase 1

Current *In Vivo* Gene Editing Approaches Are Just Scratching the Surface

Development today primarily focused on gene knockout in the liver

~7,000-10,000
monogenic diseases
impacting humanity



ARCUS Breaks Through the Surface

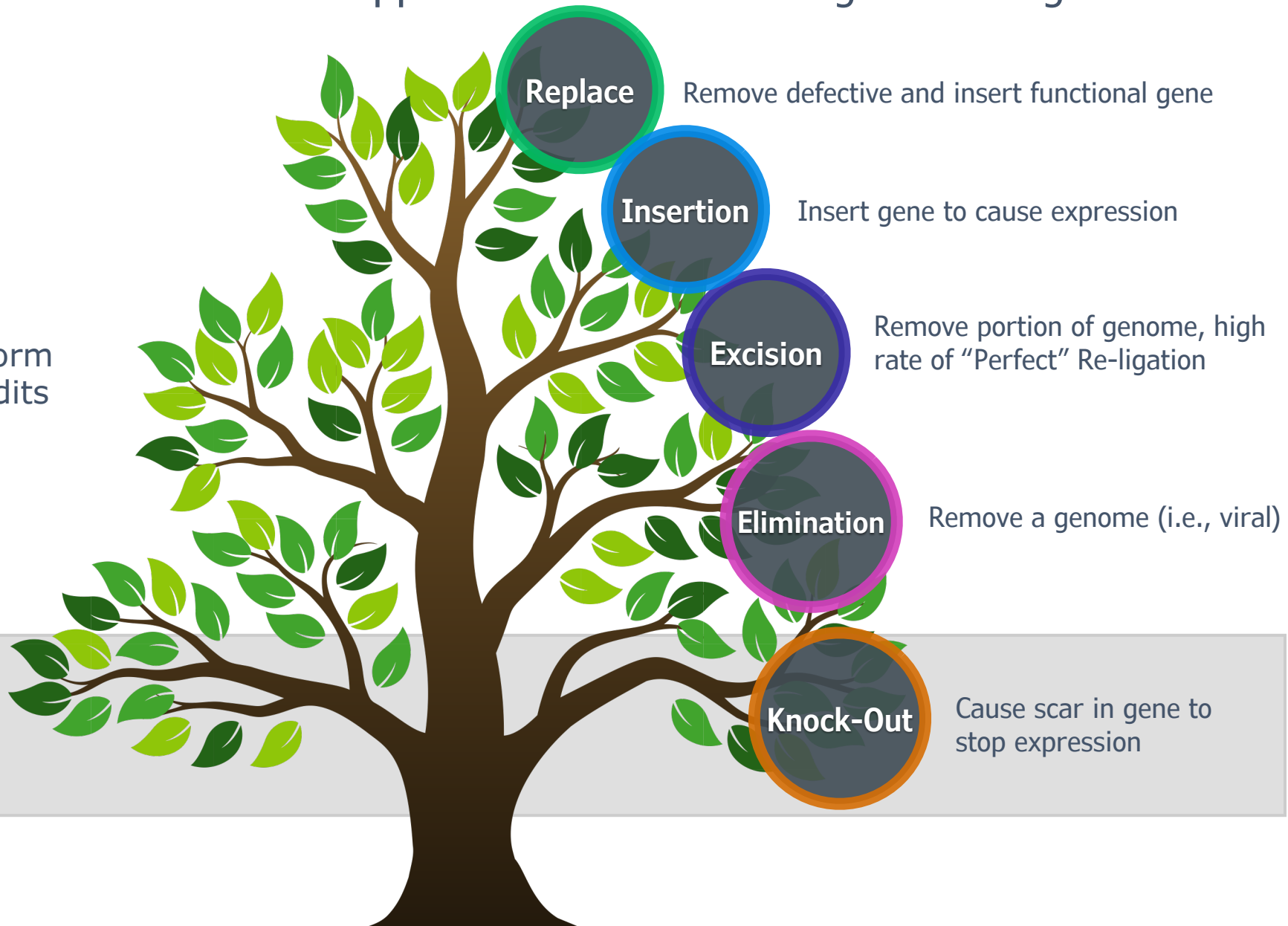
Opportunity to go beyond gene knockouts in the liver and enable gene insertions, gene excision, and gene elimination throughout the body

1. ~70% of monogenic diseases affect nervous system (CNS, etc); https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9223693/
2. Internal analysis using Beacon Intelligence database.

ARCUS for the More Sophisticated Gene Edit

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

ARCUS
Capability To Perform
"Sophisticated" Edits

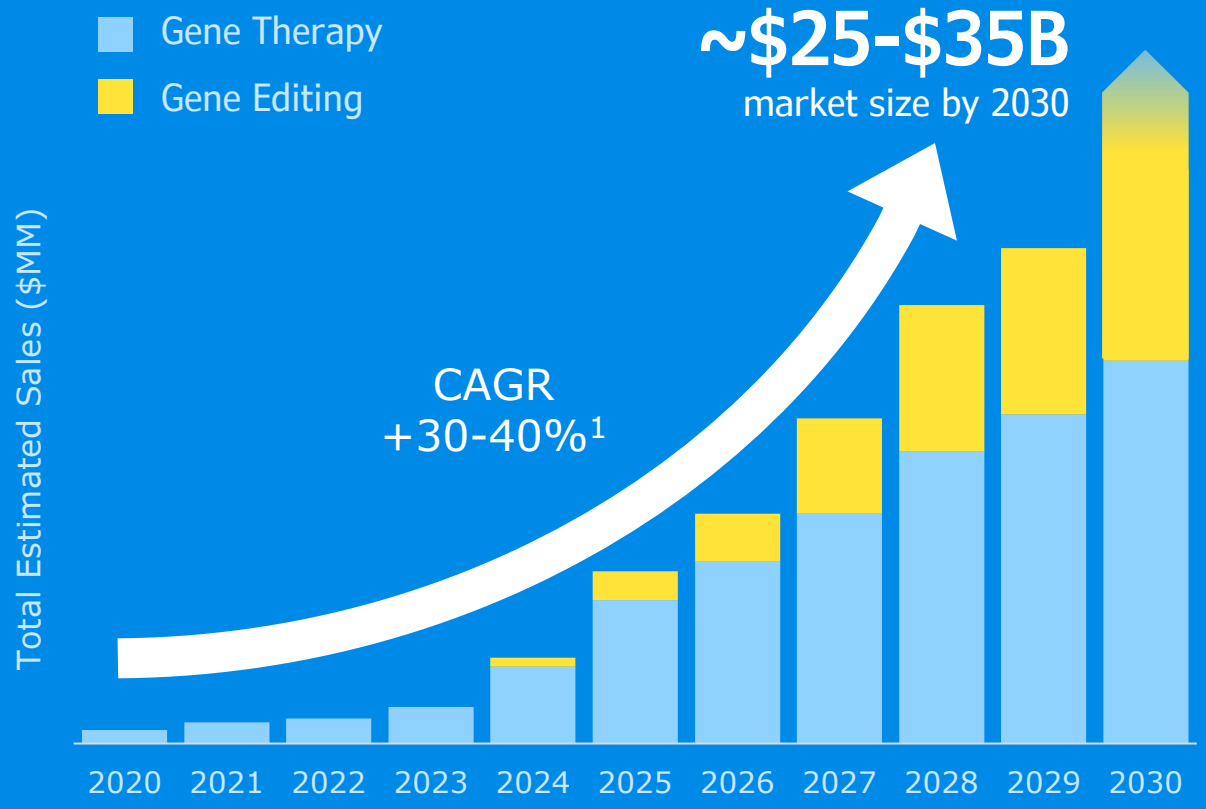


"Low Hanging Fruit"
Commoditized application for **all** gene editors

Degree of Difficulty

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

The Genetic Medicines Market Opportunity is Substantial



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

Precision's programs represent a US market opportunity to treat

400-500k patients*

Note: 1. Based on analysis from Cowen 2023, Grandview 2023, Allied 2023 and BCC 2023 research reports; * Total addressable market (TAM) assumed at 100% share

What's Important When Gene Editing?

ON TARGET EDITING

- **Specificity:** All gene editors need to cut at their specific target site, while avoiding **OFF TARGET editing**
- **Specificity** is non-negotiable for any **clinical-grade** editing technology

EDITING OUTCOMES

What happens at the DNA level **after a nuclease makes a cut**?

- For **gene knockout**, the kind of repair doesn't matter since any error prone repair can **deactivate the gene**
- For more **sophisticated** edits, the **kind of repair** after the on-target cut is critical for **therapeutic outcomes**
- The **kind of repair** achieved is driven by the **nature of the cut**, and that is where **ARCUS is differentiated**

Providing Key Framework: On-Target Gene Editing

Efficiency

Percentage of cells that are edited on-target

Defined Outcome

Predictable, highly consistent, intended = the THERAPEUTIC edit; necessary for sophisticated edits

Random Outcome

Distribution of inconsistent edits, many of which are not intended or therapeutic, potentially limiting both efficacy and safety profile; acceptable for gene knock-outs

Providing Key Framework: On-Target Gene Editing

Efficiency

Percentage of cells that are edited on-target

Defined Outcome

Drivers for Defined Outcome

Homology-Directed Repair (HDR)
Repair outcomes guided by matching identical sequence between cut and DNA repair template

Perfect Re-ligation
Seamless joining of complementary DNA ends in absence of matching DNA template

ARCUS

Random Outcome

Drivers for Random Outcome

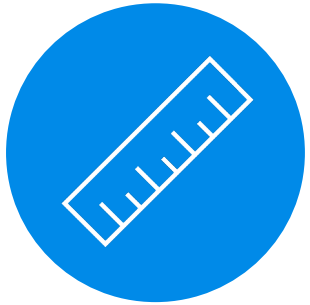
Non-Homologous End-Joining (NHEJ)
Variable and unpredictable joining of cut ends

Other Editing Technologies

ARCUS is a Sophisticated Editing Tool Designed for Defined Outcomes

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

More Defined Outcomes!

ARCUS Focused on Sophisticated Edits Where Defined Outcomes Are Essential

PROGRAM	INDICATION	TISSUE	TARGET	EDIT TYPE / DELIVERY	RESEARCH	CANDIDATE SELECTION	IND-ENABLING	PARTNER
PBGENE-HBV	Chronic hepatitis B	Liver	HBV	Elimination/LNP				
★ PBGENE-PMM	m3243 primary mitochondrial myopathy	Muscle	PMM	Elimination/AAV				
PBGENE-NVS	Sickle cell disease/ beta thalassemia	HSCs	—	Insertion/—				NOVARTIS
PBGENE-DMD	Duchenne muscular dystrophy	Muscle	DMD	Excision/AAV				Prevail THERAPEUTICS A Wholly Owned Subsidiary of Eli Lilly and Company
PBGENE-LLY2	Undisclosed	Liver	—	Insertion/—				
PBGENE-LLY3	Undisclosed	CNS	—	—				
iECURE-OTC	Ornithine transcarbamylase deficiency	Liver	OTC	Insertion/AAV				ECURE

Precision Path to Drive Stakeholder Value Through ARCUS Advantages

1 Drive Organic Development

Focus on Eliminations, Excisions and Insertions

Lead programs	**PBGENE-HBV** (Elimination)	**PBGENE-PMM** (Elimination)
Targeted CTA/IND	2024	2025

Future programs: Insertion, Excision

2 Establish Premium Partnerships

Work with leading Big Pharma/Biotech to drive differentiated programs forward

Current Partnerships	**PBGENE-DMD** **PBGENE-LLY2** **PBGENE-LLY3**	**PBGENE-NVS**	**iECURE-OTC**
	in partnership with **Prevail***	in partnership with **Novartis**	in partnership with **IECURE**

Future Partnerships: Business development partnerships will leverage ARCUS core capability for Sophisticated Edits

*Prevail is a wholly owned subsidiary of Eli Lilly and Company

The ARCUS Advantages: A Deeper Dive

Jeff Smith, PhD, Co-Founder
Chief Research Officer

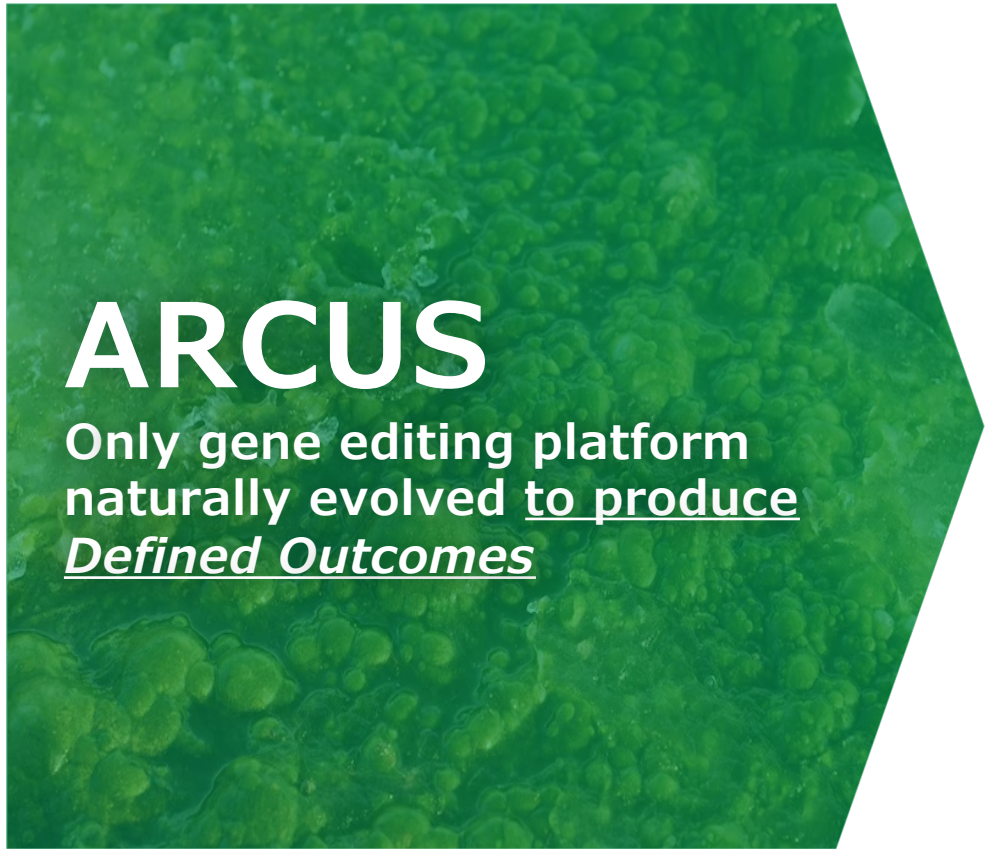
The Dream

Precision was born

The Dream

Simple, Efficient, Safe
*In Vivo g*ene editing tool to drive
Defined Outcomes in patients with genetic and hard to treat diseases

Bringing the Dream to Reality with Creation of ARCUS



- ARCUS is derived from the homing endonuclease I-CreI found in green algae
- Evolved in nature to safely edit a genome and add 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) versus Non-Homologous End Joining (NHEJ)
- DNA recognition and cutting are integrated into a single component for high specificity and efficiency

Defined Outcomes
Accomplished Through
ARCUS Advantages

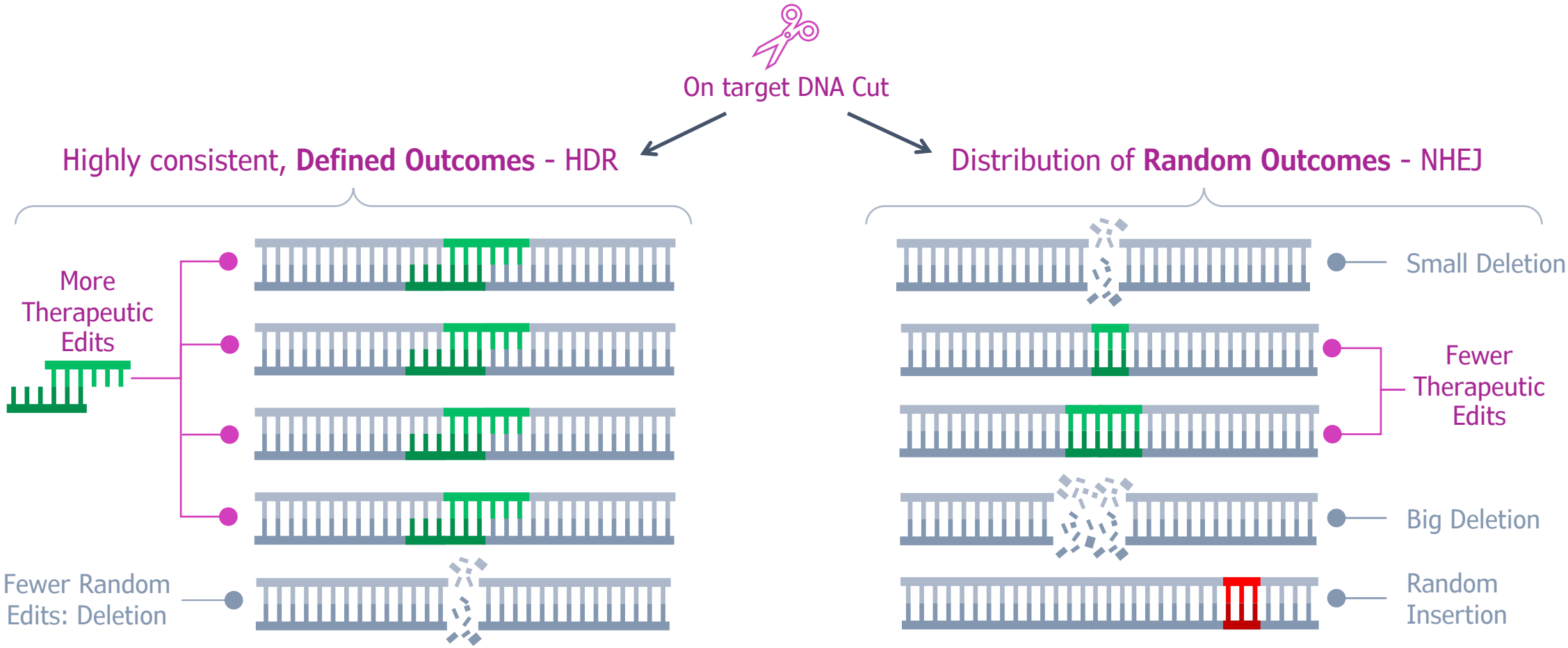
The Cut

The Size

The Simplicity

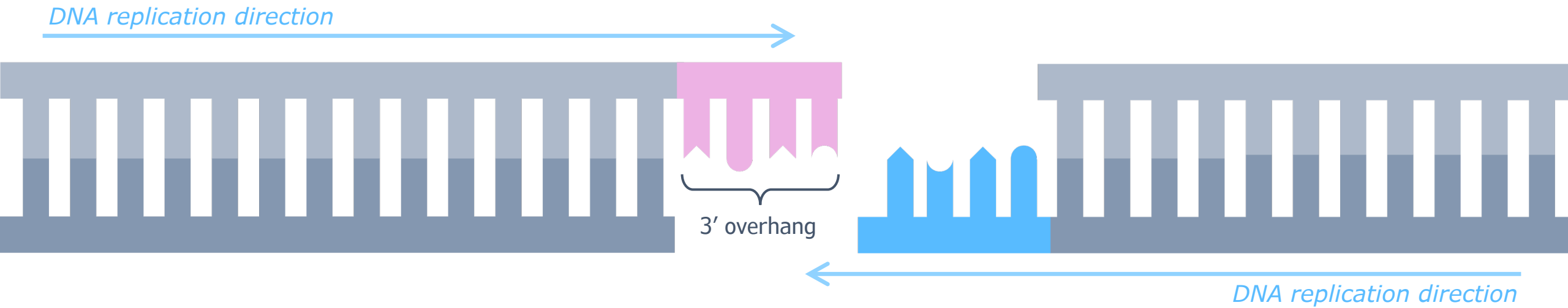
Defined Outcomes Are More Desirable than Random Outcomes:

More therapeutic edits and fewer unknown safety risks



It's All About The Cut

ARCUS's 3 prime, 4 base pair cut drives Defined Outcomes



This unique cut drives high efficiency repair by HDR OR "Perfect" Re-ligation leading to Defined Outcomes

Gene editing tools utilizing NHEJ produce more "random outcomes" carrying more risk and lower efficiency

The ARCUS Cut is Uniquely Designed to Drive Defined Outcomes

ARCUS cut leads to HDR or “Perfect” Re-ligation

Generates a 3′ overhang required for Defined Outcomes by HDR or Perfect Re-ligation

The ARCUS Cut

Cas9

Blunt cut induces NHEJ

TALEN/ZFN

Cas12a

Staggered cut in wrong 5′ direction for HDR, therefore NHEJ repair

Base Editors

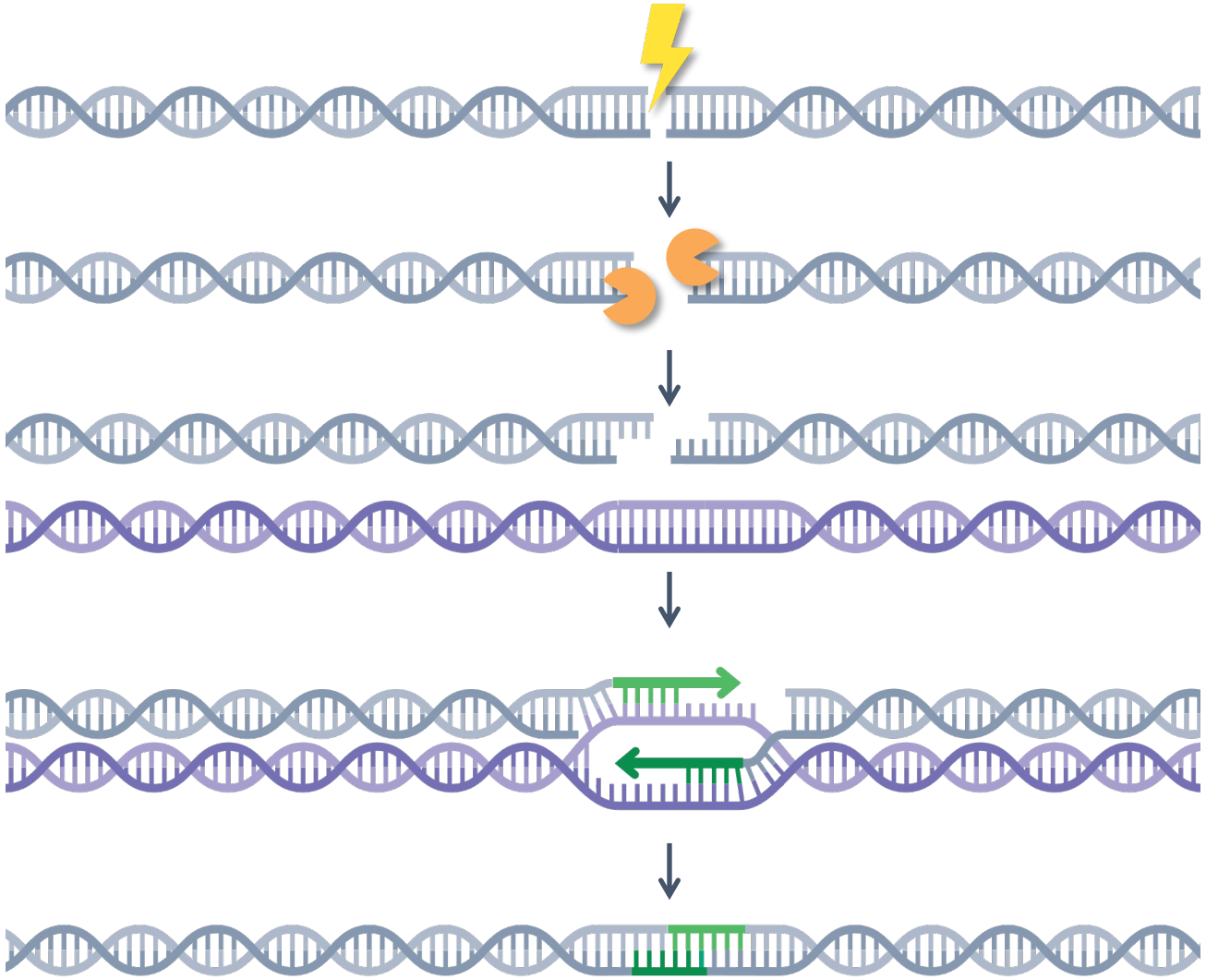
Prime Editors

Single, double, or unintended DNA breaks results in interrupted repair state*, HDR not attainable

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

ARCUS Cut Drives HDR and Starts Closer to the Defined Outcome

1. In nature DNA strands can break
2. Need Exonuclease to create an overhang
3. Broken DNA in HDR ready-state with 3’ overhang
4. The matching DNA on homology arms permit annealing
5. The damage is fixed



Competitors start here

Lower efficiency, higher chance for random events

ARCUS starts here

Designed to avoid added steps; promoting high efficiency, high likelihood of intended edit

Defined Outcome

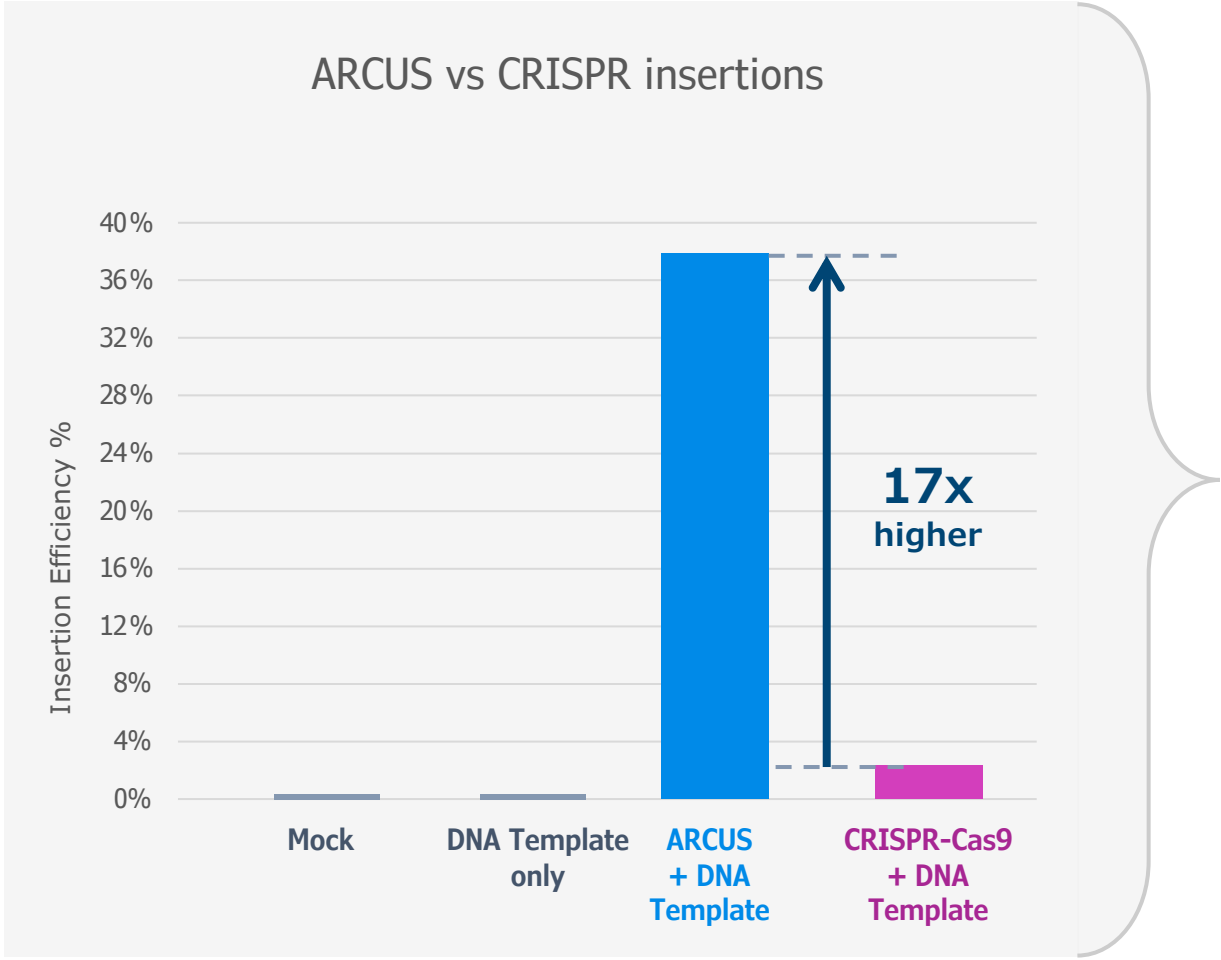
“The Proof” That It’s *All About The Cut*

