

PRECISION  
BIOSCIENCES

*Investor Update on*  
***PBGENE-HBV Program***

American Association for the  
Study of Liver Disease (AASLD)

November 13, 2023



# 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; potential product liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates; the U.S. and foreign regulatory landscape applicable to our and our collaborators’ development of product candidates; our or our collaborators’ or other licensees’ ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; our or our collaborators’ other licensees’ ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; potential manufacturing problems associated with the development or commercialization of any of our product candidates; delays or difficulties in our and our collaborators’ ability to enroll patients; changes in interim “top-line” and initial data that we announce or publish; if our product candidates do not work as intended or cause undesirable side effects; risks associated with applicable healthcare, data protection, privacy and security regulations and our compliance therewith; the rate and degree of market acceptance of any of our product candidates; the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements; our current and future relationships with and reliance on third parties including suppliers and manufacturers; our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates; potential litigation relating to infringement or misappropriation of intellectual property rights; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate key executives and personnel; market and economic conditions; effects of system failures and security breaches; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events; effects of sustained inflation, supply chain disruptions and major central bank policy actions; insurance expenses and exposure to uninsured liabilities; effects of tax rules; risks related to ownership of our common stock; our ability to meet the requirements of and maintain listing of our common stock on NASDAQ or other public stock exchanges and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarterly period ended September 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](http://www.sec.gov) and the Investors page of our website under SEC Filings at [investor.precisionbiosciences.com](http://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.



# *Opening Remarks*



**Michael Amoroso**

*President & Chief Executive Officer*



# Today's Overview

## Singular Focus on Gene Editing with ARCUS

Internal Lead Program  
PBGENE-HBV

## ARCUS Potential Curative Strategy for HBV Elimination

- › ARCUS only modality to eliminate cccDNA and inactivate HBV DNA
- › PBGENE-HBV AASLD data demonstrates strong PoC for efficacy and safety
- › **Next Step To Complete:**  
Final PBGENE-HBV clinical candidate ready, plan CTA/IND in 2024

## KOL Perspective: Quest for a Functional Cure Through ARCUS HBV Elimination Strategy



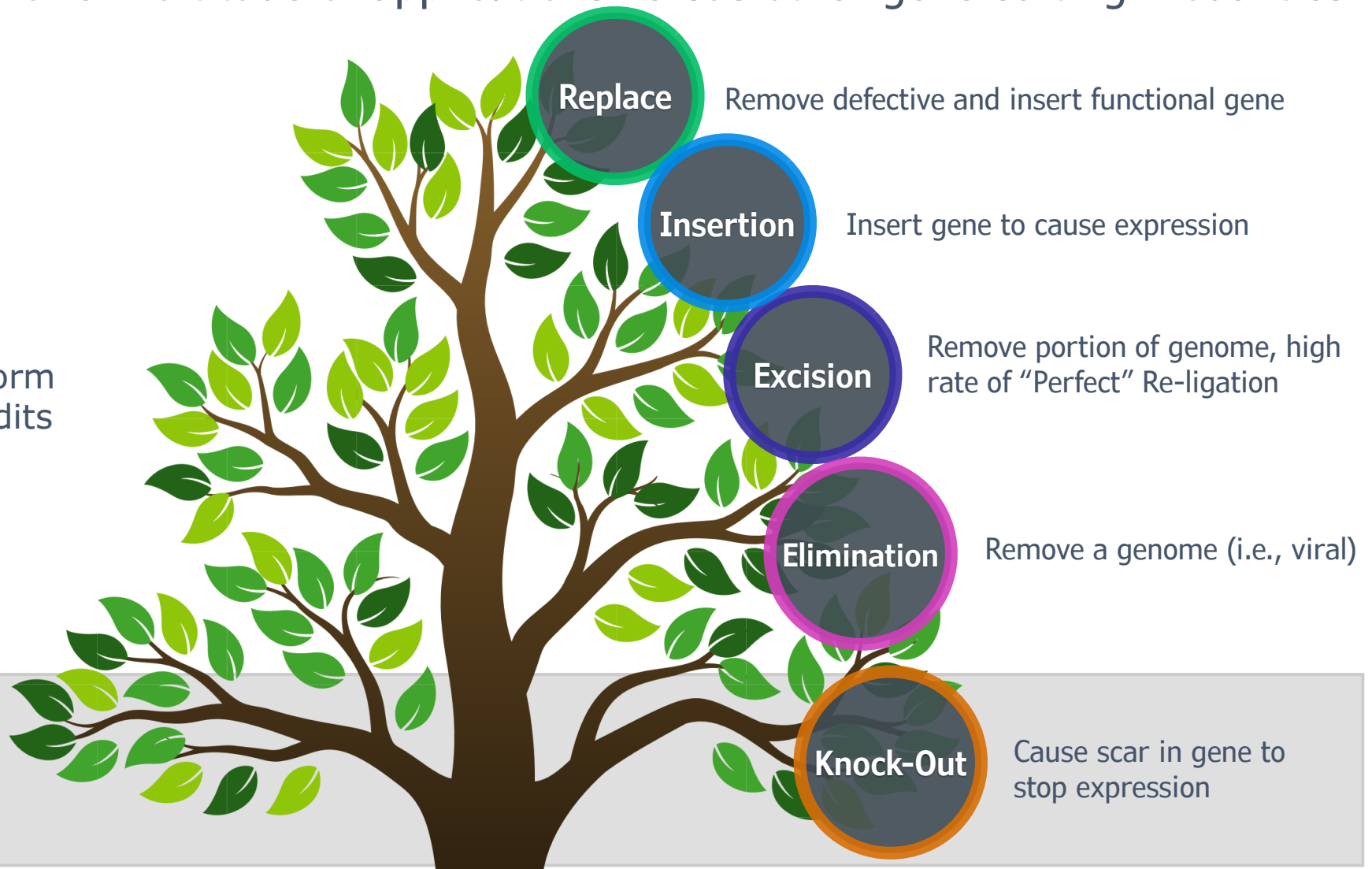
**Dr. Geoffrey Dusheiko**  
MD, FCP(SA), FRCS  
*Emeritus Professor of Medicine*  
*King's College Hospital & University*  
*College London*