Gene Insertion Experiments

- ARCUS inserted with greater efficiency than CRISPR/Cas9
- 3’ overhang cut is critical for HDR

ARCUS Inserted with 17x Higher Efficiency than CRISPR

A true head-to-head comparison



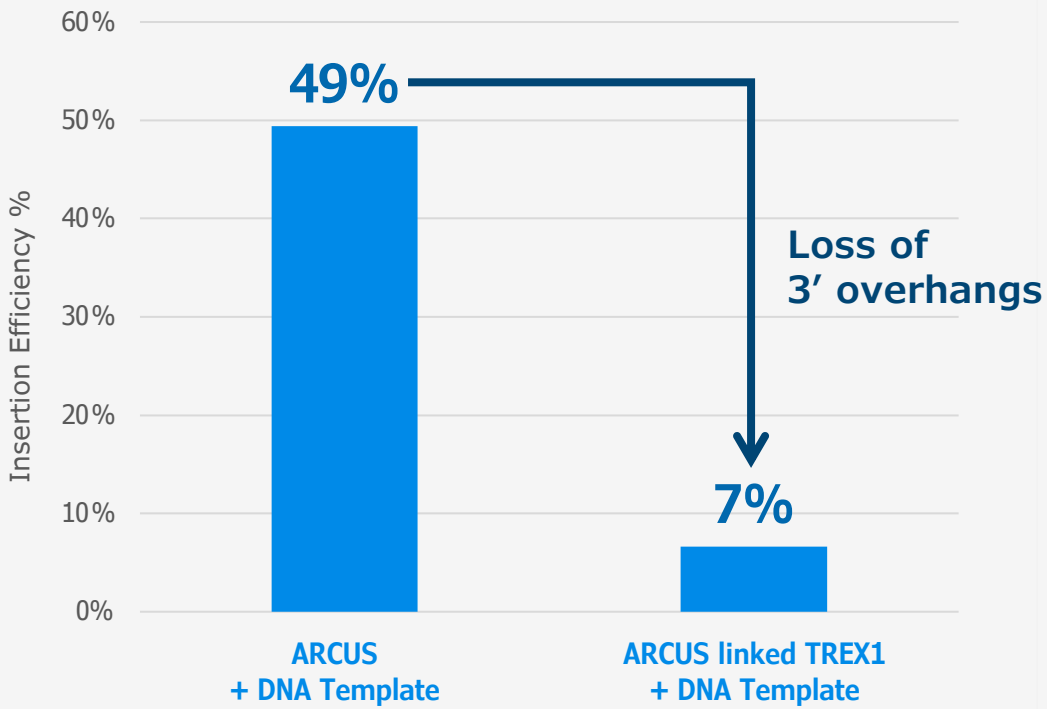
Head-to-head comparison at **same site, same dose,** with **same DNA template.**

ARCUS was More Efficient

Data on file, *in vitro* experiment conducted in primary cells

3’ Overhangs Promoted Insertion Through HDR

Chewing off the 3' overhangs impacts insertion efficiency



- TREX1 removes 3’ overhangs of ARCUS
- TREX1 generates CRISPR-like blunt cuts
- Blunt cut ablates insertion efficiency

The CUT Matters

Data on file, experiment conducted in HEK293 cells

The Cut Drives Defined Outcomes

- ARCUS generates a 3’ overhang cut
- 3’ overhang cut enables Homology-Directed Repair (HDR)
- 3’ overhang cut with complementary overhangs in ready-state for “Perfect” Re-ligation
- Higher HDR and “Perfect” Re-ligation result in higher rate of Defined Outcomes
- More Defined Outcomes drive higher therapeutic edits and fewer unknown safety risks

Defined Outcomes
Accomplished Through
ARCUS Advantages

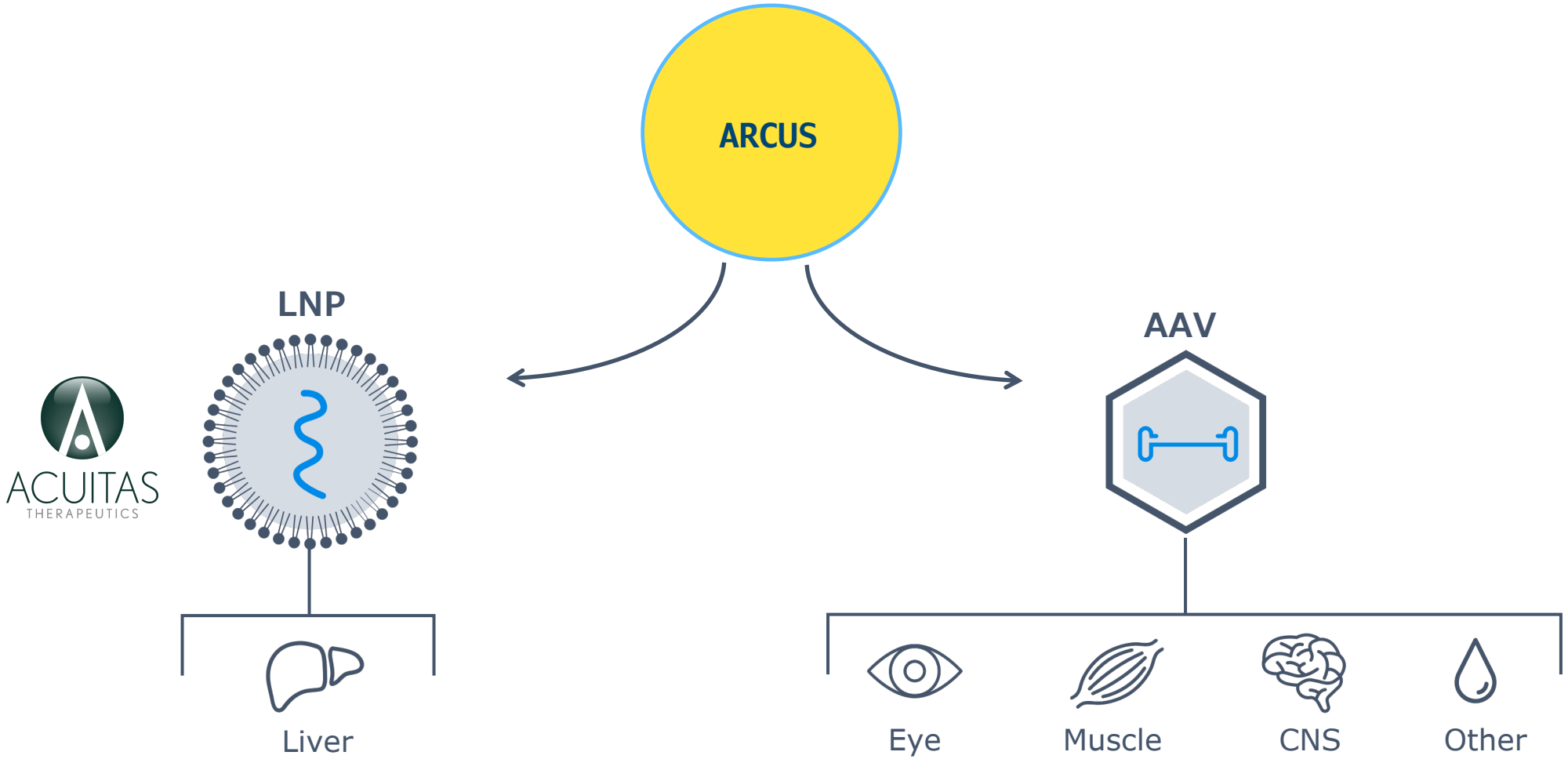
The Cut

The Size

The Simplicity

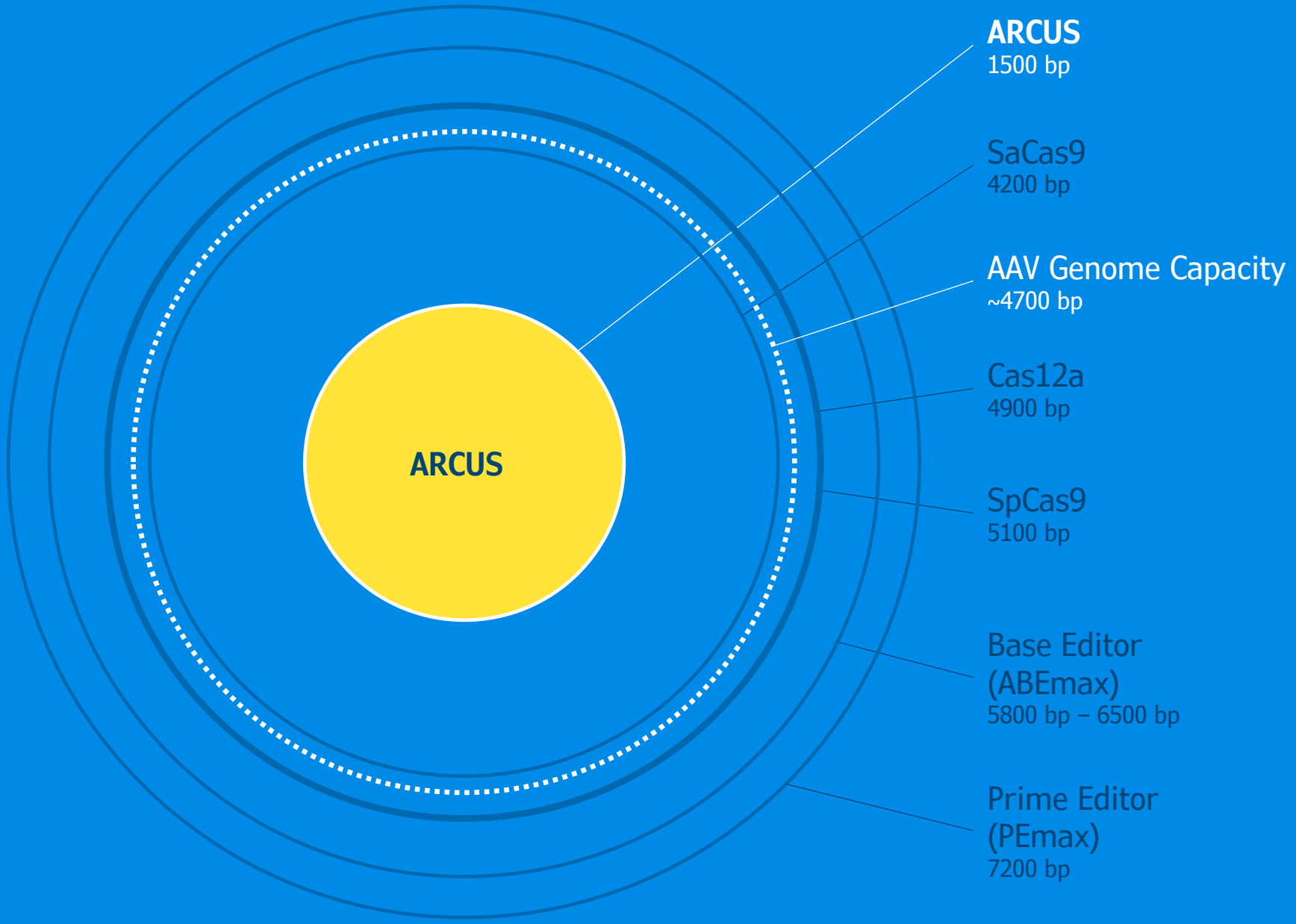
Size Matters for Where You Can Deliver

ARCUS can use different delivery vehicles to target diverse tissue types



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

ARCUS is the Smallest Gene Editing Tool in Development



Sizes include editor and expression machinery; ARCUS nuclease is 1062 bp

Size Matters for Going Beyond the Liver

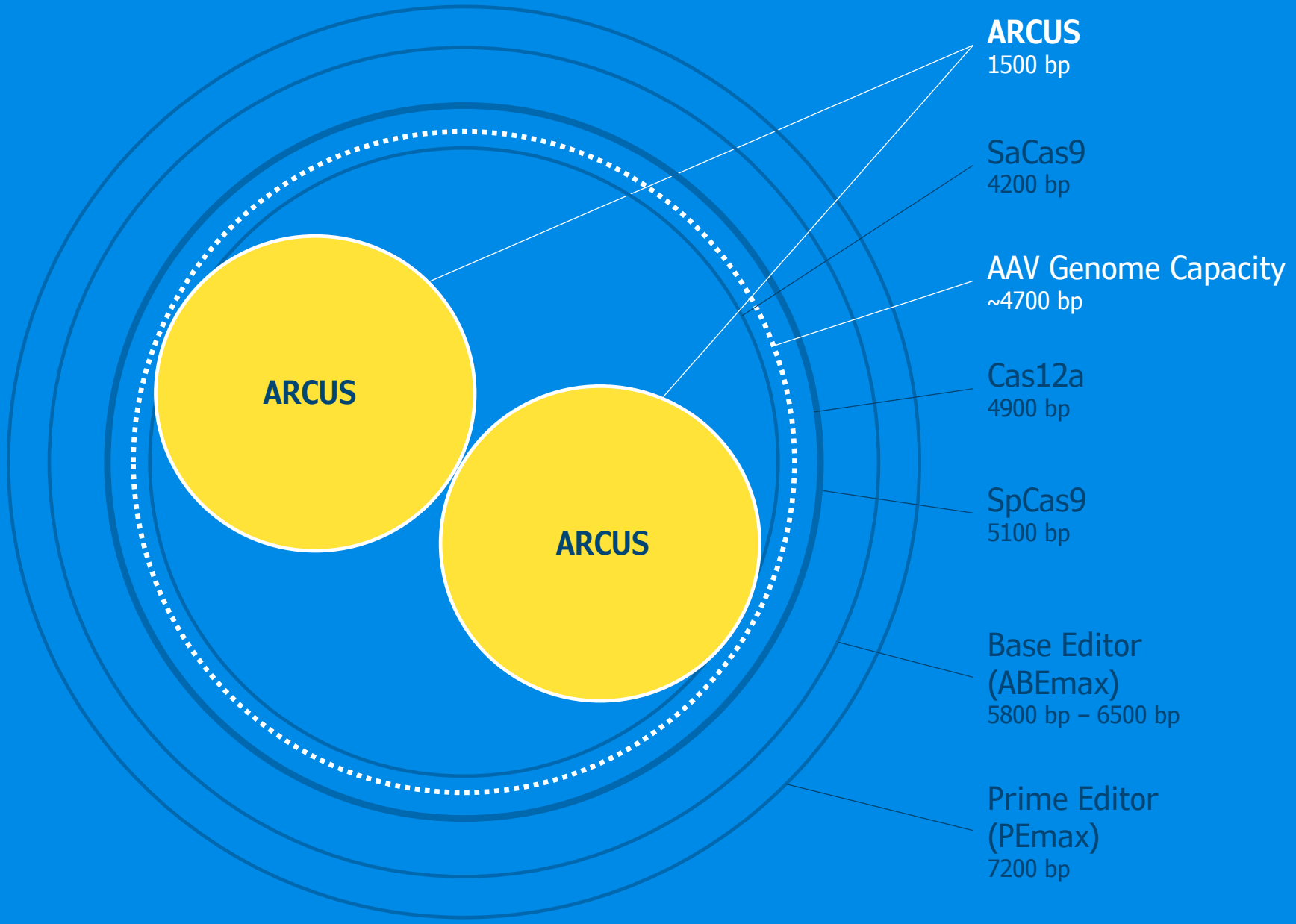
ARCUS has demonstrated editing in a breadth of diverse tissue types

Indication	Organ	Delivery	Animal model edited
Hepatitis B + undisclosed	Liver	LNP / AAV	NHP / Mouse
Duchenne Muscular Dystrophy	Muscle	AAV	NHP / Mouse
Undisclosed	CNS	TBD	NHP* / Mouse
Sickle Cell	Hematopoietic stem cells	TBD	In- Progress
Retinitis Pigmentosa	Eye	AAV	Pig / Mouse

* To Our Knowledge, Precision is First to Accomplish CNS Editing in a Non-Human Primate (NHP)

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

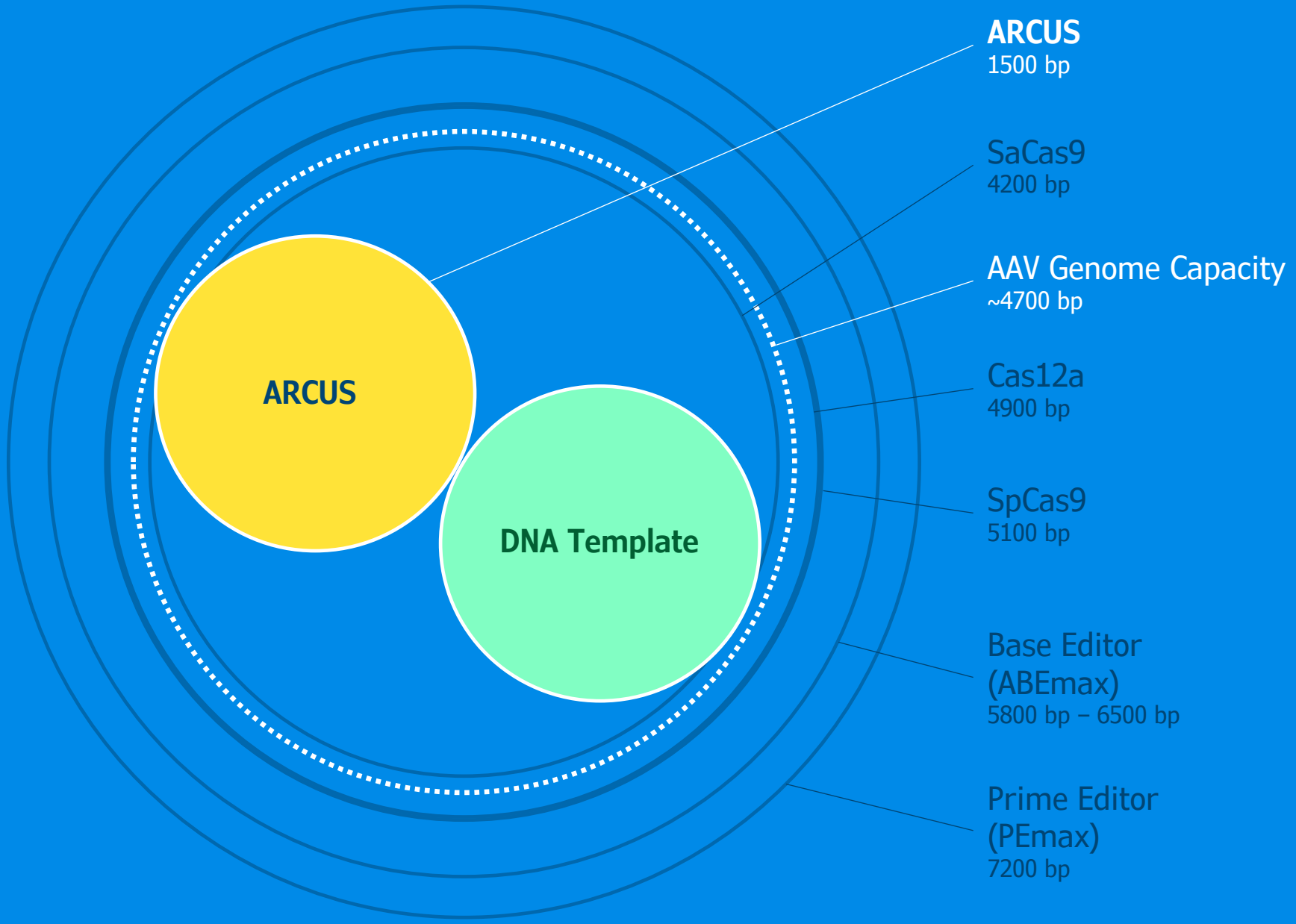
Small ARCUS Size Allows Two Nucleases in One AAV for **Gene Excision**



Sizes include editor and expression machinery; ARCUS nuclease is 1062 bp

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

Allowing Delivery with a DNA Template in a Single AAV for **Gene Insertion**



Sizes include editor and expression machinery; ARCUS nuclease is 1062 bp

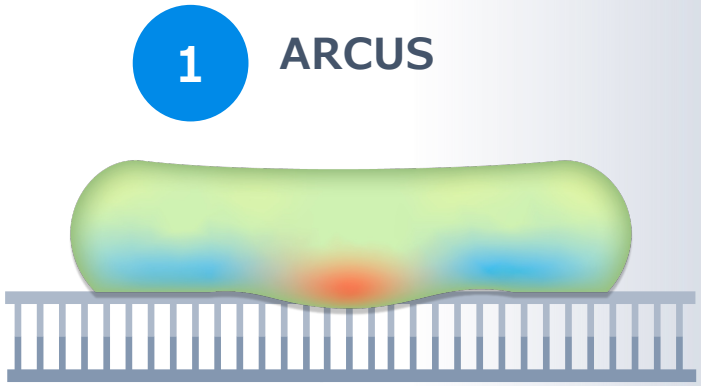
Defined Outcomes
Accomplished Through
ARCUS Advantages

The Cut

The Size

The Simplicity

Simplicity: ARCUS is the Only Single Component Editor



Single protein with a DNA recognition motif and catalytic activity all in one; **no guide RNA required**

Editing outcome not dependent on simultaneous delivery of multiple components leading to **higher efficiency**

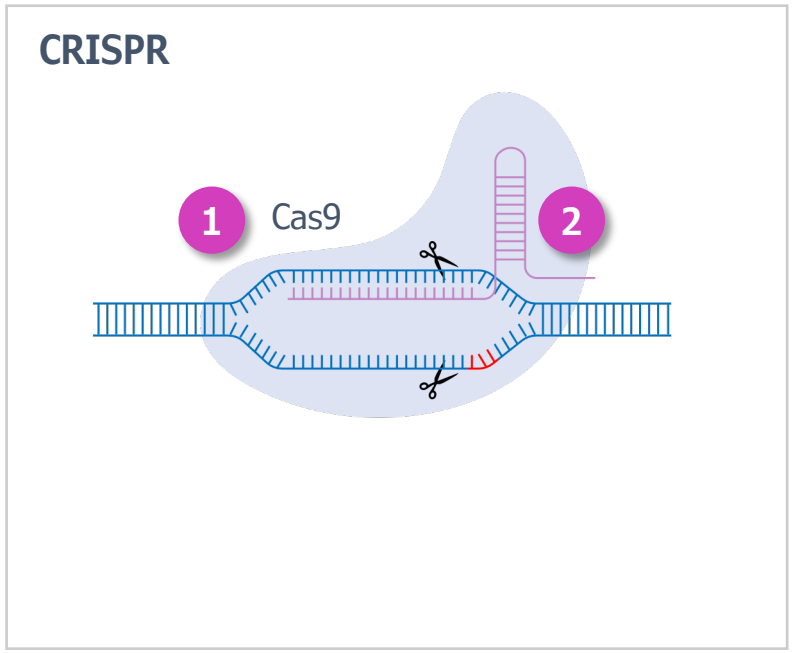
Single component **requires less** AAV and potentially less LNP

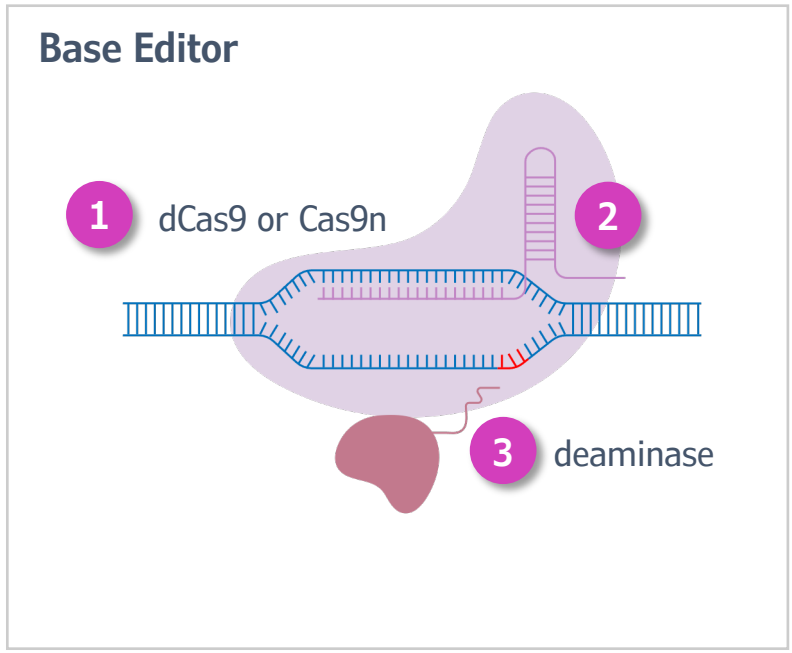
〉 **Easy to deliver**

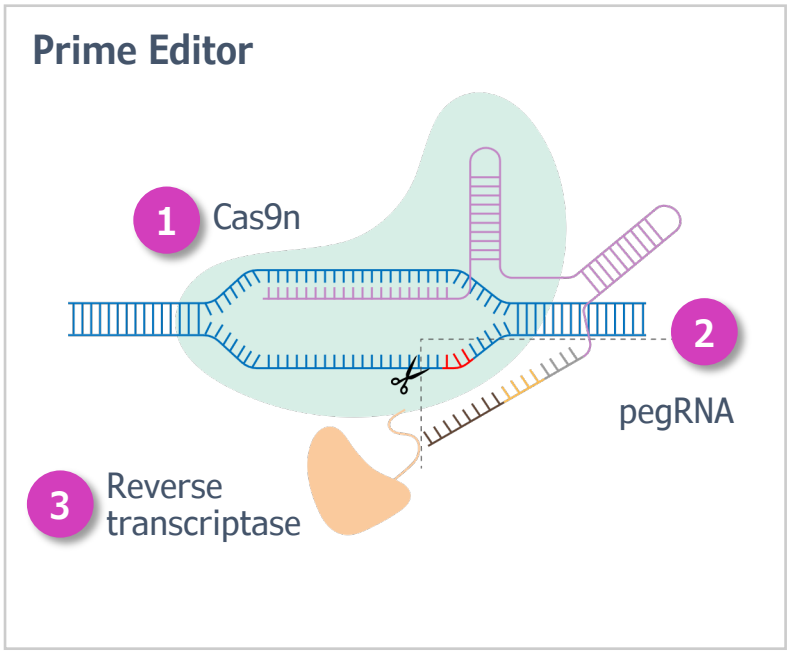
〉 **High efficiency**

〉 **Low dose improves safety**

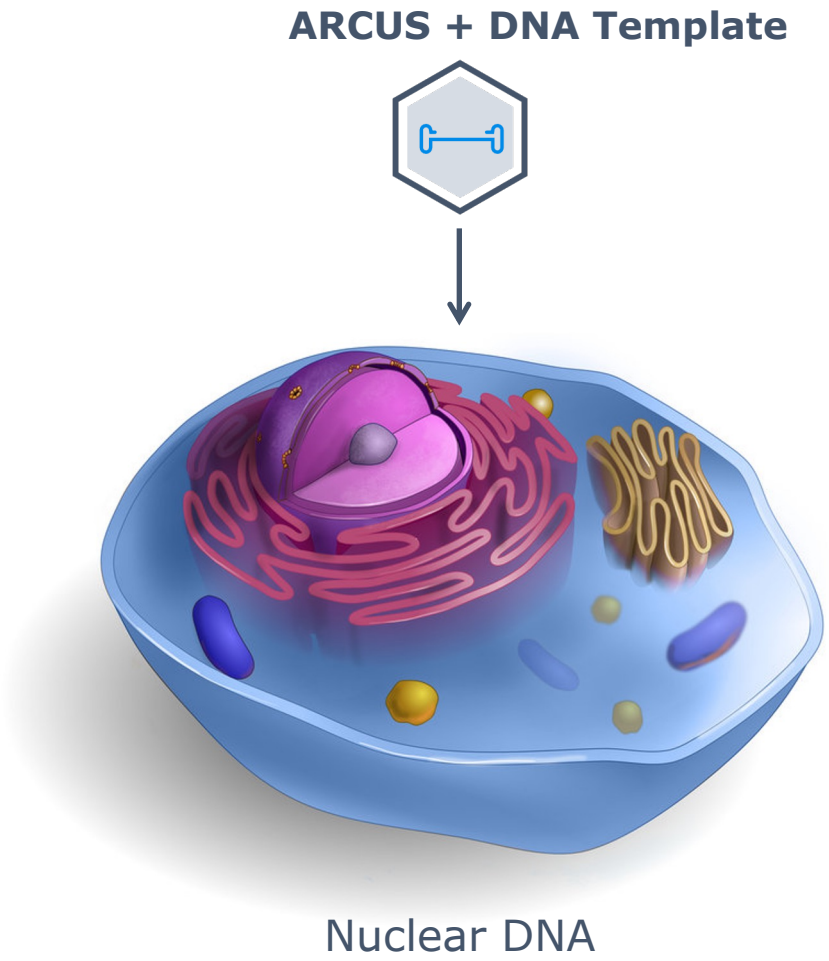
Simplicity: Simultaneous Delivery of Multiple Components in Separate Delivery Vehicles Results in Lower Efficiency

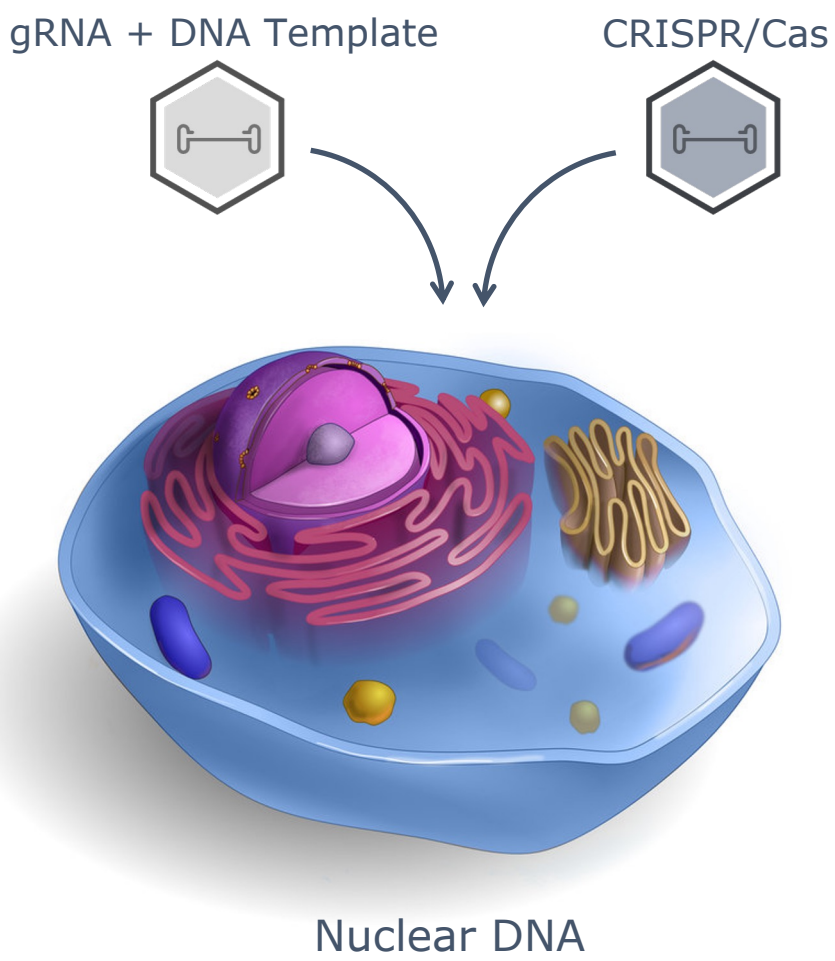




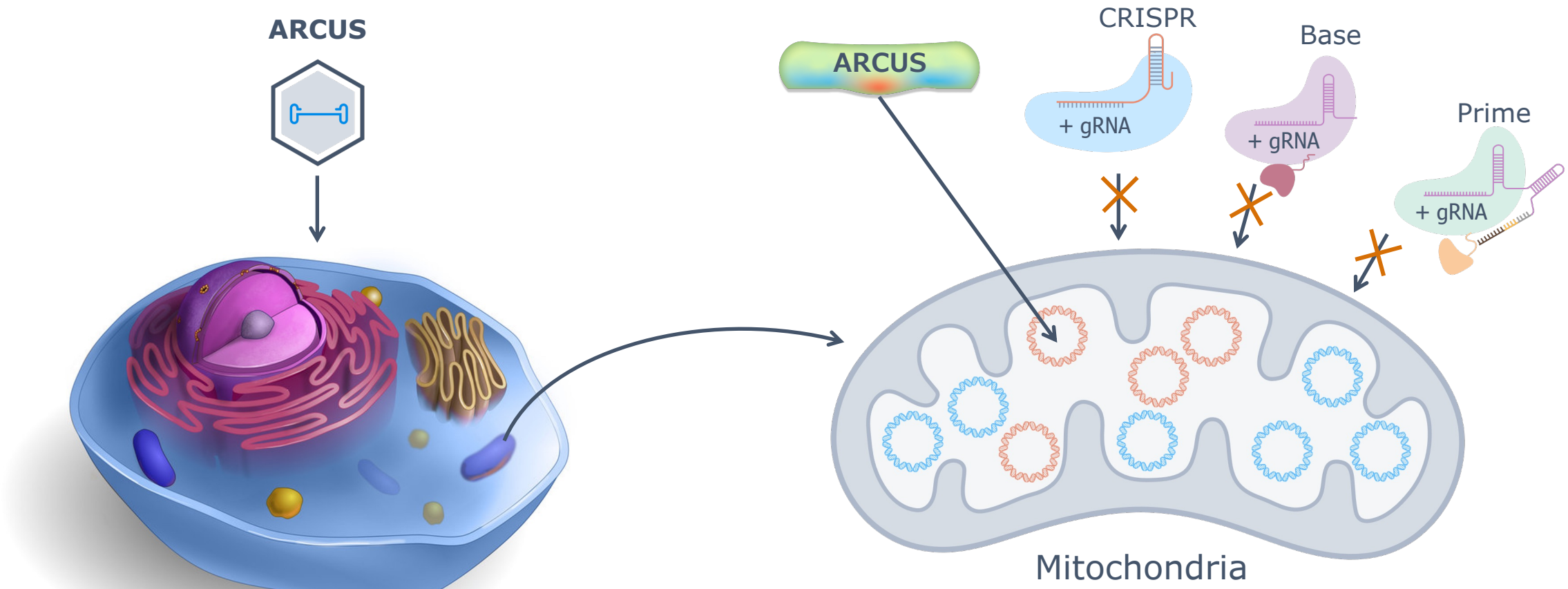


Simplicity: Fewer Components to Deliver Results In Higher Efficiency and Defined Outcomes at a Lower AAV Dose





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



ARCUS Versus Other Gene Editors in Development

		ARCUS	CRISPR	Base Editor	Prime Editor
Cut	Cut Result	3 prime overhang	Blunt end cut	Variable[1]	Variable[1]
	Large insertions	HDR	NHEJ / DNA capture	Not Applicable	Not Applicable
	Large excisions	Perfect re-ligation	NHEJ	Not Applicable	Not Applicable
Size	Kilobases (kb)	~1kb	3.2-4.1kb	4.8-5.4kb	6.4kb
	AAV delivery	Fits 2 nucleases or nuclease + repair	Limited / No	No	No
	LNP delivery	Yes	Yes	Yes	Yes
Simplicity	Complexity to deliver	1 component / Simple	2 components / Complex	3 components / Very Complex	3 components / Very Complex
	Target Site Fidelity	High	Medium	Medium	Medium
Therapeutic Outcomes		DEFINED	Random	Random	Defined But limited applicability

[1] Depends on version of editor and amount of editing; note kilobase sizing does not include expression machinery

The Cut

- 3’ Overhang Stimulates HDR
- Supports “Perfect” Re-ligation
- Designed for High Efficiency, Highly Therapeutic Gene Edit

The Size

- Smallest Gene Editor
- Enables ARCUS + Additional Payload In One Delivery
- Delivery to More Tissues Across Body

The Simplicity

- Single Enzyme / Component
- Higher Efficiency Therapeutic Edits
- Lower AAV & LNP Dose Improves Safety

Highest Probability of Defined Outcomes

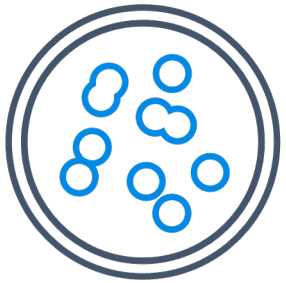
The Cut (Insertion)

Cassie Gorsuch, Ph.D.
Vice President, Gene Therapy Discovery

Gene Insertion Efficiency and Outcomes are Context-Dependent

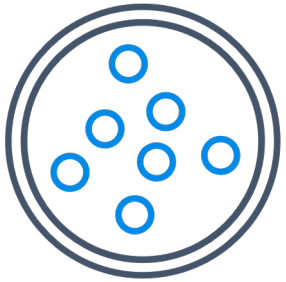
1

Dividing cells in culture



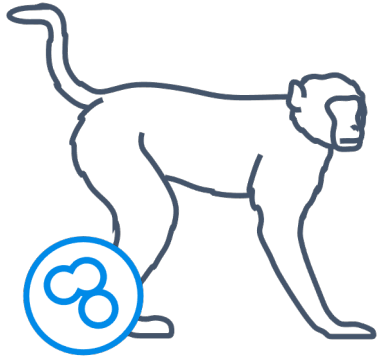
2

Non-dividing, primary cells in culture



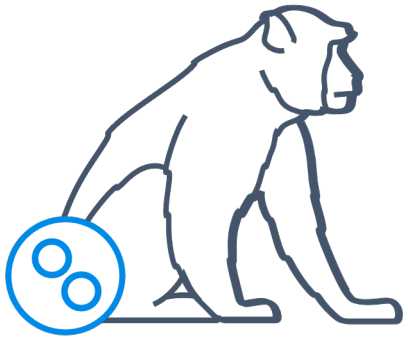
3

Dividing cells in vivo (infant/child)



4

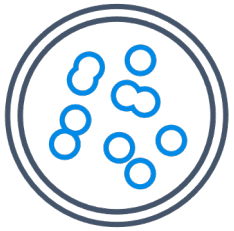
Non-dividing cells in vivo (adults)



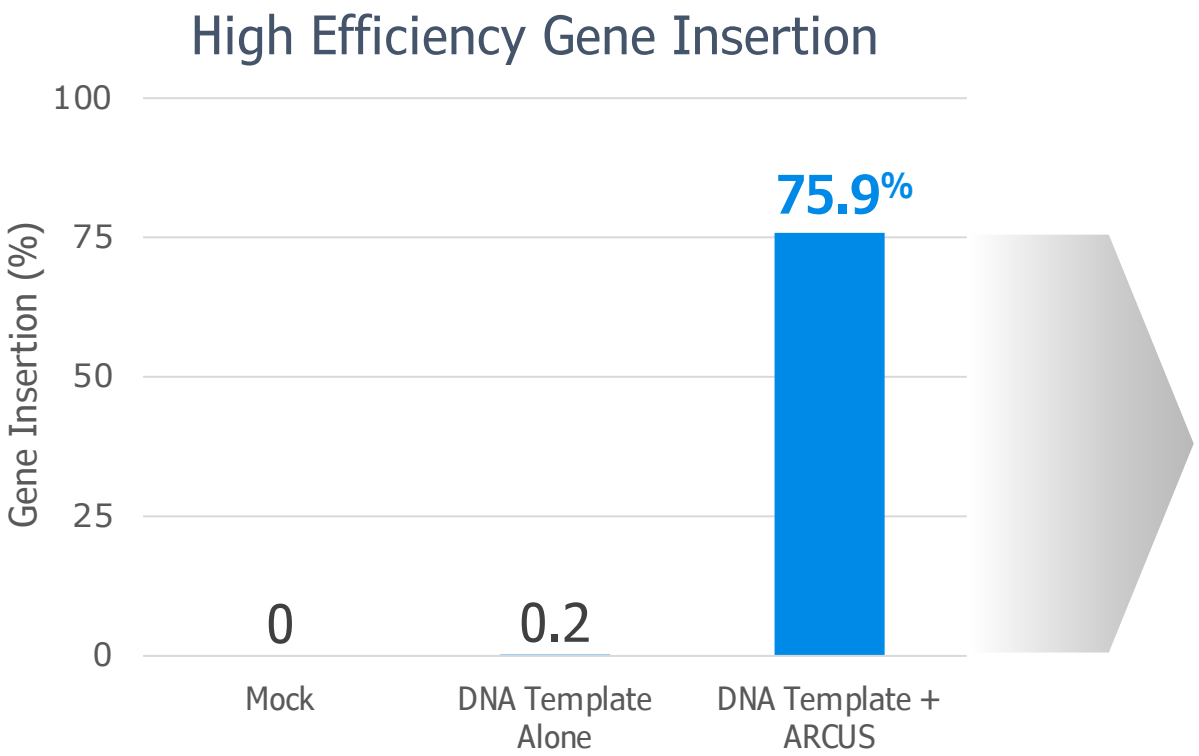
Increasing Level of Evidence & Difficulty

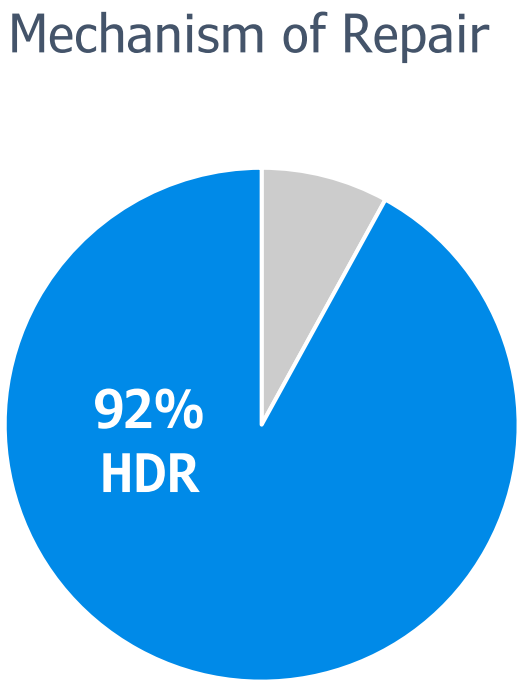
ARCUS Inserted with High Efficiency in Dividing Cells in Culture

1



Dividing cells in culture

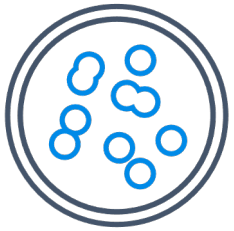




Data on file

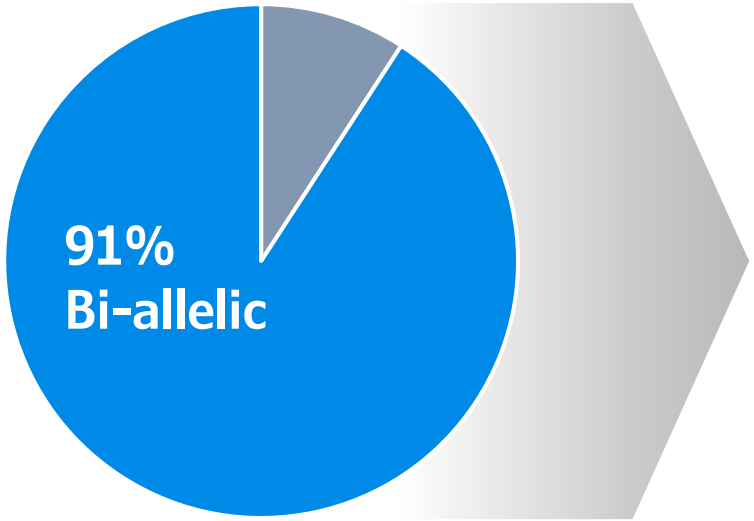
ARCUS Inserts Efficiently in Both Copies of Target Gene Resulting in High Functional Impact - Dividing Cells in Culture

1

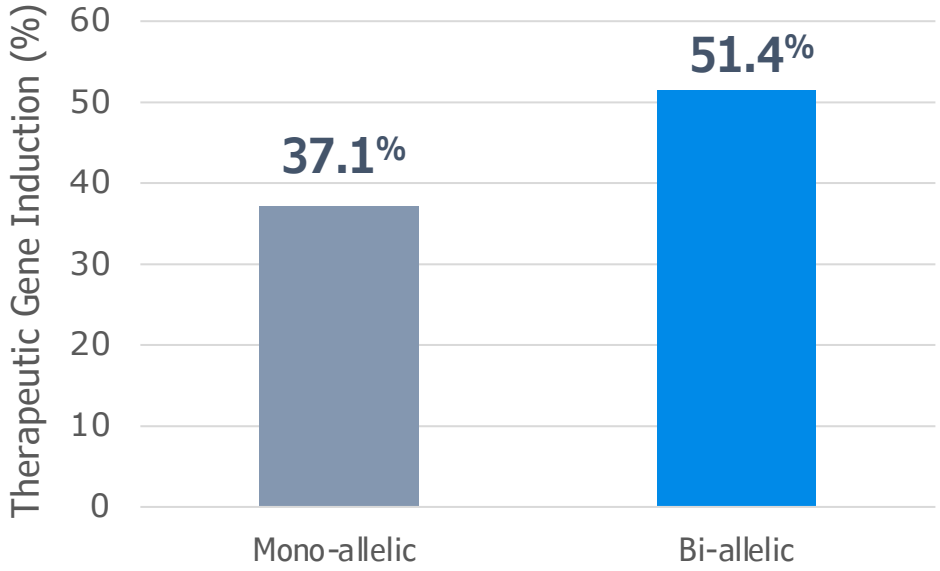


Dividing cells in culture

ARCUS inserts in both alleles*



Bi-allelic editing results in high functional impact



ARCUS Bi-Allelic Insertion Results in Robust Therapeutic Effect

Data on file; *Initial results based on PCR genotyping of single clones, sequencing confirmation in progress; based on cells with insertions.

ARCUS Can Drive Efficient HDR in Both Dividing and Non-Dividing Cells…
…Previously Thought to be Nearly Impossible for Gene Editing

"By the late 1980's, dogma in the field of DNA repair held that end joining, rather than HDR, is the dominant DSB pathway in mitotically dividing mammalian cells in culture."

–Fyodor D. Urnov,
The CRISPR Journal, V1. N1. 2018

"However, traditional HDR has very low efficiency in most human cell types, particularly in non-dividing cells, and competing non-homologous end joining (NHEJ) leads predominantly to insertion-deletion (indel) byproducts"

–Broad Institute Patent Filing
USPTO 11643652

"Inability to correct genes in non-dividing cells since currently, HDR DNA repair machinery is only expressed in dividing cells."

–Prime Medicine 10K, 2023

ARCUS Inserts Efficiently in Non-Dividing Cells - in Culture

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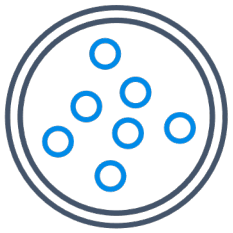
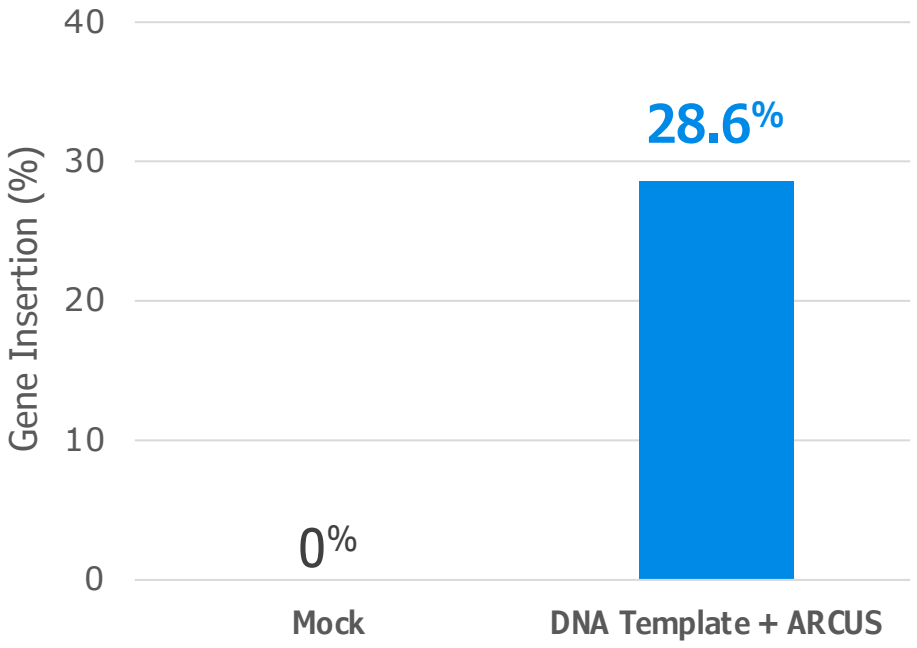
2

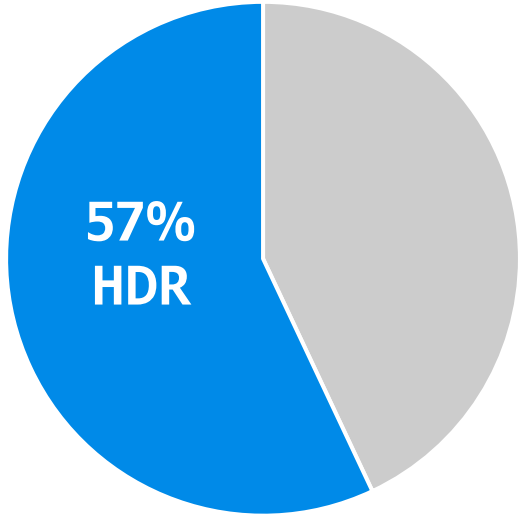


Nondividing primary cells in culture

High Efficiency Gene Insertion



Mechanism of Repair



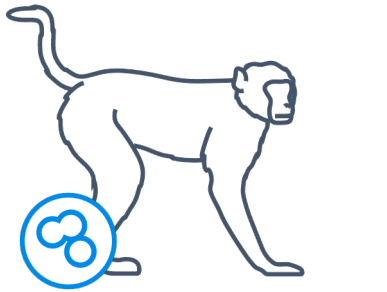
ARCUS Ability to Insert by HDR in Non-Dividing Cells is Attributable to the Unique 3' Overhang Cut

Data on file, experiment conducted in primary human hepatocytes

ARCUS Inserts with High Efficiency in Infant Nonhuman Primates; Sustained Effect Demonstrated at 12 months

3

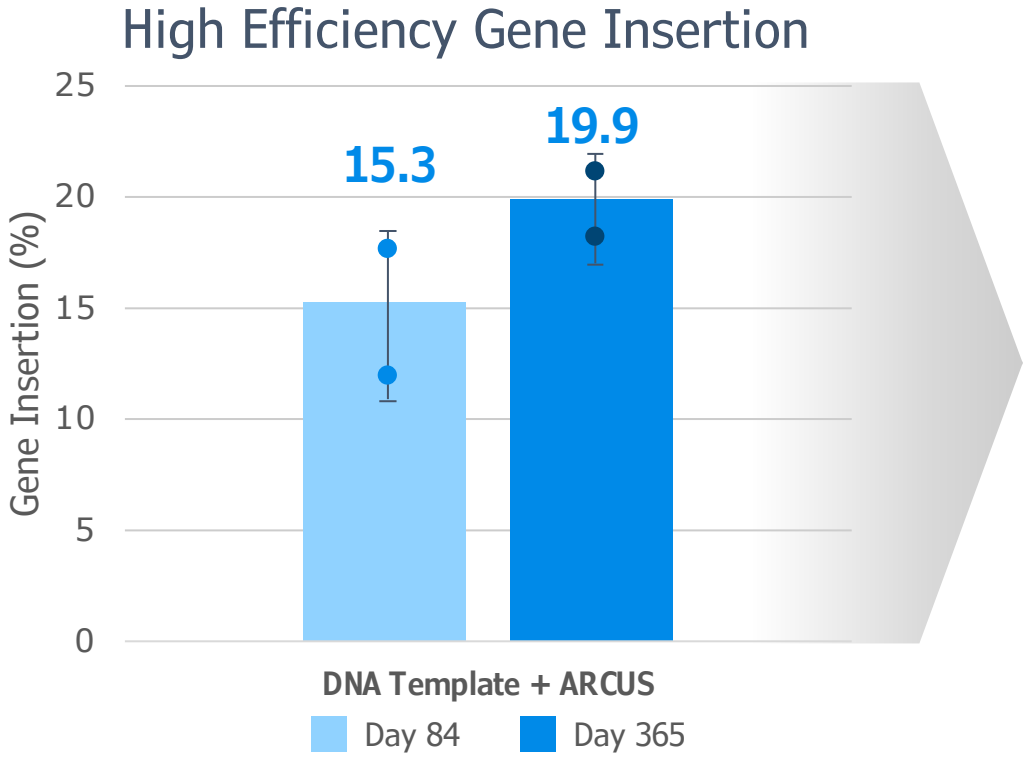
Dividing cells in vivo

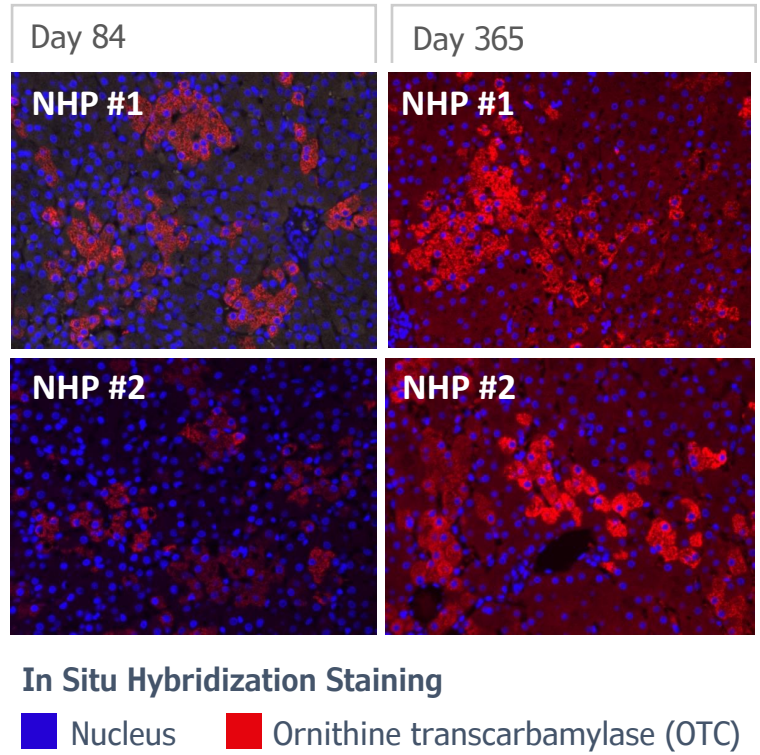


ARCUS AAV
1e13 vg/kg

+

DNA Template AAV
3e13 vg/kg





ARCUS Inserts with High Efficiency in Adult Nonhuman Primates Previously Thought to be Unachievable

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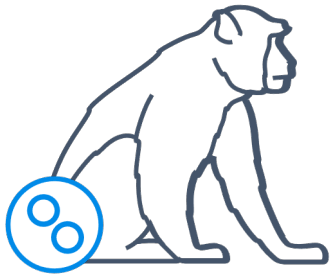
4

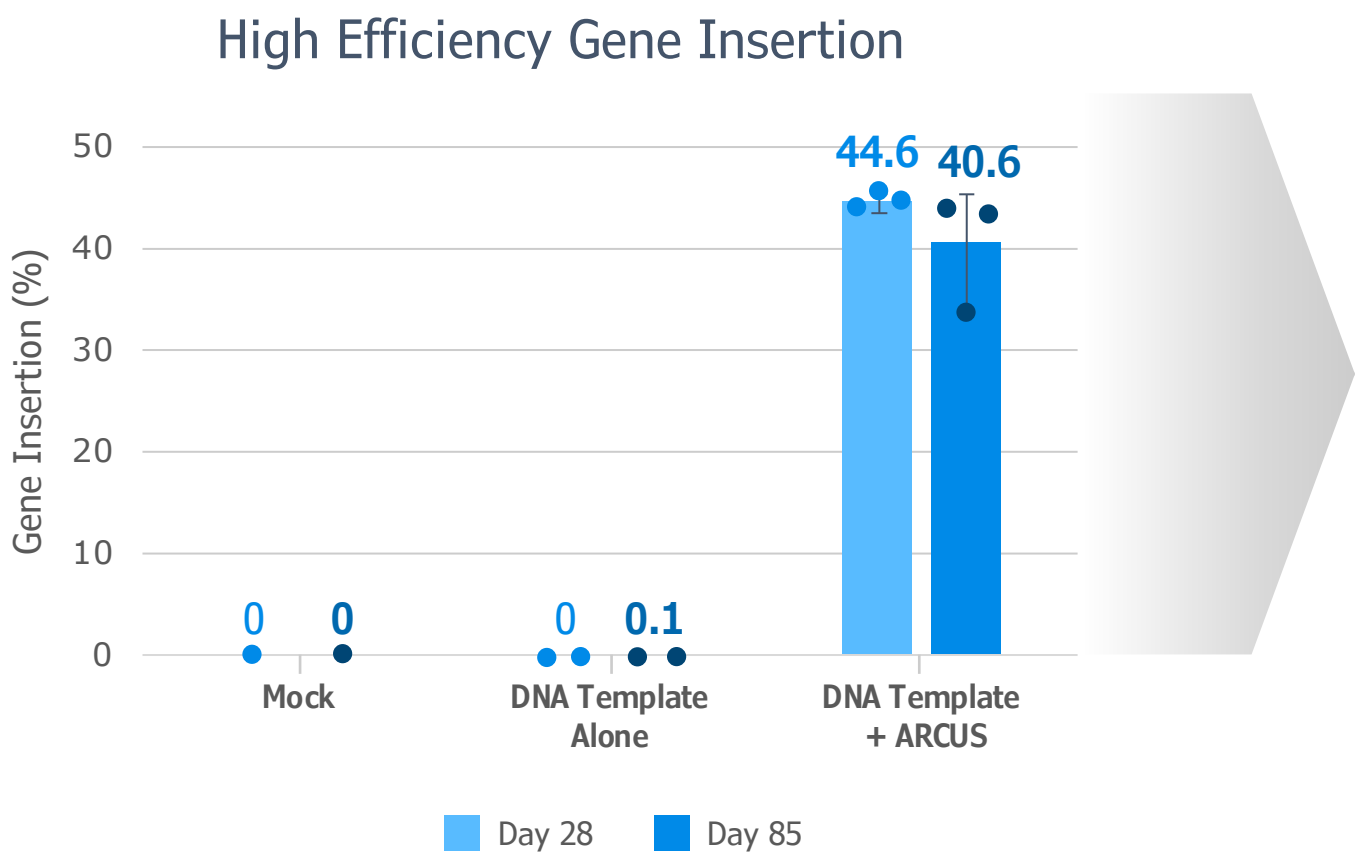
Nondividing cells in vivo



ARCUS LNP
1.75 mg/kg

+

DNA Template AAV
3e13 vg/kg



>3x
insertion efficiency of CRISPR-based approach*

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

ARCUS is Ideal for Therapeutic Gene Insertion

- ✓ High efficiency insertion rates
- ✓ High HDR observed
- ✓ Biallelic editing demonstrated

Designed to Increase Therapeutic Effect

★ **Breadth in Level of Evidence Demonstrating Insertion in Dividing and Non-Dividing Cells In Vitro and In vivo**

Gene Insertion Pipeline

PROGRAM	INDICATION	TISSUE	TARGET	COMPLEX EDIT TYPE	PARTNER
PBGENE-NVS	Sickle cell disease/ Beta thalassemia	HSCs	—	Insertion	NOVARTIS
PBGENE-LLY2	Undisclosed	Liver	—	Insertion	Prevail THERAPEUTICS A Wholly Owned Subsidiary of Eli Lilly and Company
iECURE-OTC	Ornithine transcarbamylase deficiency	Liver	OTC	Insertion	ECURE

Reasons to Believe in Precision's Gene Insertion Approaches

High efficiency gene insertion **in dividing and non-dividing cells** in vitro and in non-human primates (NHP)

In NHP study 1-year follow-up biopsies demonstrate durability with gene insertion efficiency of 20%, well **above the expected threshold for clinical benefit**[1] in OTC

Highest reported gene insertion efficiency in NHPs, >3x insertion efficiency of CRISPR-based approach

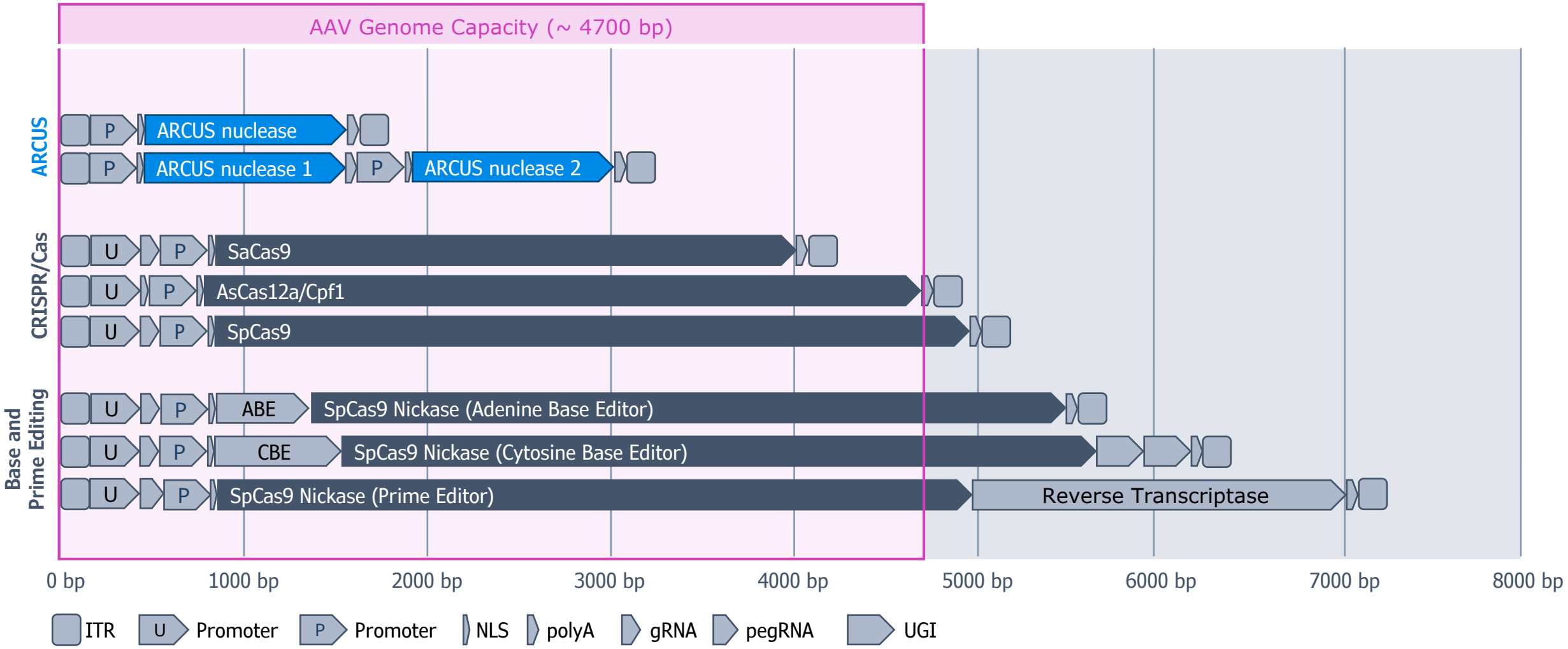
Opportunity for **one-time, potentially curative treatments** for diseases via **permanent gene insertions** vs. conventional gene therapy with waning durability

Size (Excision)

Cassie Gorsuch, PhD
Vice President, Gene Therapy Discovery

Size Matters

Only ARCUS is small enough to package two different nucleases in a single AAV



ARCUS Nucleases Excise Mutations and Restore Function in DMD

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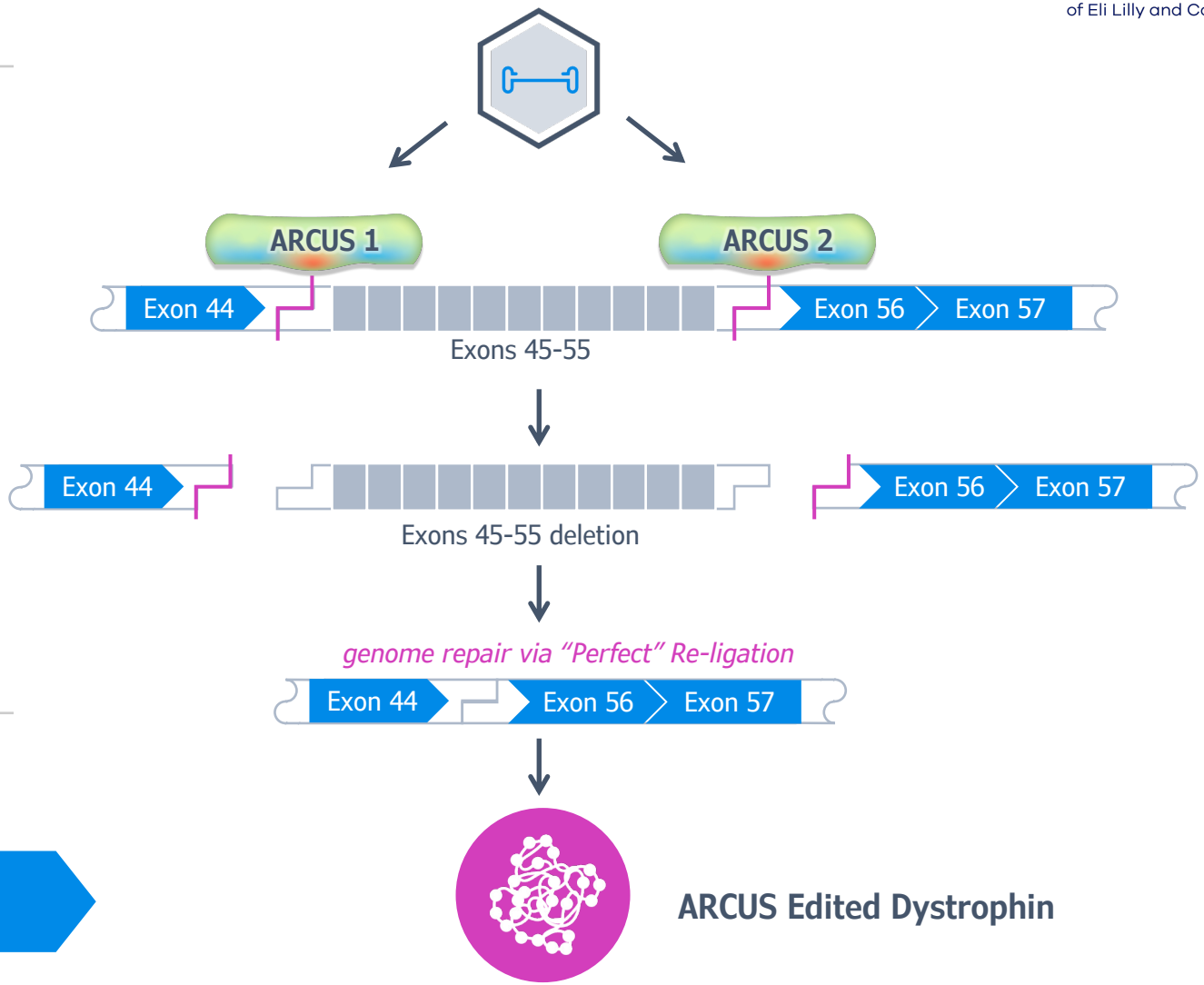
Two complementary ARCUS nucleases delivered in a single AAV are used to excise a mutation **"hot spot"** in Exons 45-55 responsible for ~50% of DMD cases



GOAL: Restore dystrophin expression

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

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Normal Dystrophin

ELEVIDYS (Sarepta)
Recently approved product

ARCUS Edited Dystrophin

ABD: actin binding domain, R: rod domain, CR: cysteine-rich domain, CT: carboxyl-terminus domain

“The Proof” That Size Matters in DMD

- ARCUS can be delivered to muscle tissues
- Two ARCUS nucleases fit into a single AAV
- ARCUS compatible 3’ overhangs enable “Perfect” Re-ligation

In Vivo Functional POC Study Design

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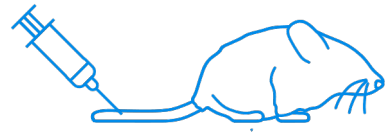

Objective:

Assess muscle function in a humanized, murine model of DMD

Test Article:

A single AAV with 2 early generation ARCUS nucleases, expression driven by a muscle specific promoter

Readouts:

- Excision of Exons 45-55
- Dystrophin restoration
- Force frequency
- BaseScope for editing in Pax7^{+} cells

Due to the Cut, ARCUS Excision Results in “Perfect” Re-ligation

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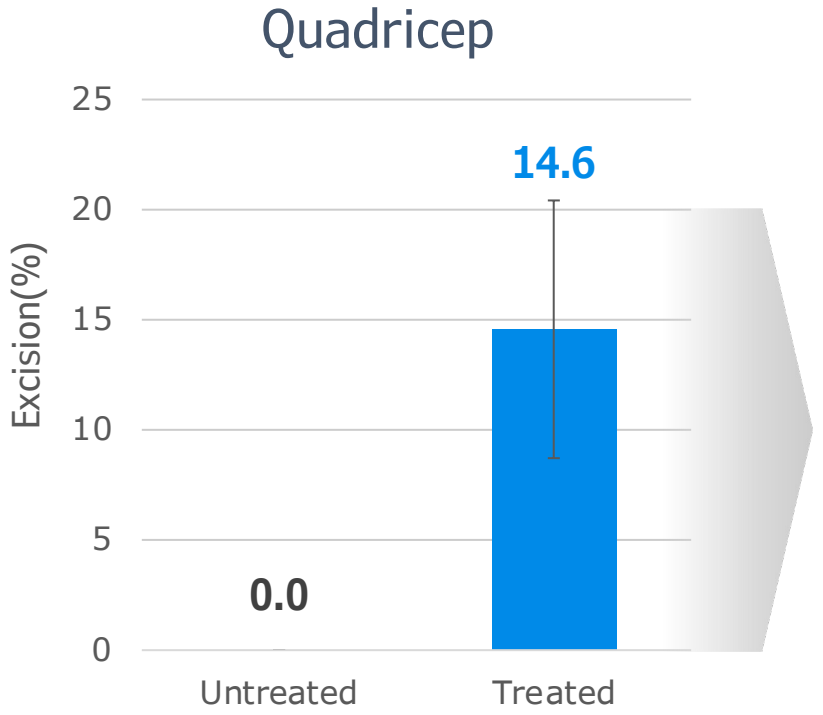
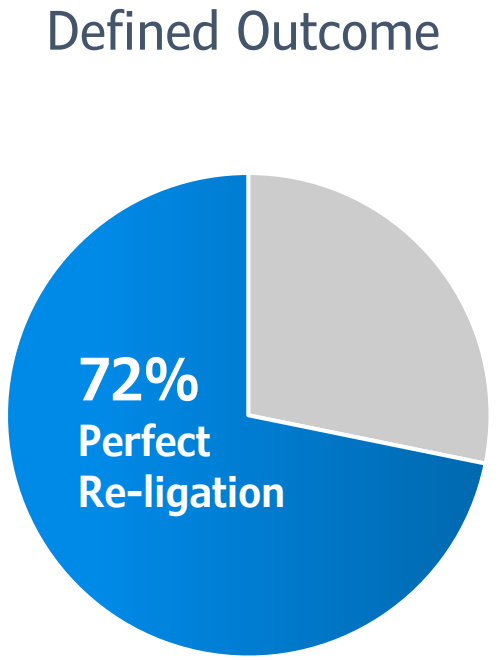
Genome repair via direct re-ligation





Edited Dystrophin Protein Variant Expressed in Target Tissues

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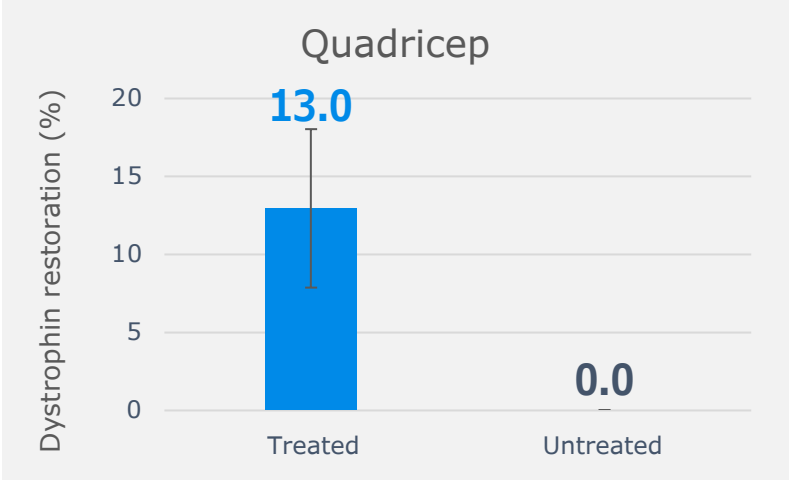
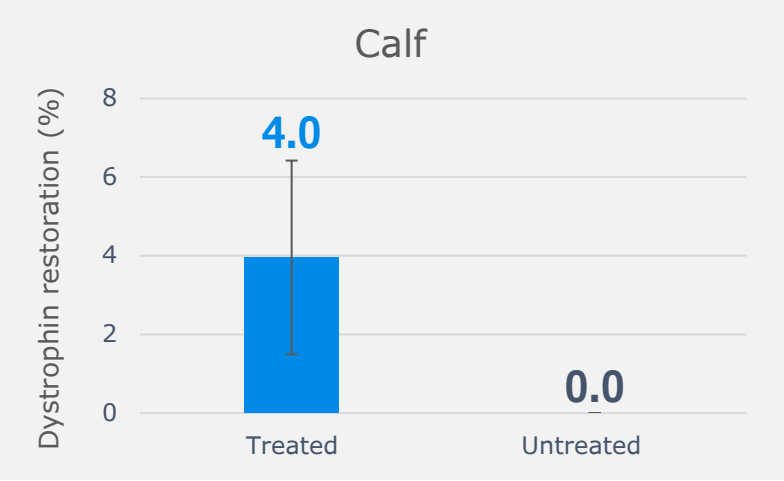
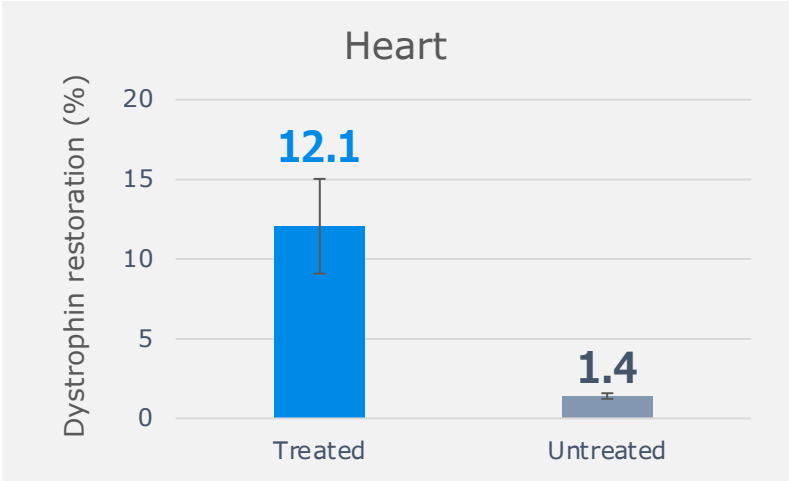
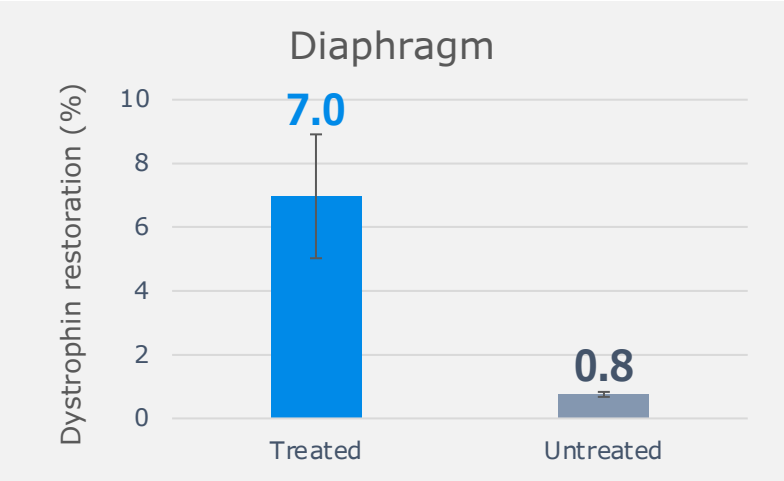
Truncated dystrophin protein produced from splice edited mRNA









Maximum Force Output in ARCUS-Treated Mice was Significantly Improved

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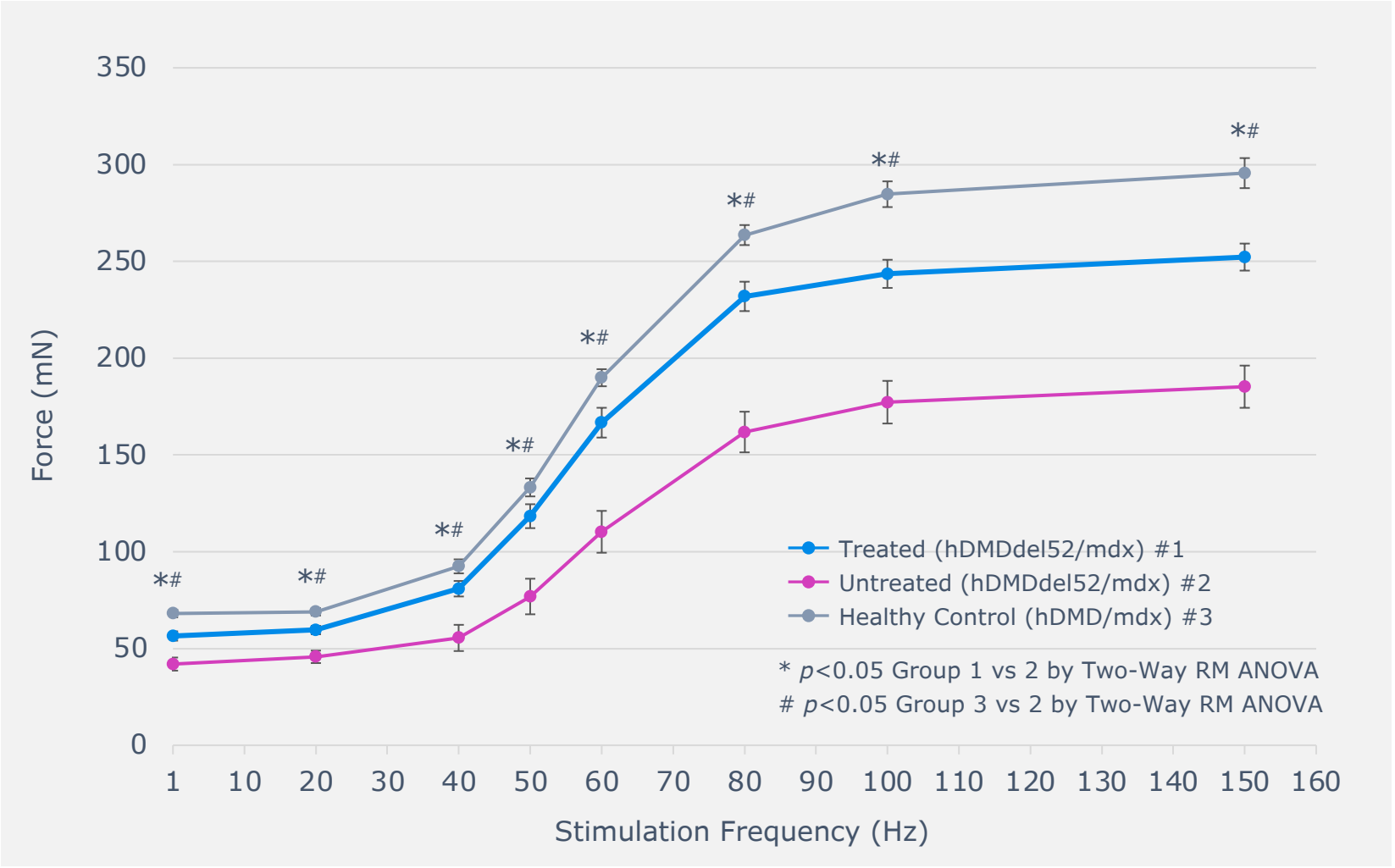

ARCUS-treated mice achieved

86% Maximum Force Output Levels

compared to non-diseased, control mice in the calf

ARCUS Ability to Edit Muscle Satellite Stem Cells Suggests Maintained Muscle Function Over Time

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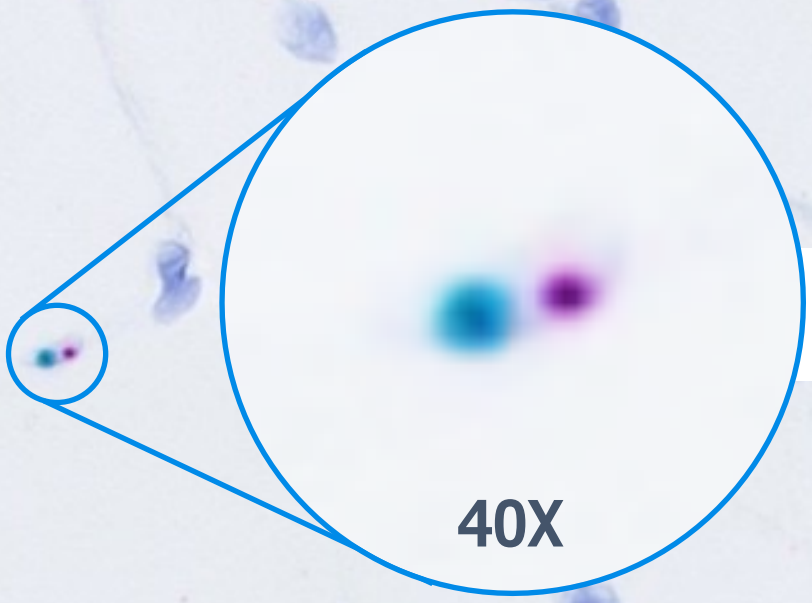
We observed evidence of the edited dystrophin mRNA transcript in PAX7+ cells, **a marker for muscle satellite stem cells**



Pax7+
Edited DMD 44-56 mRNA

Reasons to Believe in Precision-Prevail Approach for DMD

Small size of ARCUS enables delivery of **two nucleases in a single AAV** to excise hot-spot region of dystrophin and the **unique cut** yields complementary 3’ overhangs and for “**Perfect” Re-ligation**

Edited Dystrophin protein variant **expressed across various muscle tissues;** resulting in **86% force restoration** in calf muscle

ARCUS-edited dystrophin protein **preserves more functional domains** than micro dystrophin approaches

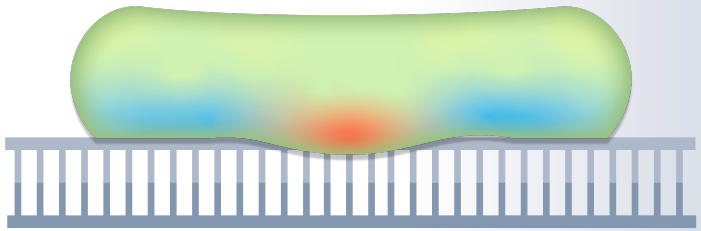
Evidence of **satellite cell editing** suggests potential for durable outcomes compared to standard gene therapy approaches

Simplicity

Cassie Gorsuch, PhD
Vice President, Gene Therapy Discovery

Simplicity: ARCUS is the Only Single Component Editor

1 ARCUS



Single protein with a DNA recognition motif and catalytic activity all in one; **no guide RNA required**

Editing outcome not dependent on simultaneous delivery of multiple components leading to **higher efficiency**

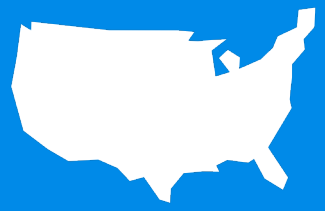
Single component **requires less** AAV and potentially less LNP

Hepatitis B Virus (HBV)
Precision’s Program: PBGENE-HBV

HBV Currently Lacks a Curative Treatment

Hepatitis B is a leading cause of morbidity in the US and death globally, with **no current curative options**

> 1,000,000
cHBV infections in the US



> 300 million
cHBV infections globally

An estimated
15% to **40%** of patients

with HBV infections may develop complications, such as cirrhosis, liver failure, or liver cancer, which account for the majority of HBV-related deaths.

Current HBV treatments require life-long chronic treatment that may result in viral suppression by reducing circulating HBV DNA, but **these therapies do not eradicate HBV cccDNA and therefore rarely lead to functional cure**.

The Quest for a Functional Cure Through HBV Elimination Strategy

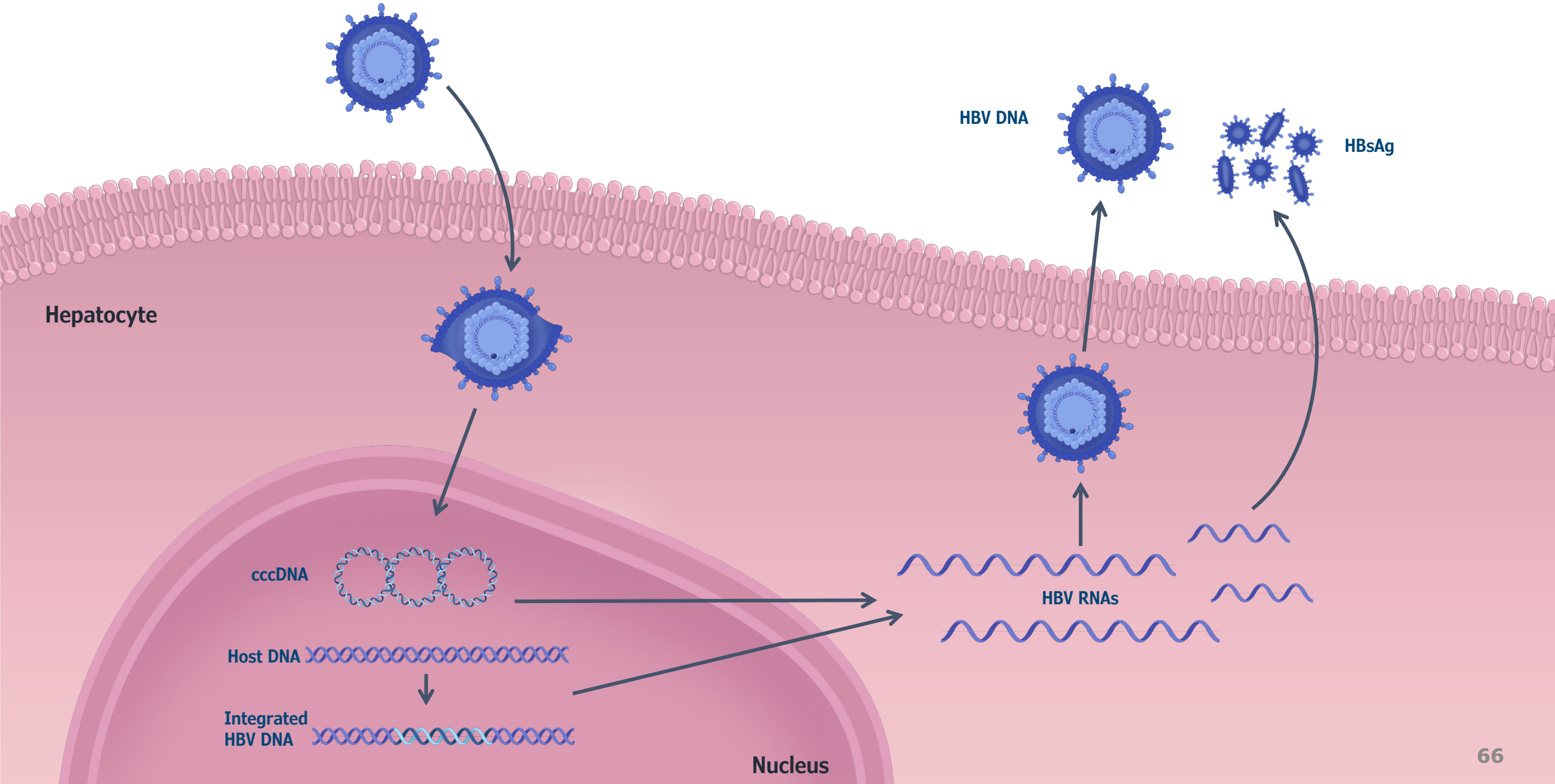
Functional Cure = Sustained Undetectable Circulating HBV Surface Antigen (HBsAg) and HBV DNA After a Finite Course of Treatment.

"Ability to achieve functional cure today is extremely limited…

Gene editing therapies would enhance the possibility of functional cures. A high rate of functional cure with gene editing therapy…would be a remarkable step up in our management of Chronic Hepatitis B"

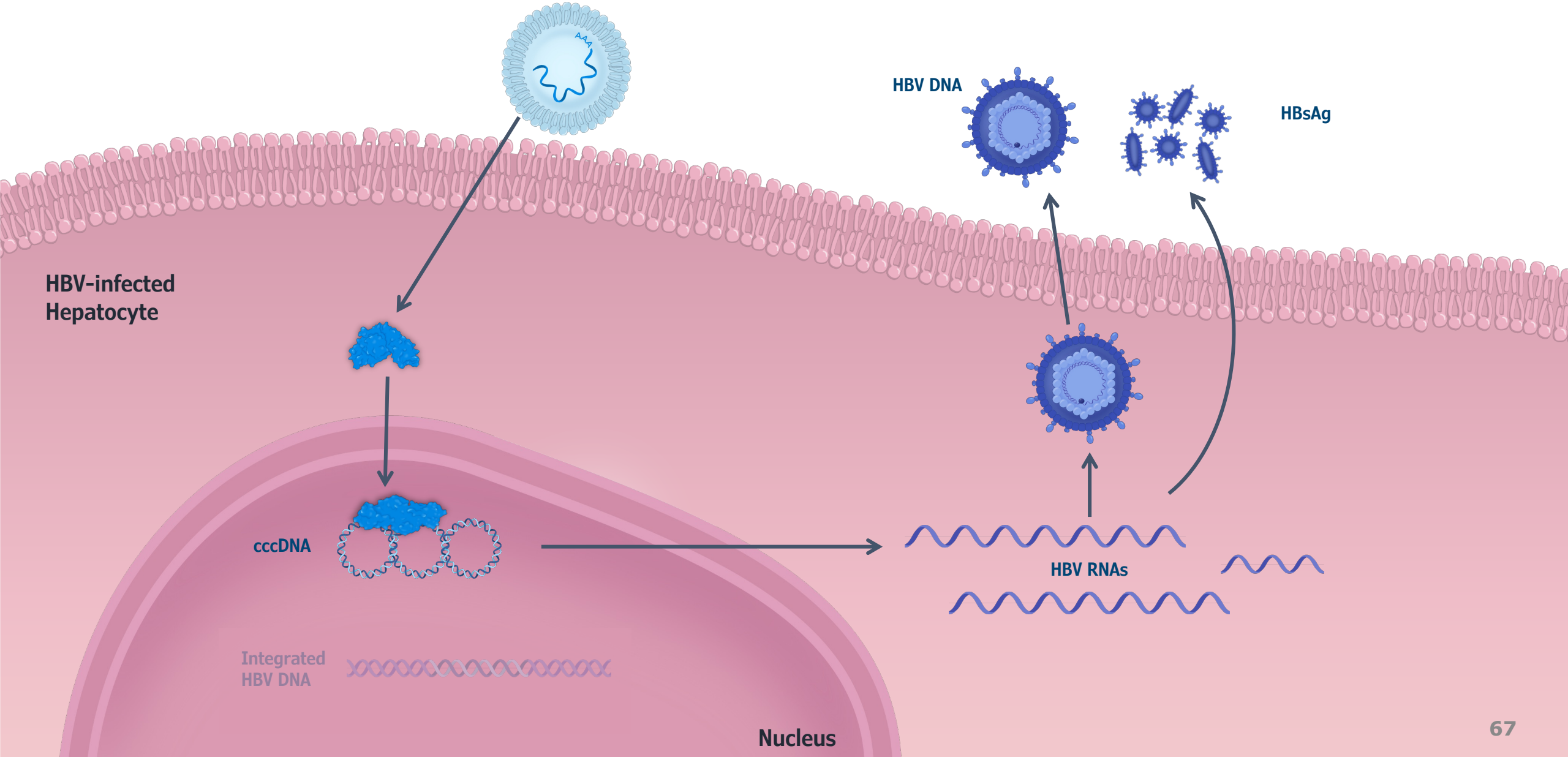
– Dr. Geoffrey Dusheiko, FCP(SA), FRCS
Emeritus Professor of Medicine
Royal Free Hospital & University College

Hepatitis B Viral Lifecycle



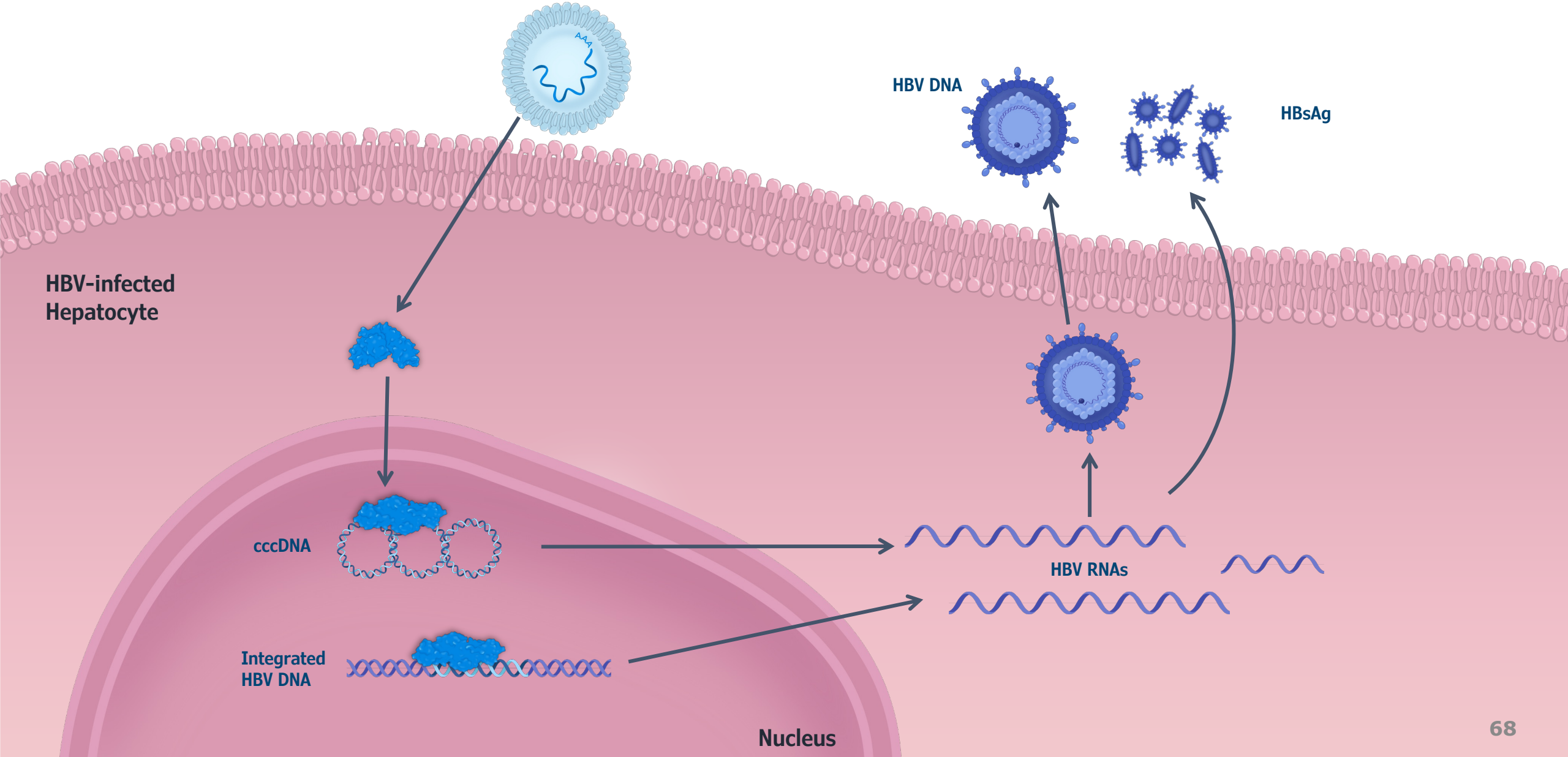
ARCUS Approach for a Functional Cure

ARCUS eliminates cccDNA and inactivates integrated HBV to drive durable antigen loss



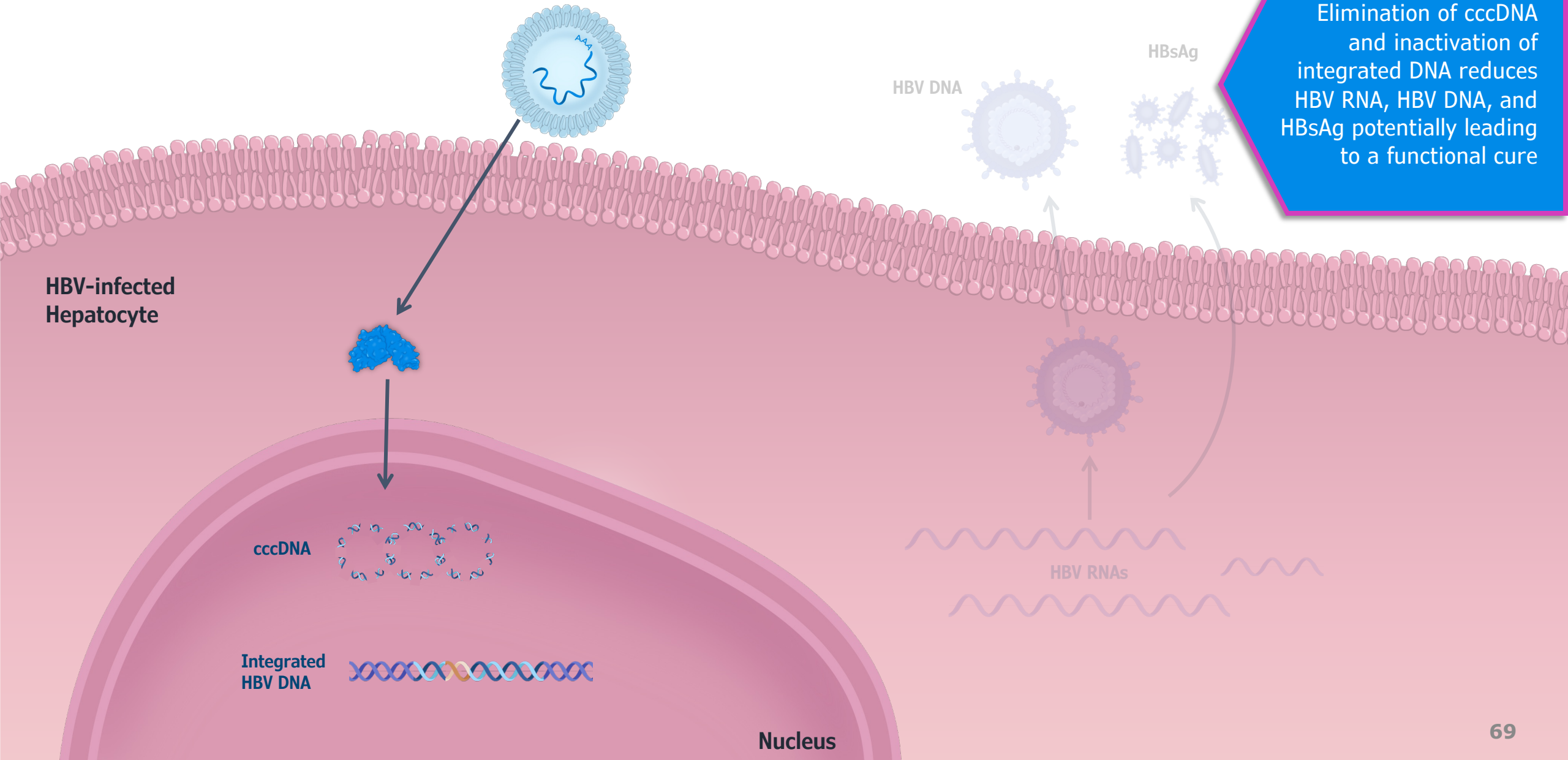
ARCUS Approach for a Functional Cure

ARCUS eliminates cccDNA and inactivates integrated HBV to drive durable antigen loss



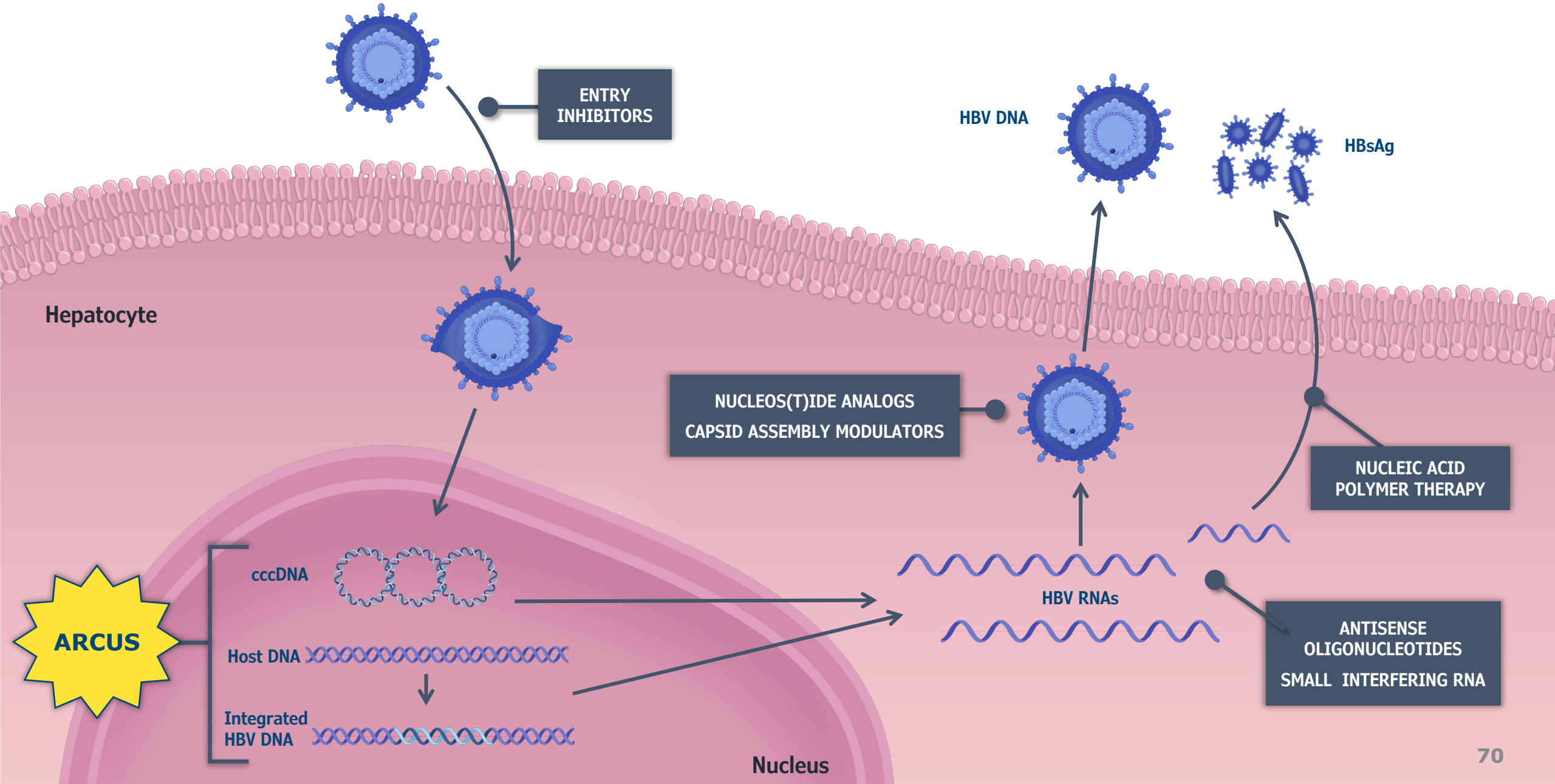
ARCUS Approach for a Functional Cure

ARCUS eliminates cccDNA and inactivates integrated HBV to drive durable antigen loss

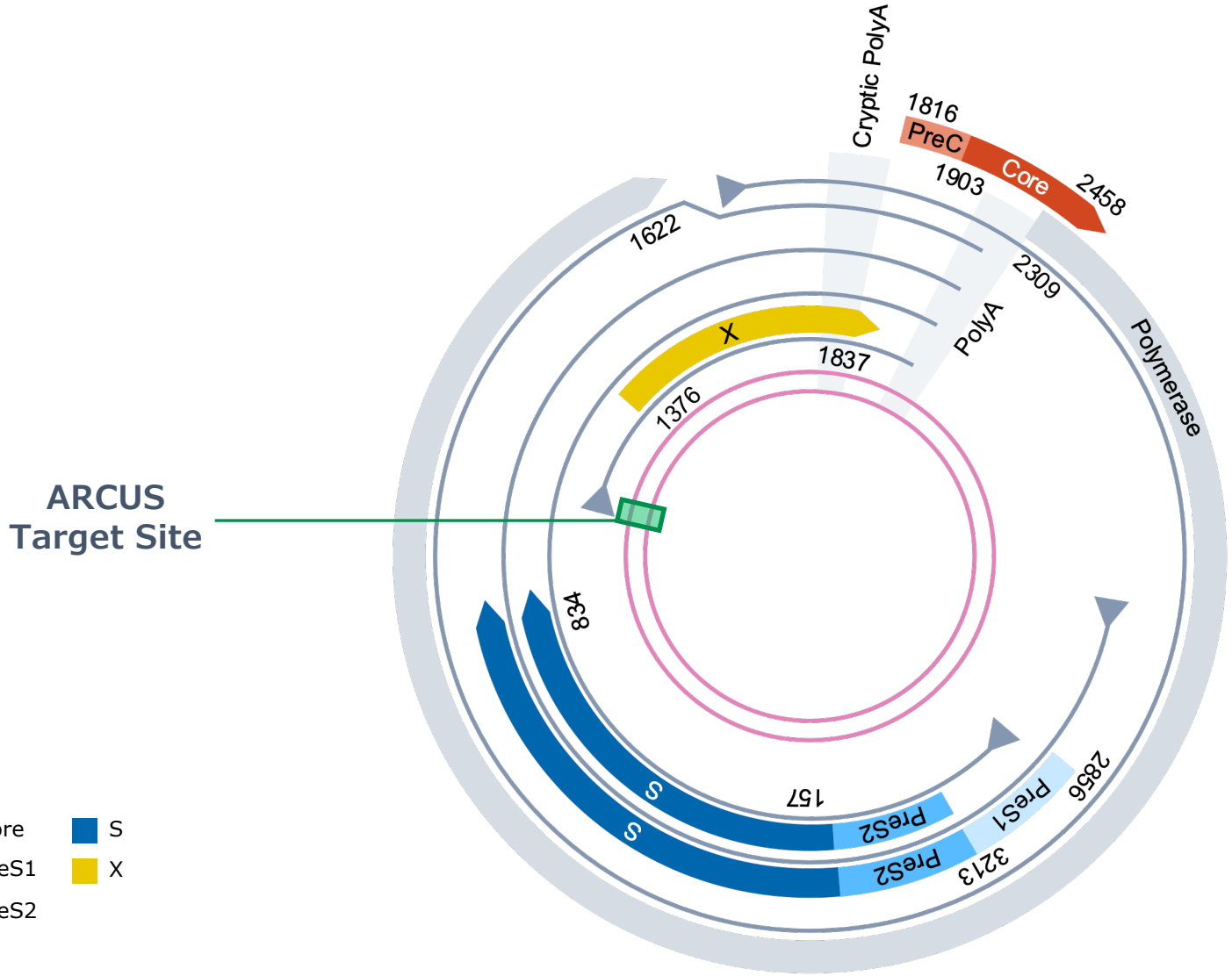


Elimination of cccDNA and inactivation of integrated DNA reduces HBV RNA, HBV DNA, and HBsAg potentially leading to a functional cure

Hepatitis B – ARCUS is Differentiated Versus Other Approaches



Selecting Target Site:
ARCUS Recognizes a Highly Conserved Sequence in cccDNA



Target site conserved in

92% of isolates across genotypes[1,2]

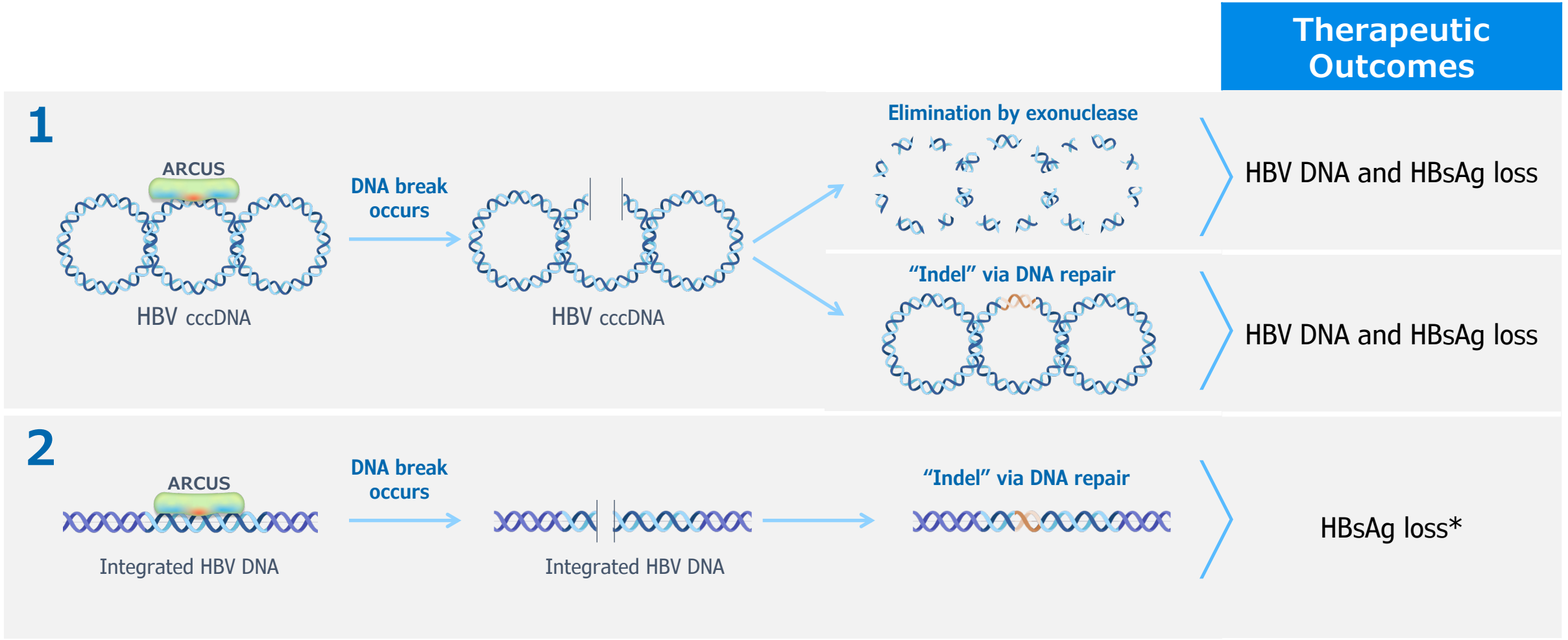
1. Gorsuch CL, et al. Mol Ther. 2022;30(suppl 9):2909-2922. 2. Image source adapted from: Tu T, et al. *Viruses.* 2021;13(2):180.

Selecting Target Site:
ARCUS Recognizes a Highly Conserved Sequence in Integrated HBV DNA

Targeted region is present in the vast majority of integrations[1]

1. van Buuren, N, et al. *JHEP* Rep. 4.4 (2022): 100449. Published 2022 Feb 12. doi:10.1016/j.jhepr.2022.100449

ARCUS Approach to Eliminate cccDNA and Inactivate Integrated HBV to Drive Durable Antigen Loss with Goal of Functional Cure

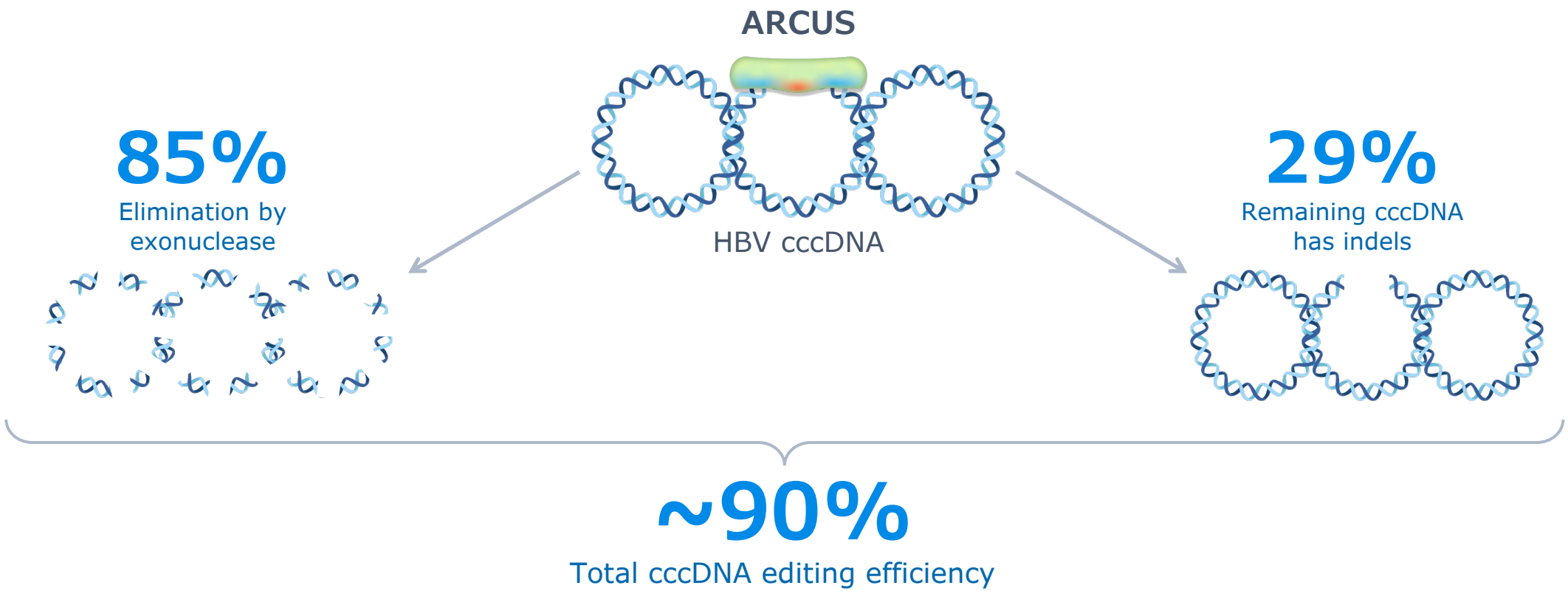


*Note: Integrated DNA does not produce HBV DNA

“The Proof” HBV Program

- ARCUS designed to eliminate cccDNA and inactivate integrated HBV DNA
- POC demonstrated both in vitro and in novel animal models
- mRNA improvements to achieve efficiencies needed for HBV

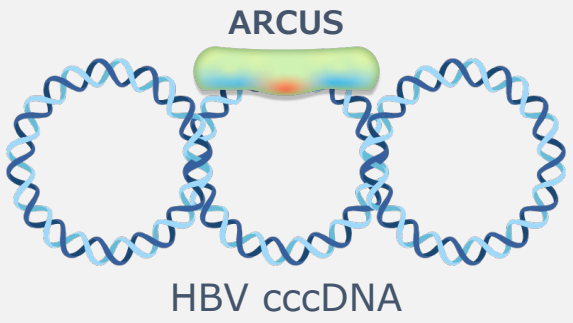
ARCUS Eliminated cccDNA in HBV-infected Primary Human Hepatocytes



Gorsuch et al, 2022. *Molecular Therapy*

ARCUS Dual Mechanism Drives Desired Therapeutic Outcomes

cccDNA elimination and integrated HBV inactivation led to sustained HBsAg loss

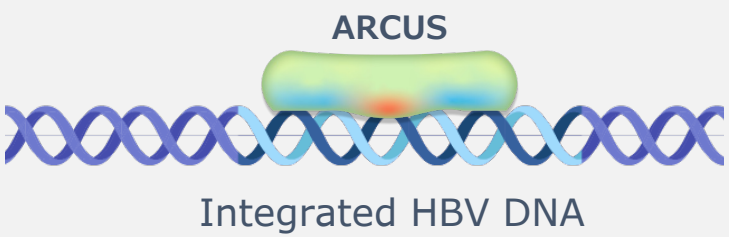


90%
editing efficiency

Therapeutic Outcome

80%
sustained loss of HBV DNA

77%
sustained loss of HBsAg



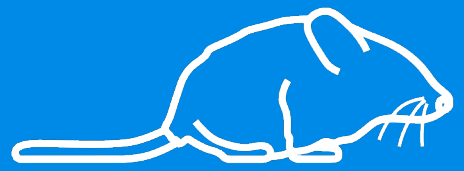
87%
editing efficiency

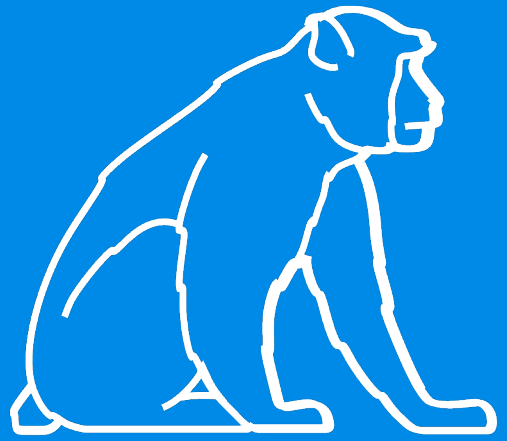
Therapeutic Outcome

80%
sustained loss of HBsAg

Gorsuch et al, 2022. *Molecular Therapy;* Note: Integrated DNA does not produce HBV DNA

HBV Episomal *In Vivo* Model





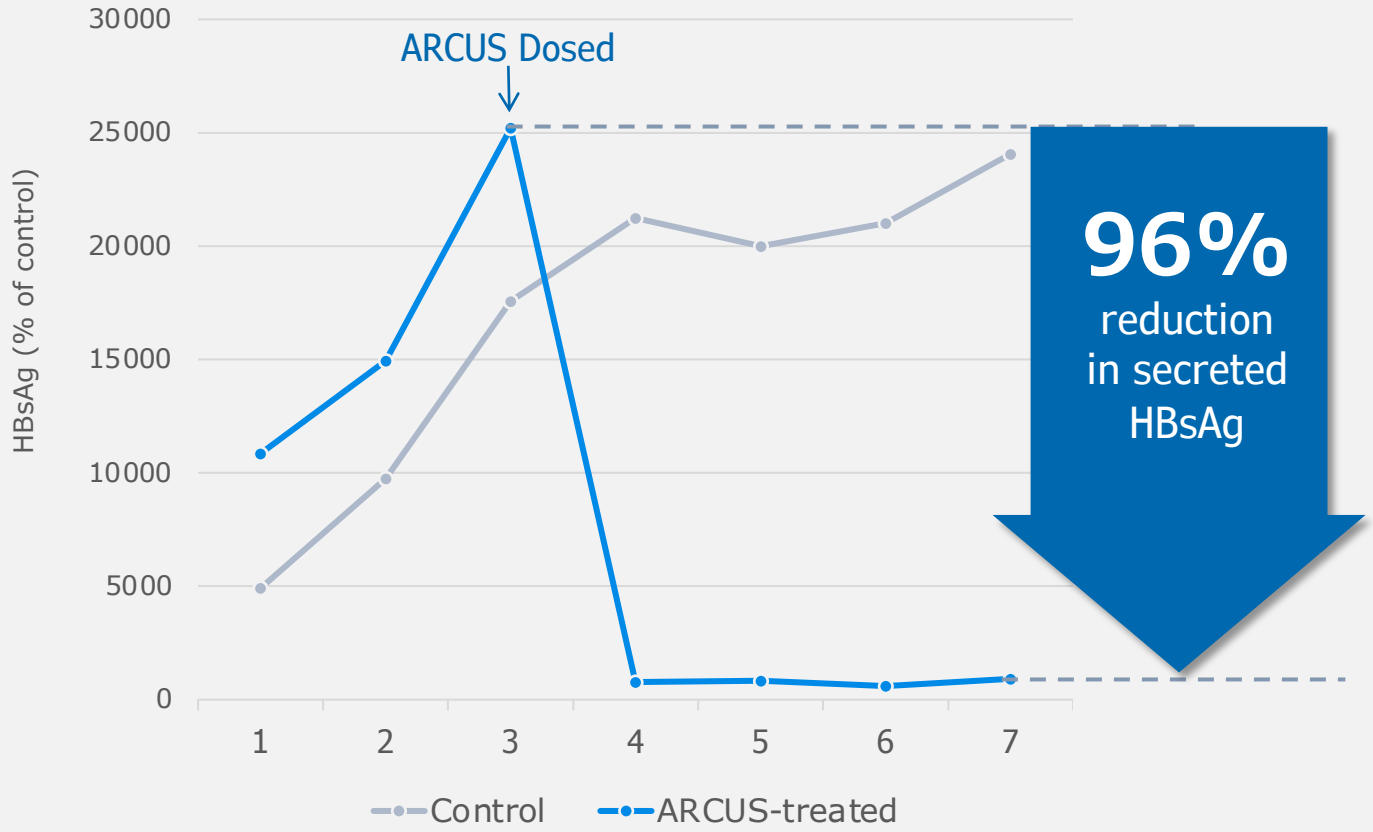
Step 1: ARCUS Inactivated Viral DNA and Durably Reduced HBsAg By 96%

Editing Efficiency

40%
reduction in viral copy number

86%
indels in remaining viral DNA

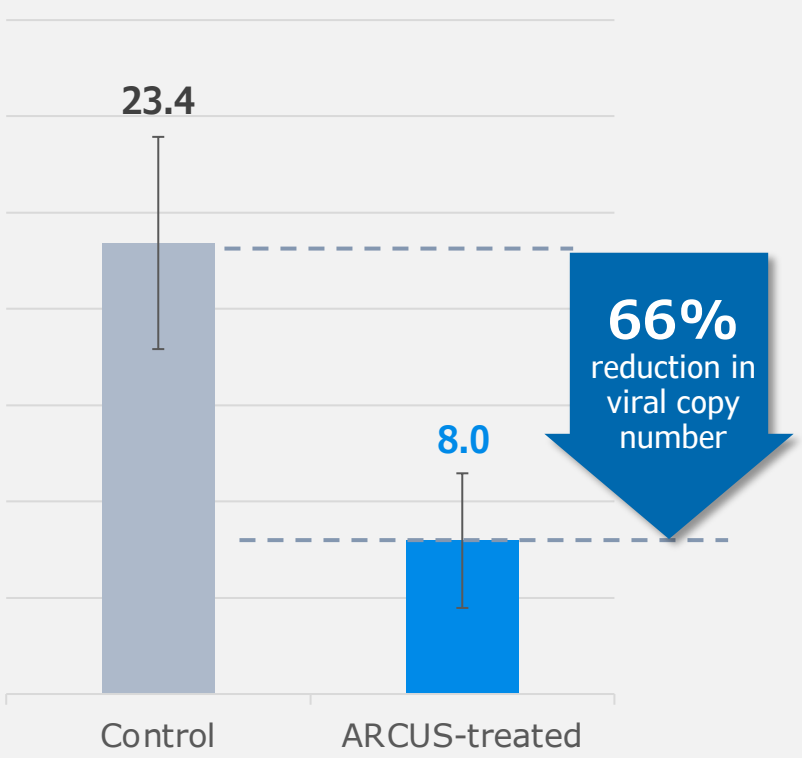
Therapeutic Outcome



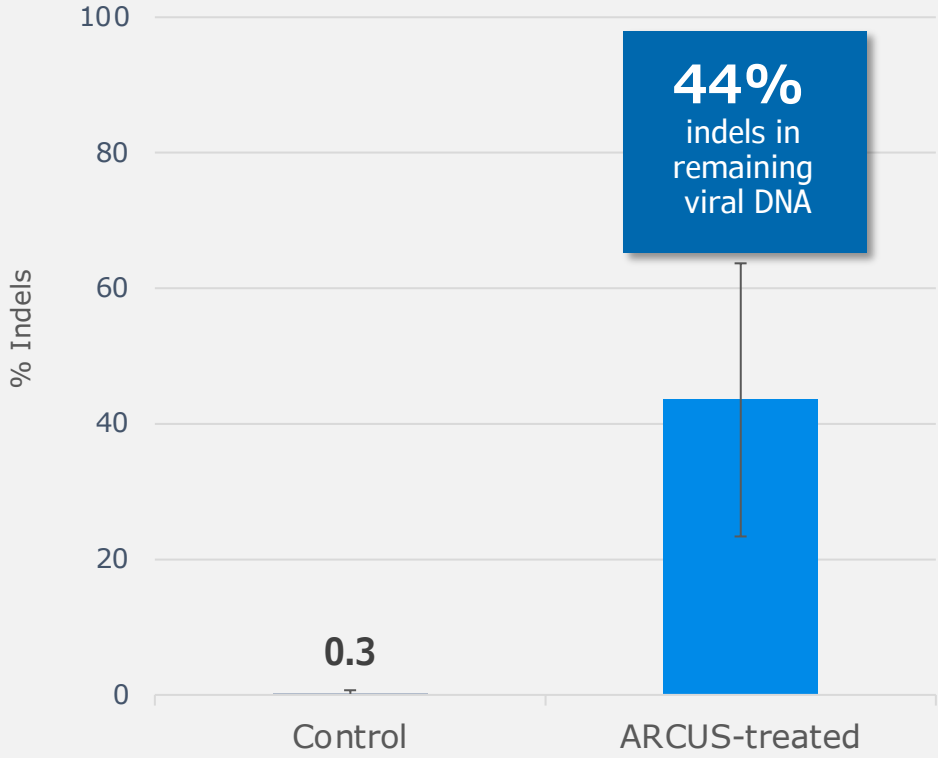
96%
reduction in secreted HBsAg

Gorsuch et al, 2022. *Molecular Therapy; Episomal mouse model*

Step 2: ARCUS Eliminated and Inactivated >80% Total Viral DNA



Of remaining **34%**

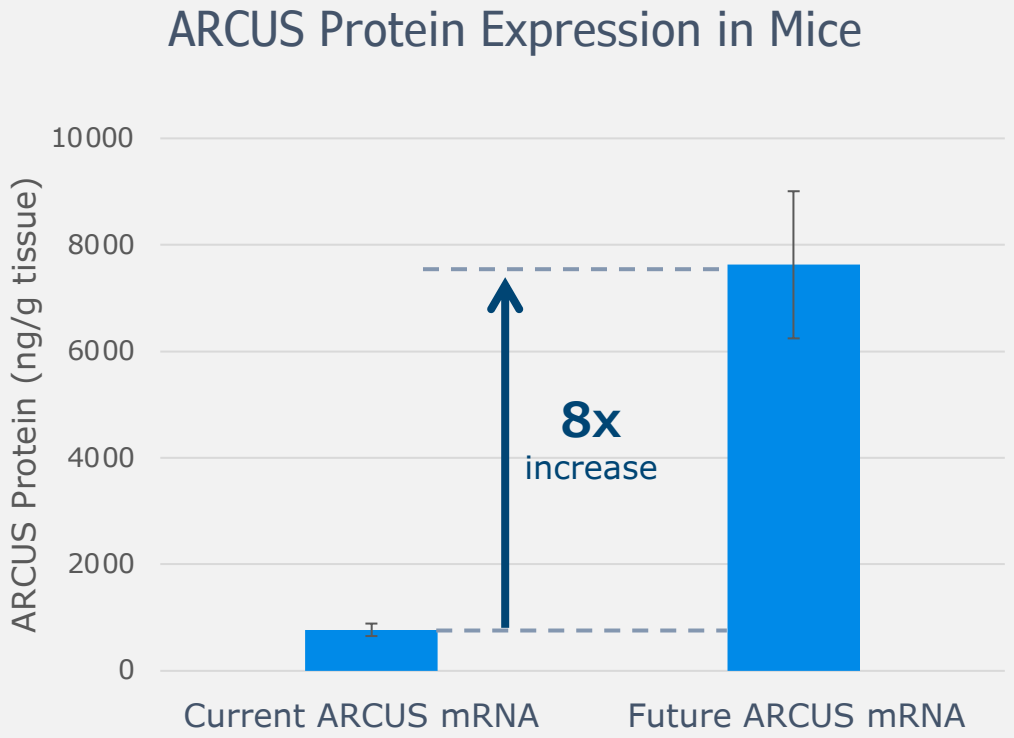


Total Efficiency: >80% Viral Editing

Gorsuch et al, 2022. *Molecular Therapy;* Episomal NHP Model
HBsAg cannot be measured in NHP model due to immune clearance

Enhancing HBV Efficacy via mRNA Optimization

mRNA Sequence Optimization



Reasons to Believe in Precision's Approach for HBV

Target CTA/IND
2024

ARCUS is only approach for HBV **targeting both elimination of cccDNA and inactivation of integrated HBV DNA**

80% reduction in HBV DNA and 96% reduction in HBsAg after a finite course of treatment in preclinical animal models

Precision has made platform improvements in mRNA resulting in 8-fold increase in ARCUS protein expression, designed to boost efficacy

In vivo gene editing offers a novel approach for HBV patients and a **path for a functional cure; target CTA and/or IND in 2024**

HBV Expert Discussion

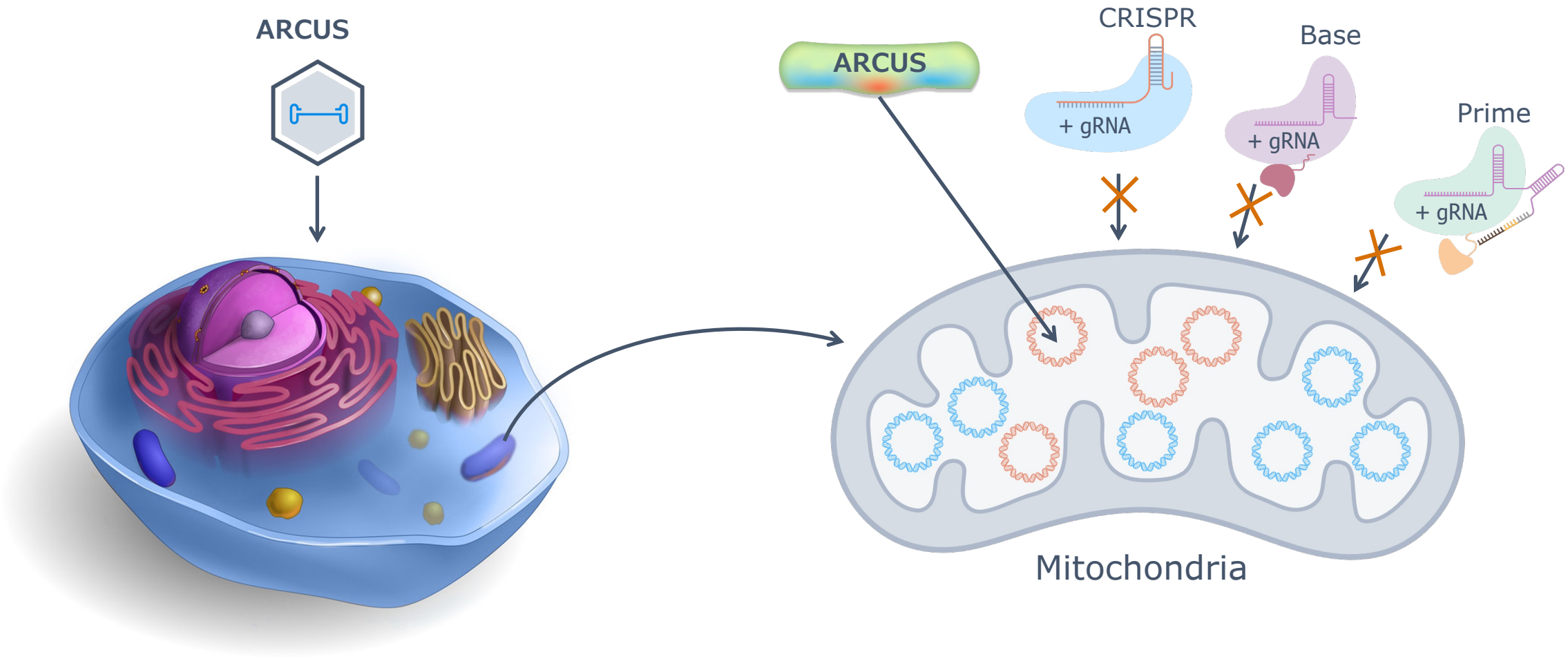
Alan List, MD
Chief Medical Officer
Precision BioSciences, Inc.

Mark Sulkowski, MD
Chief, Division of Infectious Diseases
John Hopkins University School of Medicine

Primary Mitochondrial Myopathy

Wendy Shoop, PhD
Research Leader – Mitochondrial Programs

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



Primary Mitochondrial Myopathy (PMM) Currently Lacks a Curative Treatment

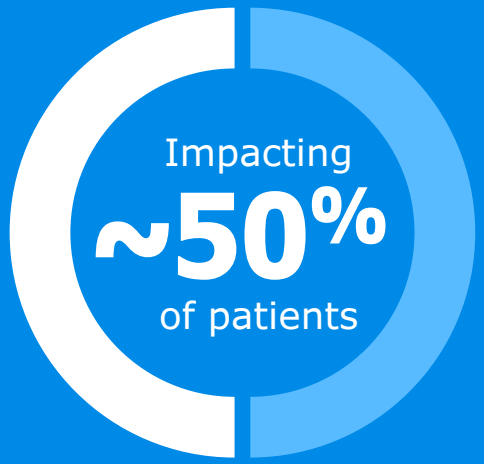
Mitochondrial diseases (MDs)

are the most common hereditary metabolic disorders and have an overall frequency[2]

1 in 4,300

A key manifestation of mitochondrial disease is[3]

PMM

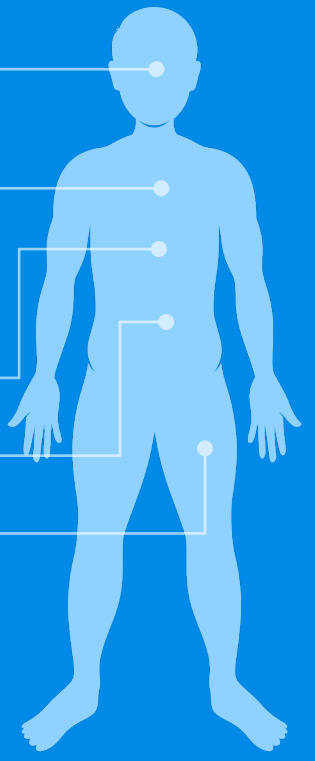


Primary mitochondrial myopathies (PMM)

are genetically defined disorders leading to defects in energy production predominantly affecting skeletal muscle

PMM is debilitating[1]:

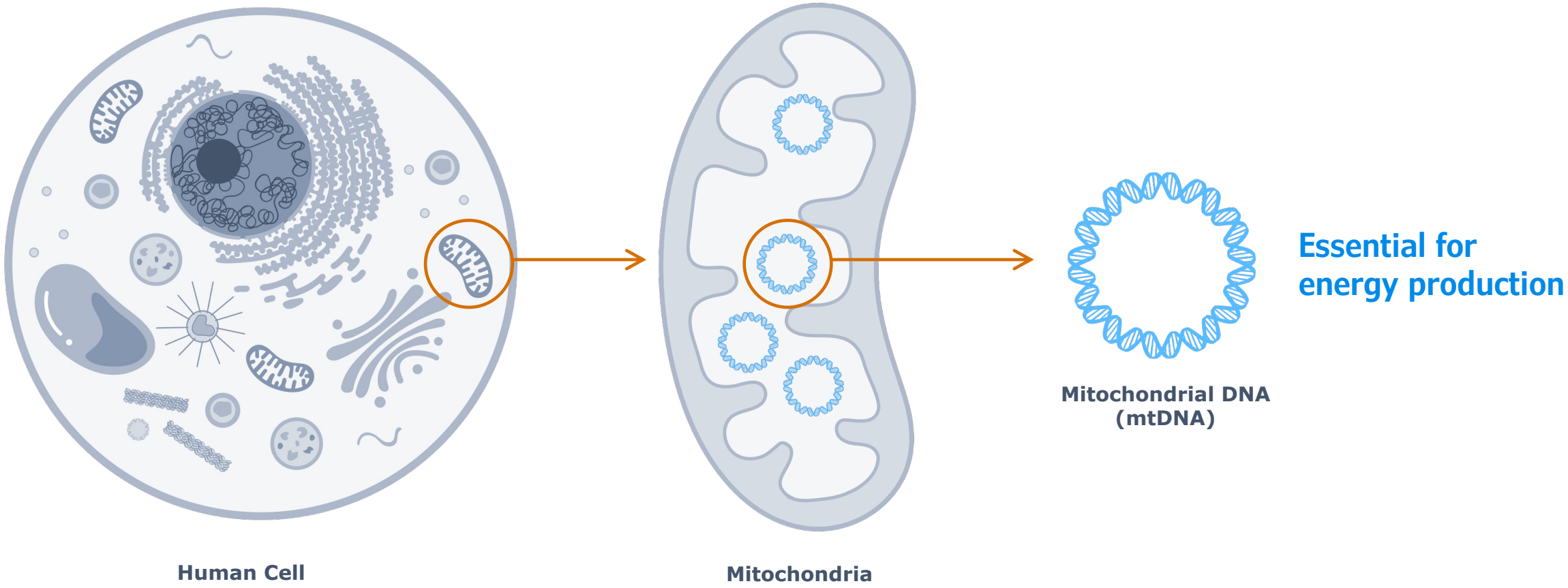
- Chronic progressive external ophthalmoplegia
- Respiratory failure
- Exercise Intolerance
- Multi organ dysfunction
- Impaired Mobility
- Generalized weakness



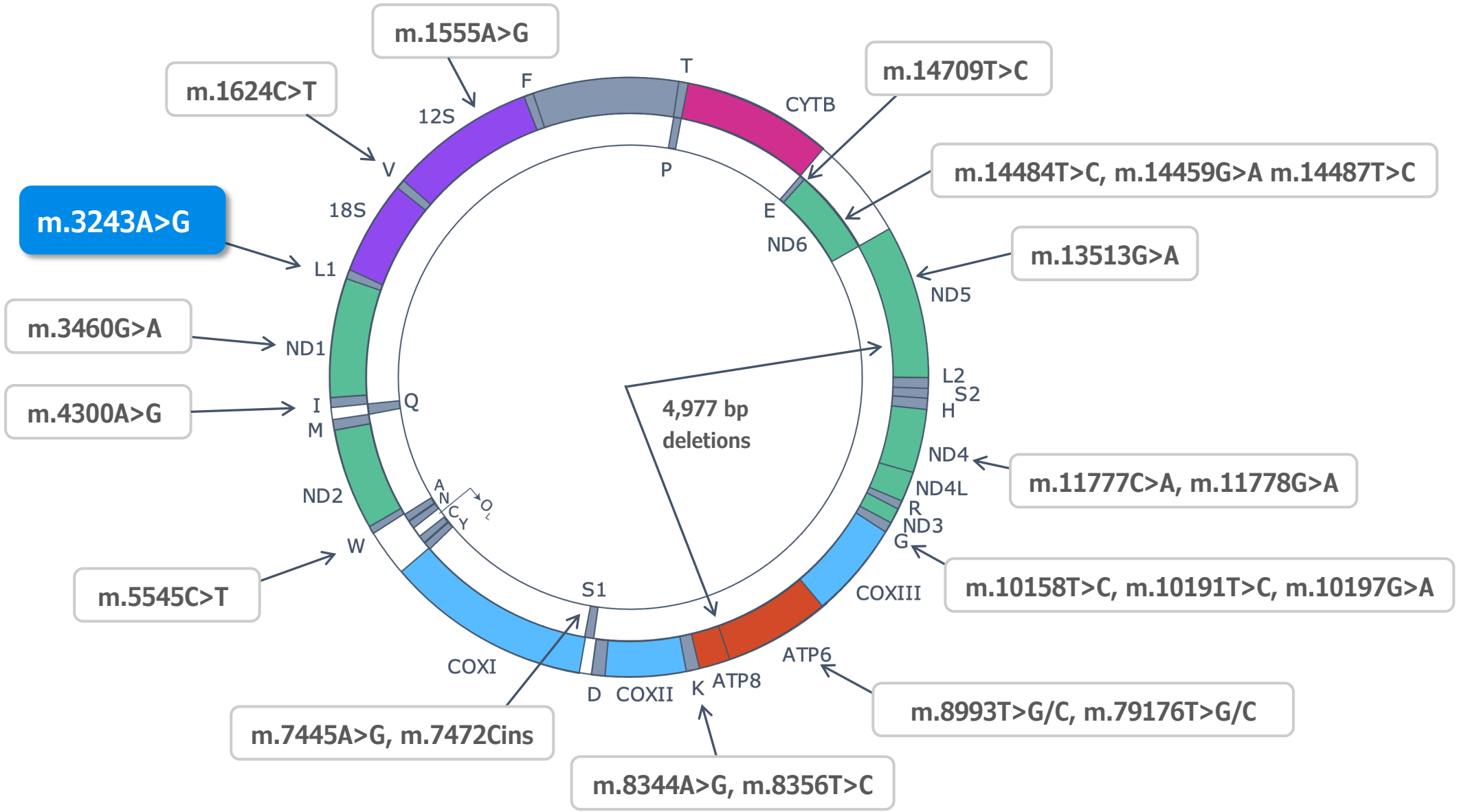
Patients today lack curative treatments and receive supportive care only through "mito cocktails"[1]

Sources:
1. https://www.ninds.nih.gov/health-information/disorders/mitochondrial-myopathies; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6938233/
2. https://ng.neurology.org/content/6/6/e519
3. Chinnery et al., Molecular Pathology …1997 Brain 120, 1713-1721; myopathy can reach up to 80% of patients depending on driver mutation (e.g., m.3243)
4. https://pubmed.ncbi.nlm.nih.gov/25652200/

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



The mtDNA is Prone to Mutation, Leading to Mitochondrial Disease



mtDNA, mitochondrial DNA.

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

m.3243A>G

- **Mutation Prevalence of 1/500**[1]
- **~36% of Mitochondrial Diseases are driven by m.3243A>G**[2]

m.3243 associated PMM estimated at **~14k patients in the US alone**[3]

Mutant mtDNA sequence

5′-C A G **G** G C C C G G T A A T C G C A T A A A-3′

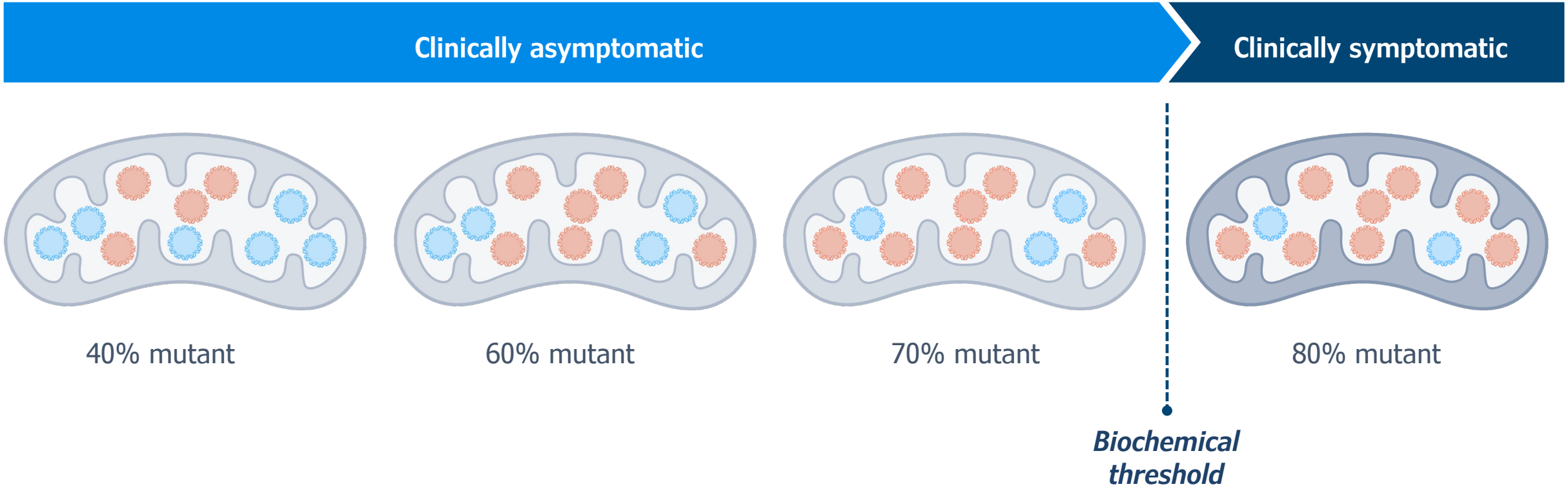
5′-C A G **A** G C C C G G T A A T C G C A T A A A-3′

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;
3. Calculated based disease epidemiology studies and secondary literature

mtDNA Mutations Are Commonly Heteroplasmic

Situation where two or more mtDNA variants exist in same mitochondria



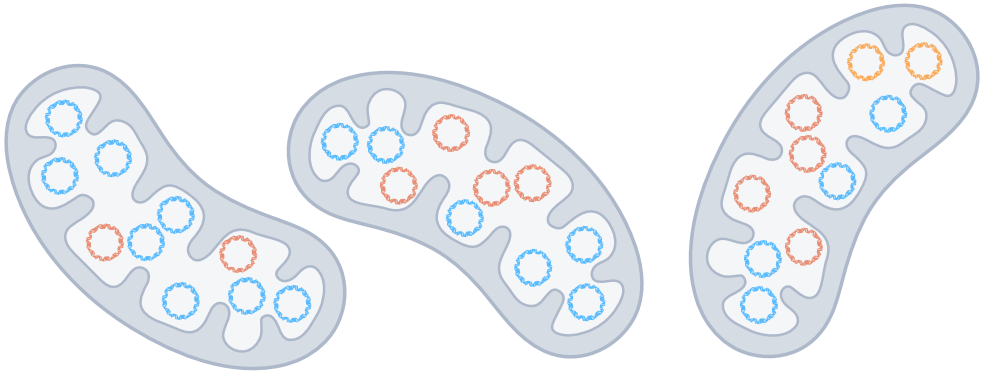
mtDNA, mitochondrial DNA.

Key Differences Between Editing Nuclear DNA and Mitochondrial DNA

Nuclear DNA

- Most cells contain one nucleus
- Nuclear DNA is diploid (two copies per cell)
- Mechanisms exist to repair DSBs – can result in **multiple outcomes** including repair to wild-type, deletion, insertion, excision, etc.

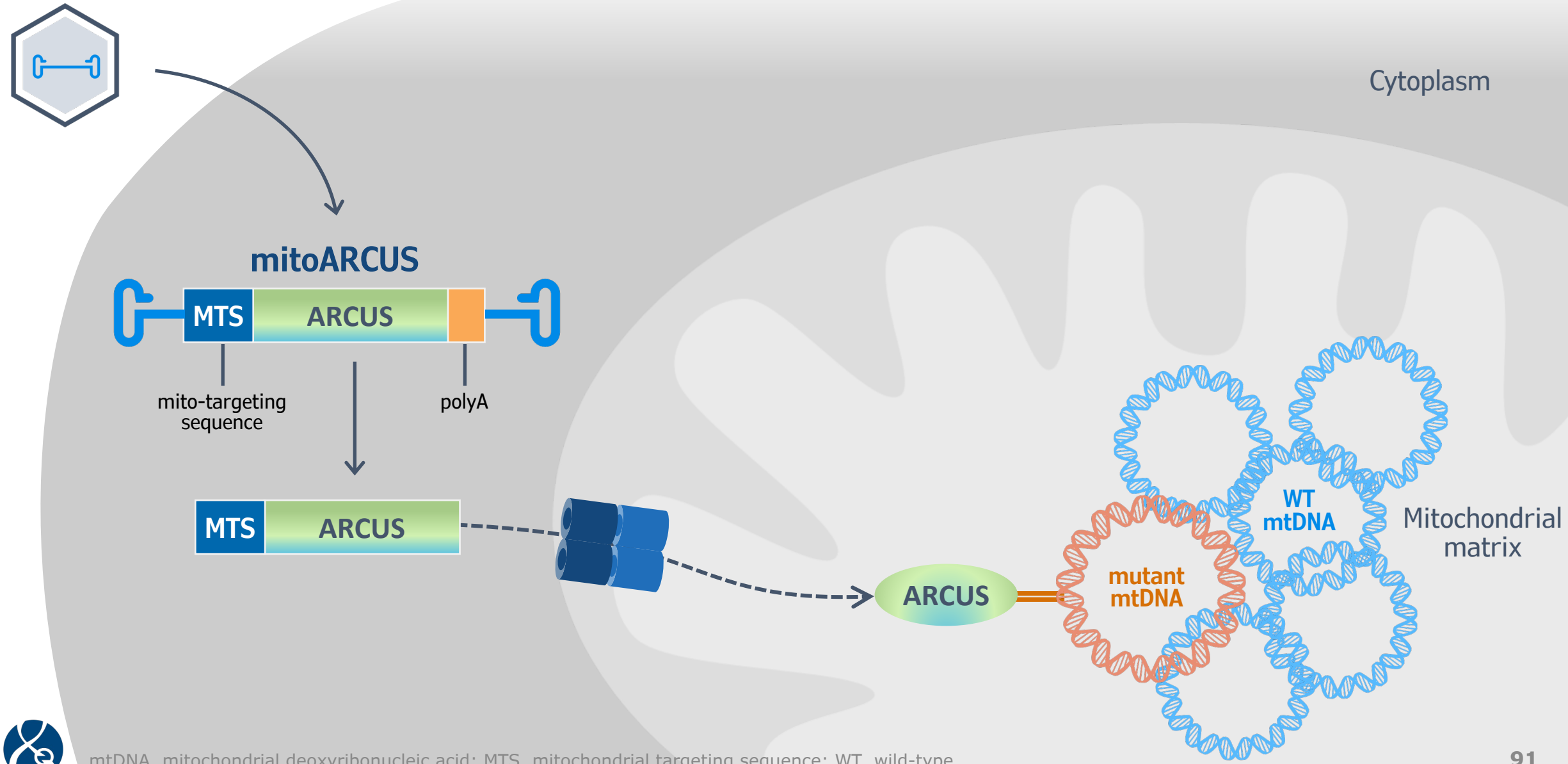
mtDNA



- Each cell contains many mitochondria
- mtDNA is polyploid (hundreds to thousands of copies per cell)
- No efficient DSB repair mechanisms exist — **one outcome**, linearized mtDNA molecules are degraded
- mtDNA copy number is tightly regulated

DSB, double-strand break; mtDNA, mitochondrial DNA.

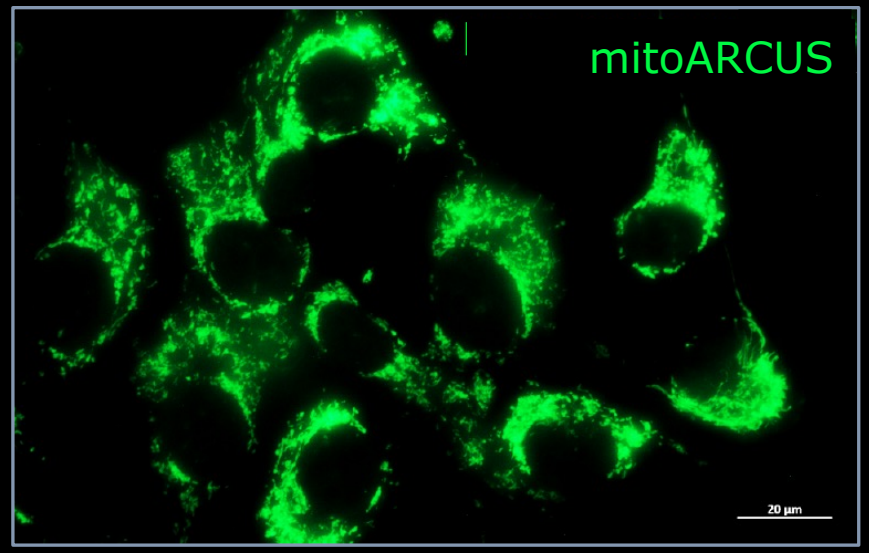
mitoARCUS Therapeutic Approach to Shift Heteroplasmy

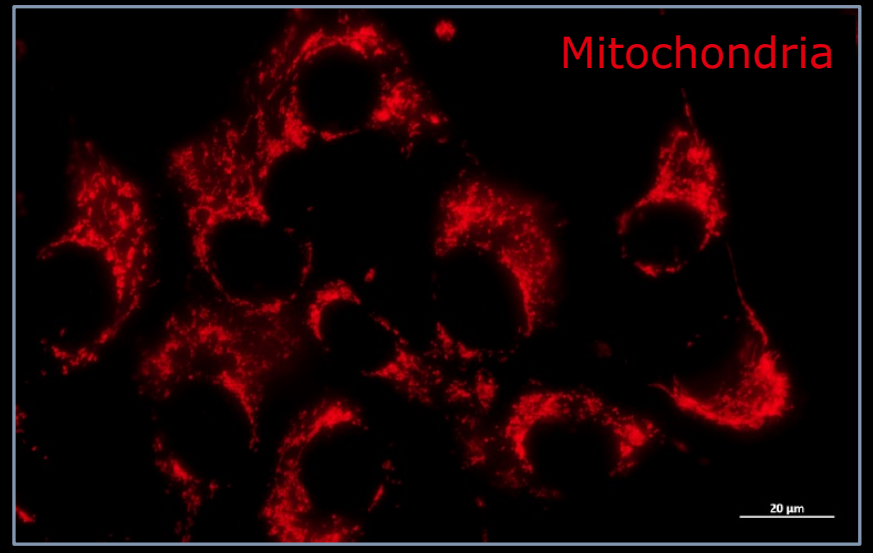


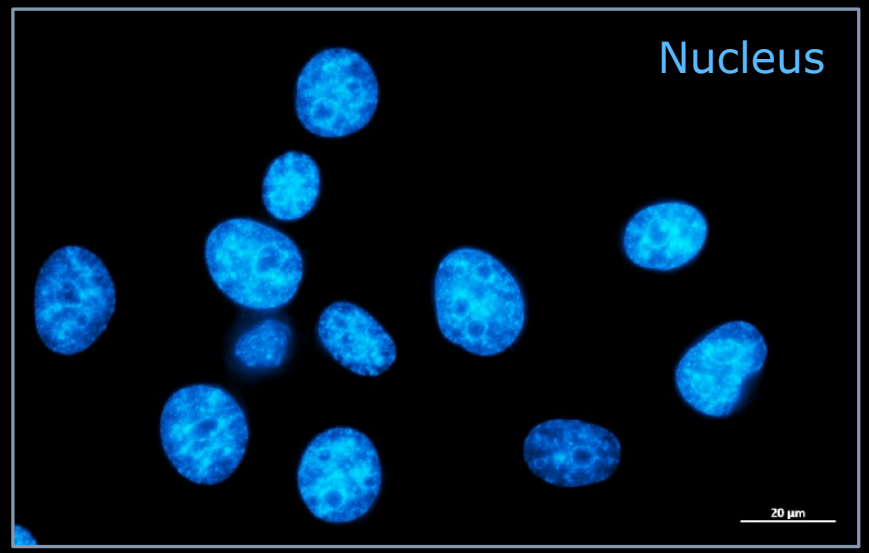
mtDNA, mitochondrial deoxyribonucleic acid; MTS, mitochondrial targeting sequence; WT, wild-type.

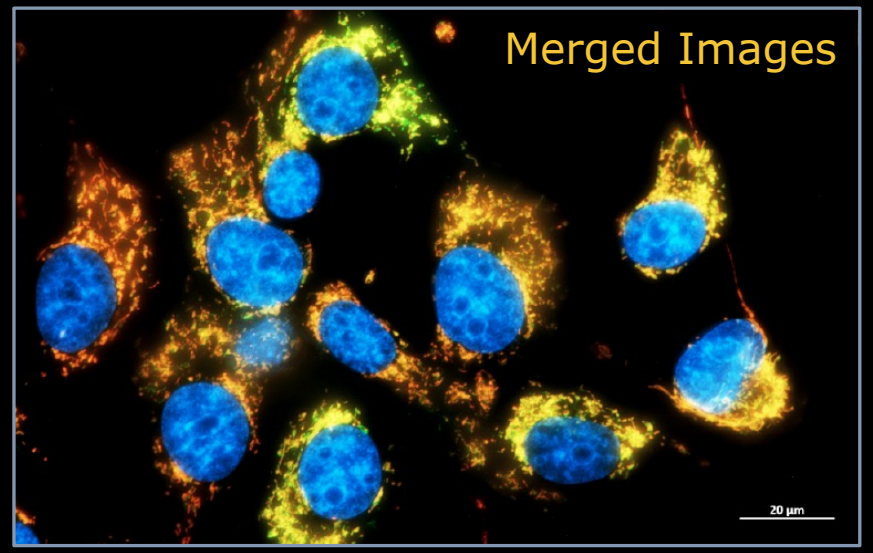
mitoARCUS Localizes Exclusively to Mitochondria

ARCUS fused to a Mitochondrial Targeting Sequence (MTS) localized to mitochondria in vitro







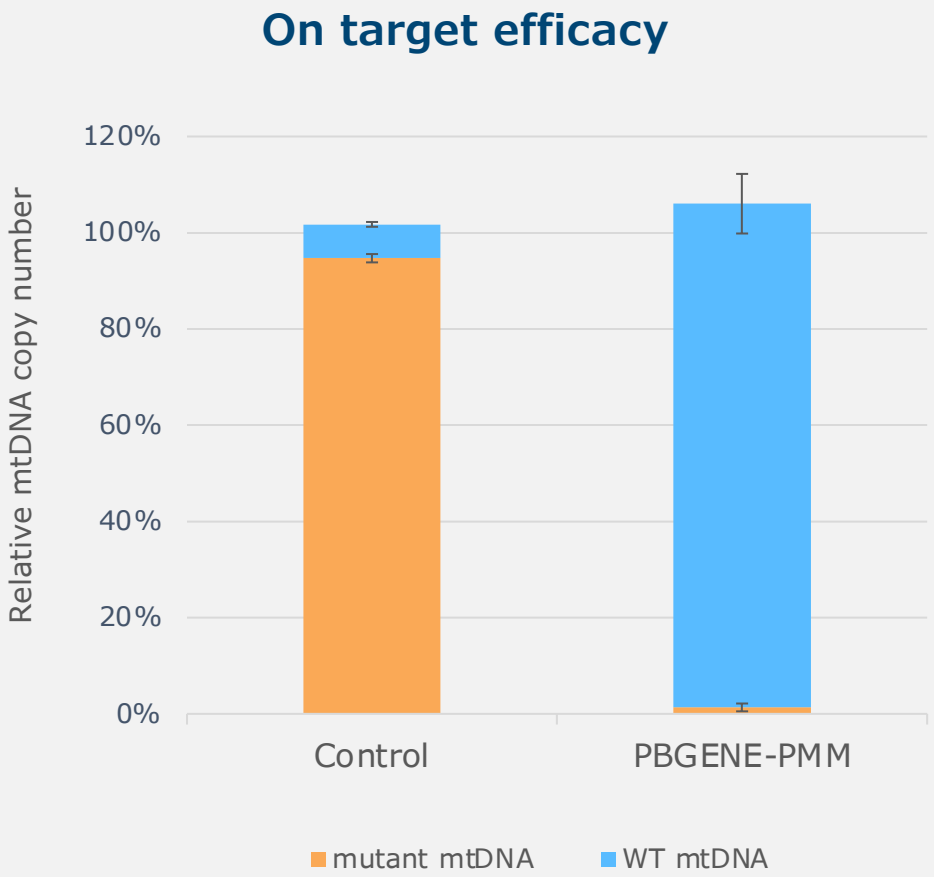


MTS, mitochondrial targeting sequence.
Shoop, et al. ESGCT MIT. Poster 422.

“The Proof” PMM Program

- Single component nature of ARCUS allows specific editing of mutant mtDNA with no off-target editing
- ARCUS-induced heteroplasmy shift resulted in respiratory improvement in edited cells
- POC of in vivo mtDNA editing with mitoARCUS

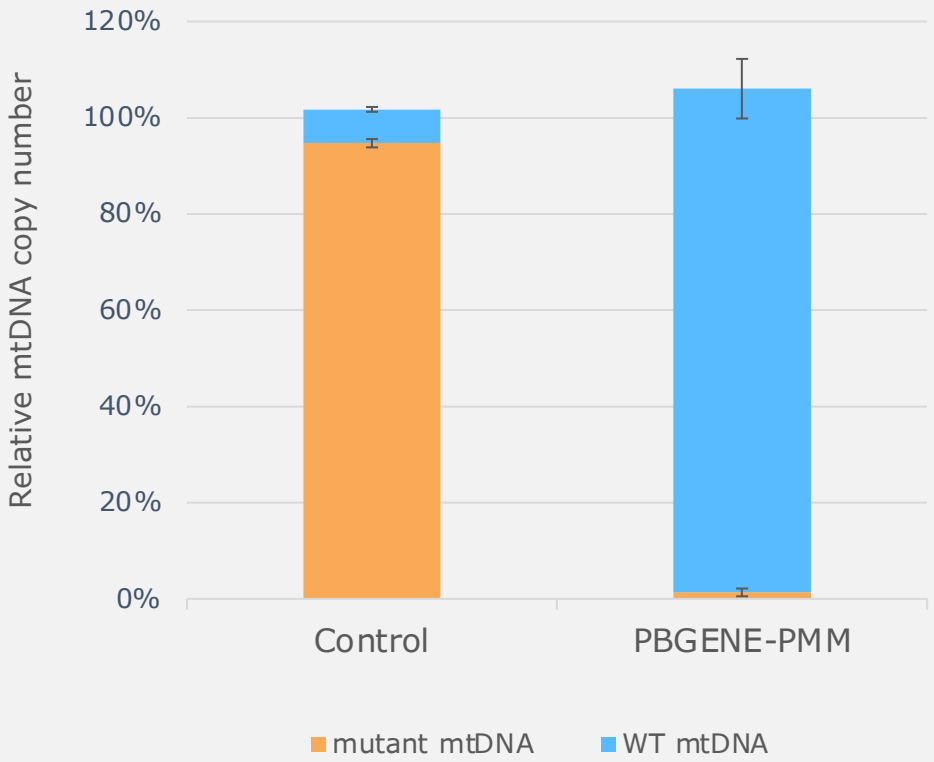
PBGENE-PMM Shifts Heteroplasmy



mtDNA, mitochondrial DNA; WT, wild-type.

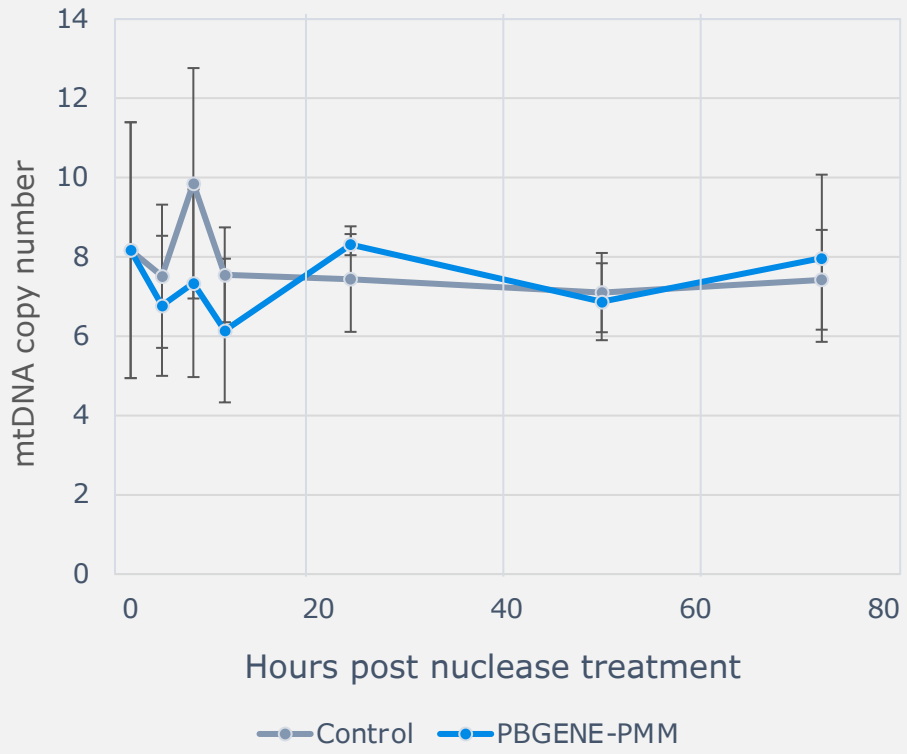
PBGENE-PMM Specifically Eliminated Mutant but Not Wildtype mtDNA

On target efficacy



3x higher dose

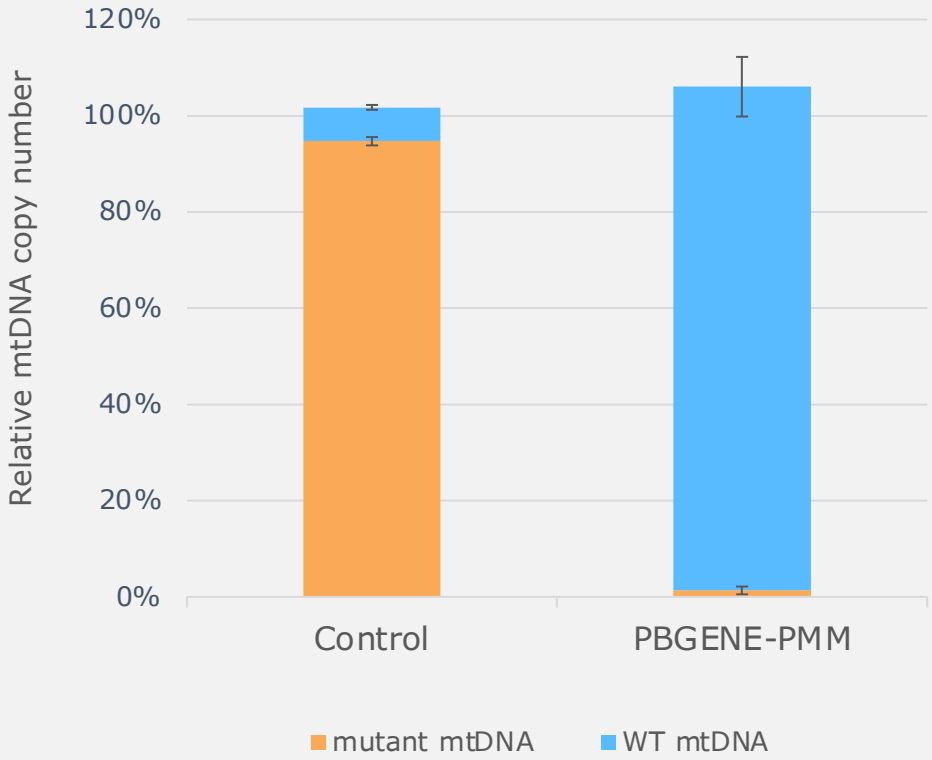
Mitochondrial off target specificity



mtDNA, mitochondrial DNA; WT, wild-type.

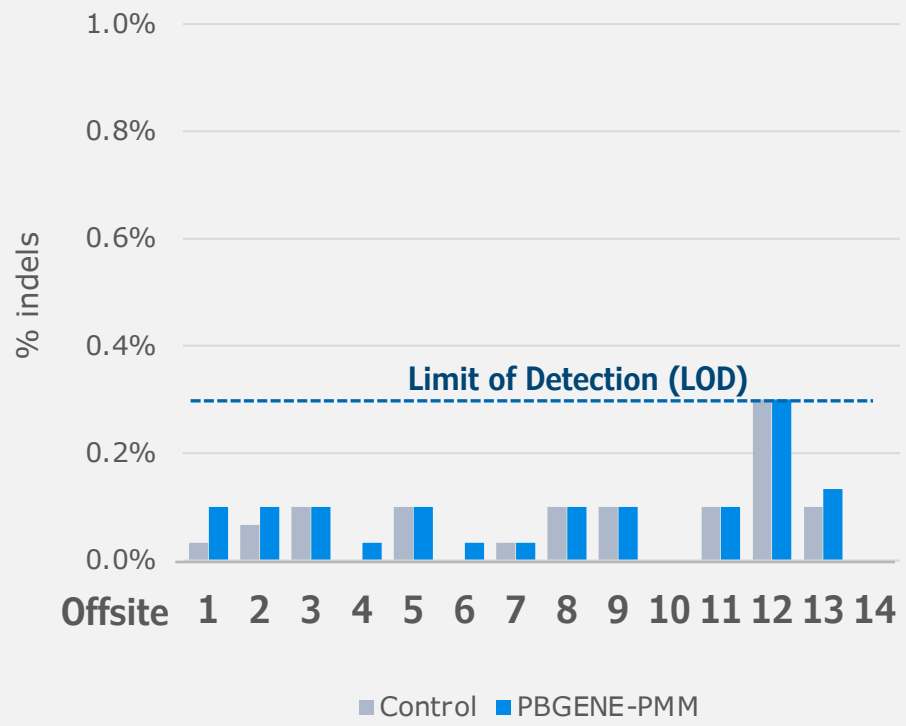
PBGENE-PMM Designed Not to Cut Nuclear DNA

On target efficacy



20x higher dose

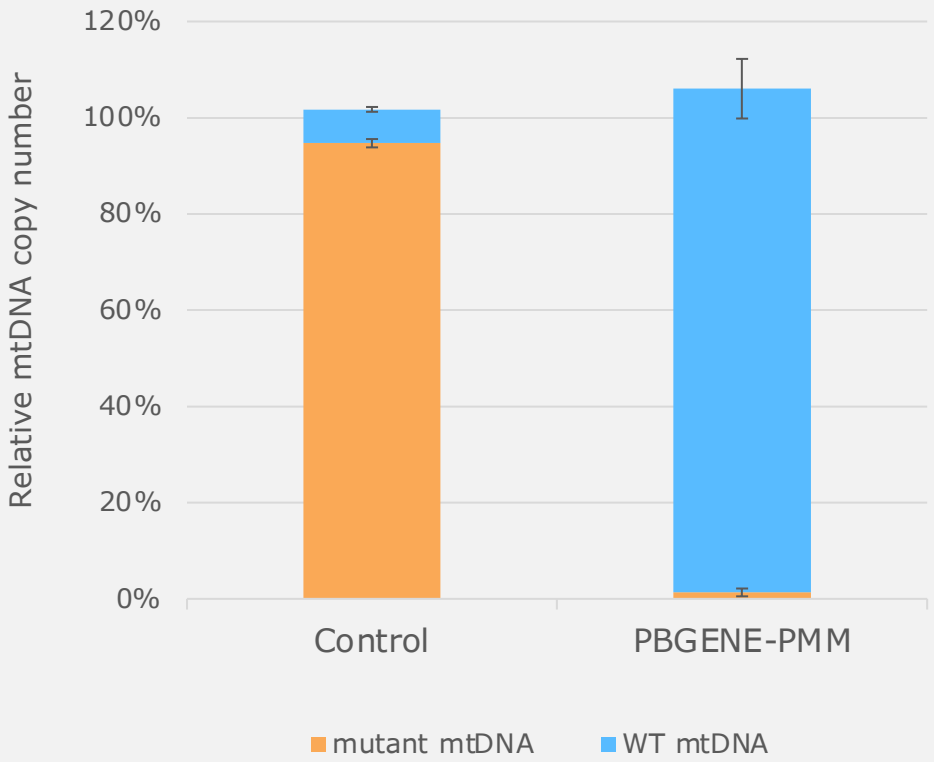
Nuclear off target specificity



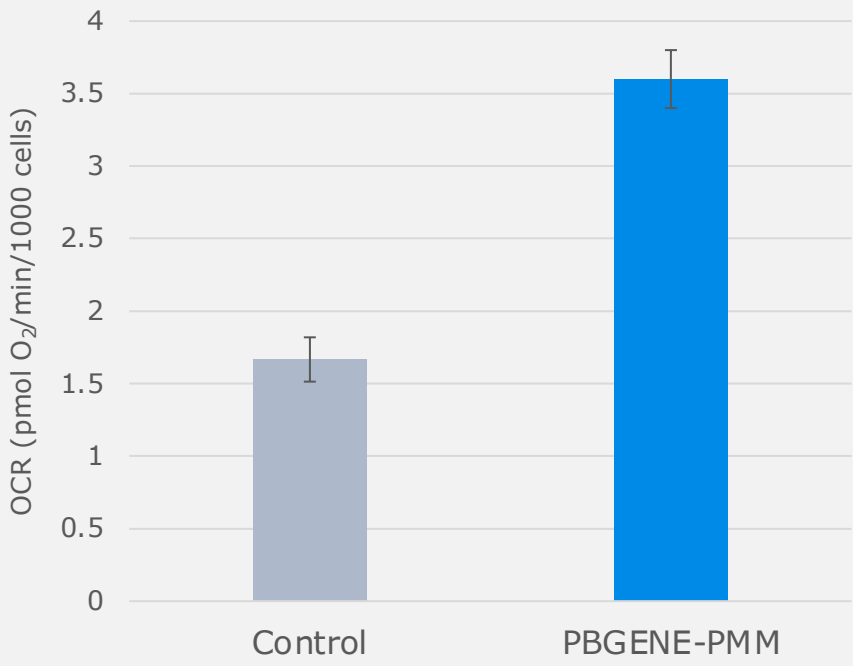
mtDNA, mitochondrial DNA; WT, wild-type; indel, insertion and/or deletion.

PBGENE-PMM Improved Mitochondrial Function

On target efficacy

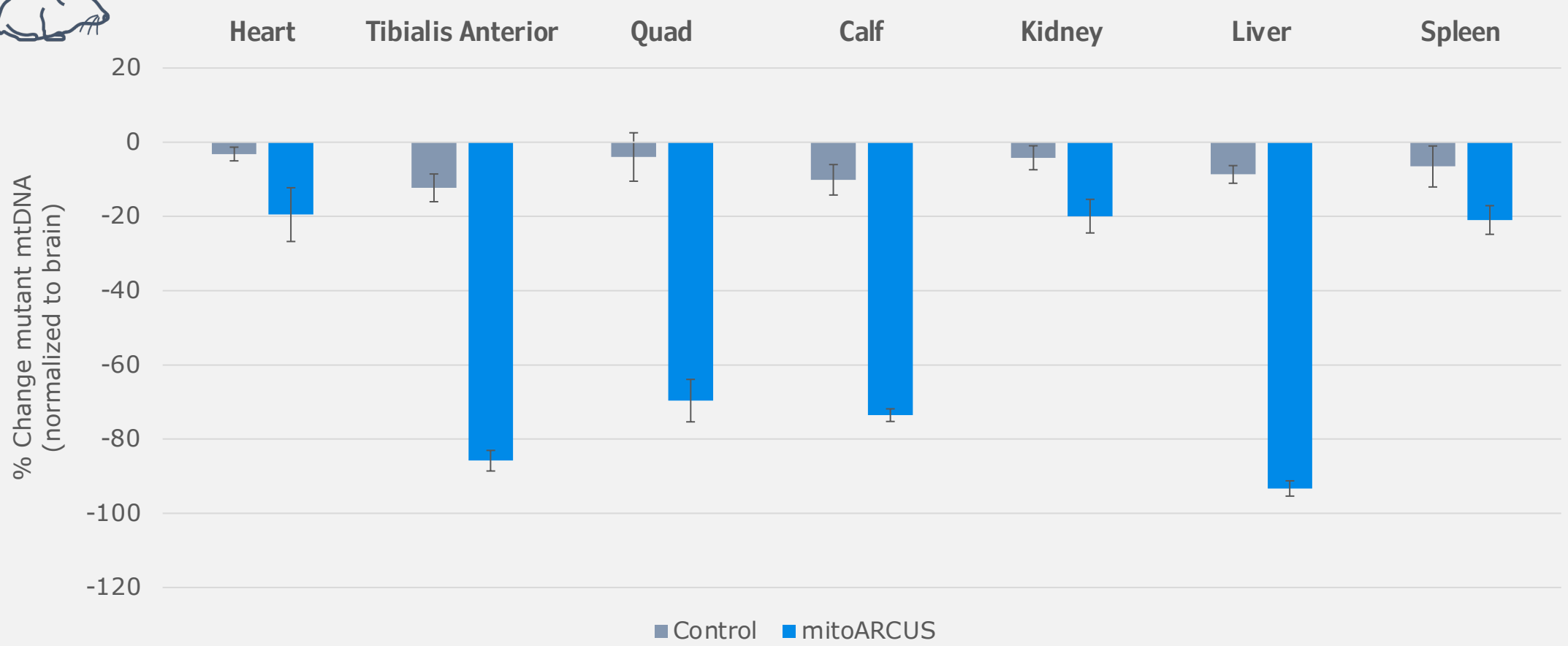


Impact on energy production



mtDNA, mitochondrial DNA; WT, wild-type.

mitoARCUS Shifted Heteroplasmy in *In Vivo* Mouse Model



mtDNA, mitochondrial DNA.

Zekonyte U, et al. *Nat Commun*. 2021. 2021;12(1):3210.

PBGENE-PMM Strategy

Attributes of PBGENE-PMM Construct

Delivery

Single-vector AAV delivery drives gradual nuclease expression

Tissue-Specific Expression

Muscle-specific promoter limits nuclease expression to target tissues

Subcellular Localization

MTS traffics mitoARCUS nuclease to mitochondria

Specificity

PBGENE-PMM specifically cuts mutant m.3243G mtDNA

ARCUS gene editing therapy delivered by AAV directly and specifically edits m.3243A>G-mutant mitochondrial genomes leading to a shift in heteroplasmy to wild-type

AAV, adeno-associated virus; mtDNA, mitochondrial DNA; MTS, mitochondrial targeting sequencing.

Reasons to Believe in Precision's Approach to Treat PMM

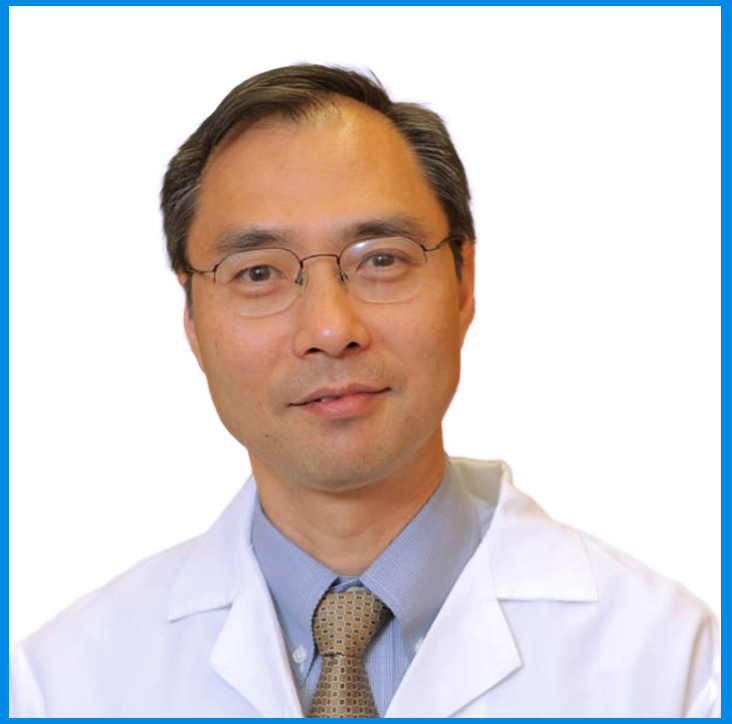
Target CTA/IND
2025

- 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"
- 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

Mitochondrial expert discussion

Alan List, MD
Chief Medical Officer
Precision BioSciences, Inc.

Carlos T. Moraes, PhD
Esther Lichtenstein Professor of Neurology
University of Miami Miller School of Medicine



Michio Hirano, M.D.
Chief, Division of Neuromuscular Disorders;
New York-Presbyterian/Columbia University
Irving Medical Center

Concluding Remarks

Michael Amoroso

President & Chief Executive Officer

More Defined Outcomes Accomplished Through ARCUS

The Cut

- 3’ Overhang Stimulates HDR
- Supports Perfect Re-ligation
- Designed for High Efficiency, Highly Therapeutic Gene Edit

The Size

- Smallest Gene Editor
- Enables ARCUS + Additional Payload In One Delivery
- Delivery to More Tissues Across Body

The Simplicity

- Single Enzyme / Component
- Higher Efficiency Therapeutic Edits
- Lower AAV & LNP Dose Improves Safety

Highest Probability of Defined Outcomes

Next Steps: Precision to Drive Stakeholder Value Through ARCUS

Drive Organic Development in Sophisticated Edits

Focus on Insertions, Excisions and Eliminations

	PBGENE-HBV (Elimination)	PBGENE-PMM (Elimination)
Lead programs		
Key next steps	2023 ☑ Positive INTERACT FDA feedback received– alignment on on/off target assessment ☑ Final Clinical Candidate ☑ Initiate GLP Tox Starting Material 2023/24 ☐ GLP Tox Study Planning and Execution	2023 ☑ Final Clinical Candidate ☑ PoC and Dose Finding Studies underway 2024 ☐ Initiate GLP Tox
Target CTA/IND	2024	2025

Partnered Programs

IECURE
target filing OTC CTA/IND in H2 2023

NOVARTIS & PREVAIL
partnerships progressing well, further updates to be provided by respective partners

Thank you

Appendix

Glossary of Terms

AAV
Adeno Associated Virus, common viral delivery vehicle for gene therapy

Defined Outcome
Predictable, highly consistent, intended and THERAPEUTIC edit.

DNA template
Exogenously supplied DNA with homologous sequence to the cut target to direct repair

Efficiency
Percentage of cells that are edited

Elimination
Remove a genome (viral, mitochondrial)

Excision
Remove portion of genome

Heteroplasmy
Mixture of mutant and wild type mitochondrial DNA (mtDNA)

Homology-Directed Repair (HDR)
Matching of identical sequence between cut DNA and DNA template to guide repair outcome; also known as homologous recombination

Insertion
Insert gene to cause expression

Knockout
Cause scar in gene to stop expression

LNP
Lipid Nano Particles, common non-viral delivery vehicle to liver

Mitochondrial DNA (mtDNA)
DNA genome in the mitochondria

Mutant mitochondrial DNA Sequence
Mitochondrial genome that contains a base change, insertion, or deletion that disrupts function

Non-Homologous End-Joining (NHEJ)
Variable and unpredictable joining of cut ends

Nuclear DNA
DNA that is located within the nucleus

Off-Target Effects
Unexpected, unwanted, or even adverse alterations to the genome as a result of actions on untargeted genomic sites

On-Target Effect
Expected and desired alterations to the genome as a result of actions on intended genomic sites

Perfect Re-ligation
Seamless joining of complementary ends

Random Outcome
Distribution of inconsistent edits, many of which are not therapeutic or intended thereby effecting both the efficacy and safety profile

Repair
Remove defective and insert functional gene

Target Site Fidelity
How reliability the nuclease recognizes and binds it target site

Wild-type mitochondrial DNA Sequence
Mitochondrial genome that does not contain a base change, insertion, or deletion that disrupts function

Hemoglobinopathies are a Major World Health Problem

Sickle Cell Disease

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

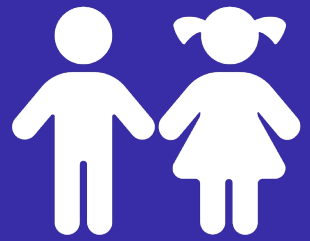
Sickle Cell Disease Affects **>300,000 newborns annually**

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

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



~68,000 children born with thalassemia each year

Ornithine Transcarbamylase (OTC) Deficiency is a Severe, Ultra Rare Genetic Condition with Extremely High Unmet Medical Needs

OTC Deficiency (OTCD)

- Results from genetic defect in a liver enzyme driving detoxification of ammonia.
- Patients with OTC build up excessive levels of ammonia in their blood, potentially resulting in acute and chronic neurological deficits and toxicities.
- Current treatments don't eliminate the risk of future metabolic crises and must be taken multiple times a day. The only curative approach is liver transplantation

Neonatal onset has been associated with **mortality rates** as high as **74%** [1]

~10,000

People with OTCD worldwide

- ~4,2-6.6k in the US[2]
- Disease prevalence is between 1 in 60,000 and 1 in 72,000

Neonatal onset disease occurs only in males, presents as severe disease, and can be fatal at an early age.

Mortality up to 90% [1]

[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 ≥ 150 µmol/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.

Duchenne Muscular Dystrophy Currently Lacks a Curative Treatment

On average, children **lose their ability to walk** by

age 12

Mutation on the X chromosome interferes with dystrophin protein production, which is needed to form and maintain healthy muscle

Affects approximately

1 in 3,500

live male births