# 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

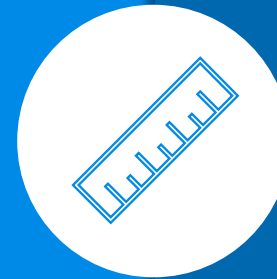
Degree of Difficulty



PBGENE-HBV  
Leverages the ARCUS  
Advantages of  
**Size & Simplicity**



The Cut



**The Size**

PBGENE-HBV Program

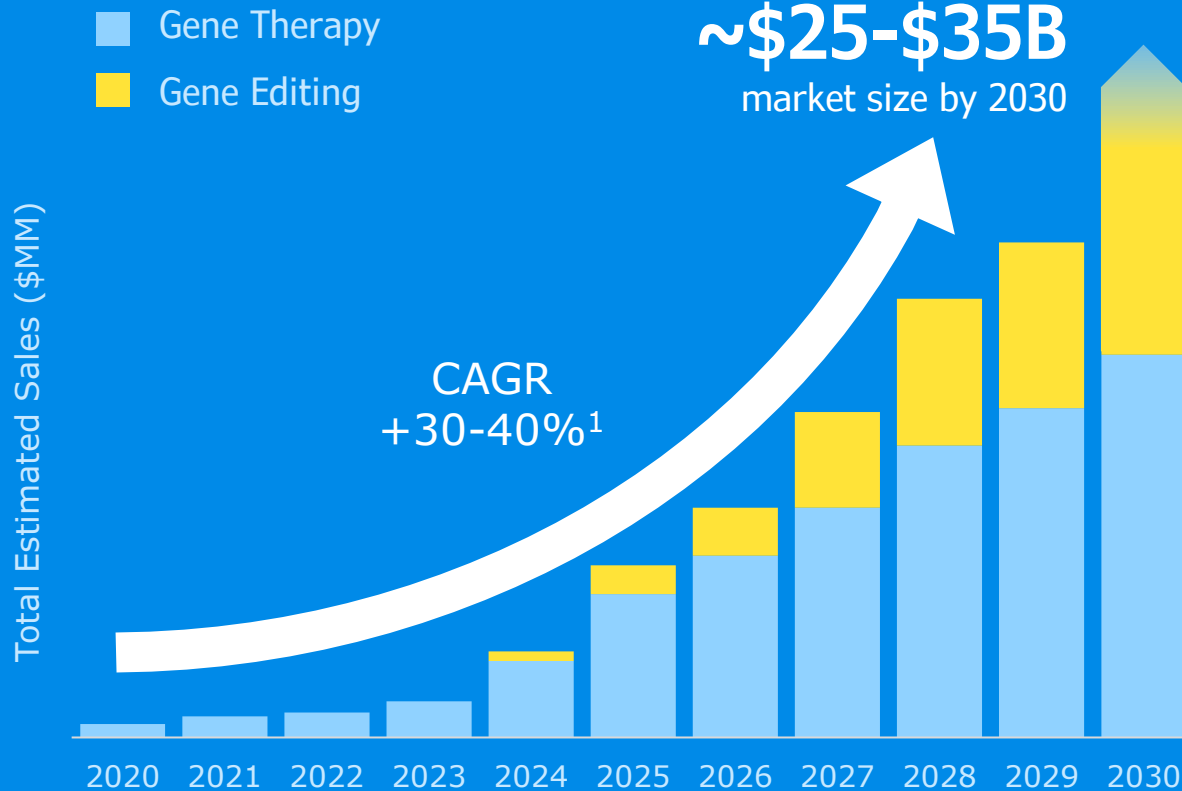


**The Simplicity**



# ARCUS Potential to Capture a Significant Portion of Genetic Medicines Market

## The Genetic Medicines Market Opportunity is Substantial



Precision's PBGENE-HBV program represents a market opportunity to treat

200-300k patients in US

with potential to treat an additional ~4.5M patients worldwide\*



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; worldwide patients include EU5, China and Japan that are currently drug treated with nucleos(t)ides analogs

# *ARCUS Potential Curative Strategy for HBV Elimination*



**Cassie Gorsuch, PhD**

*Vice President, Head of Gene Therapy Discovery*





# PBGENE-HBV Program Accomplishments

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

FDA INTERACT Meeting in July

Final Clinical Candidate Nominated

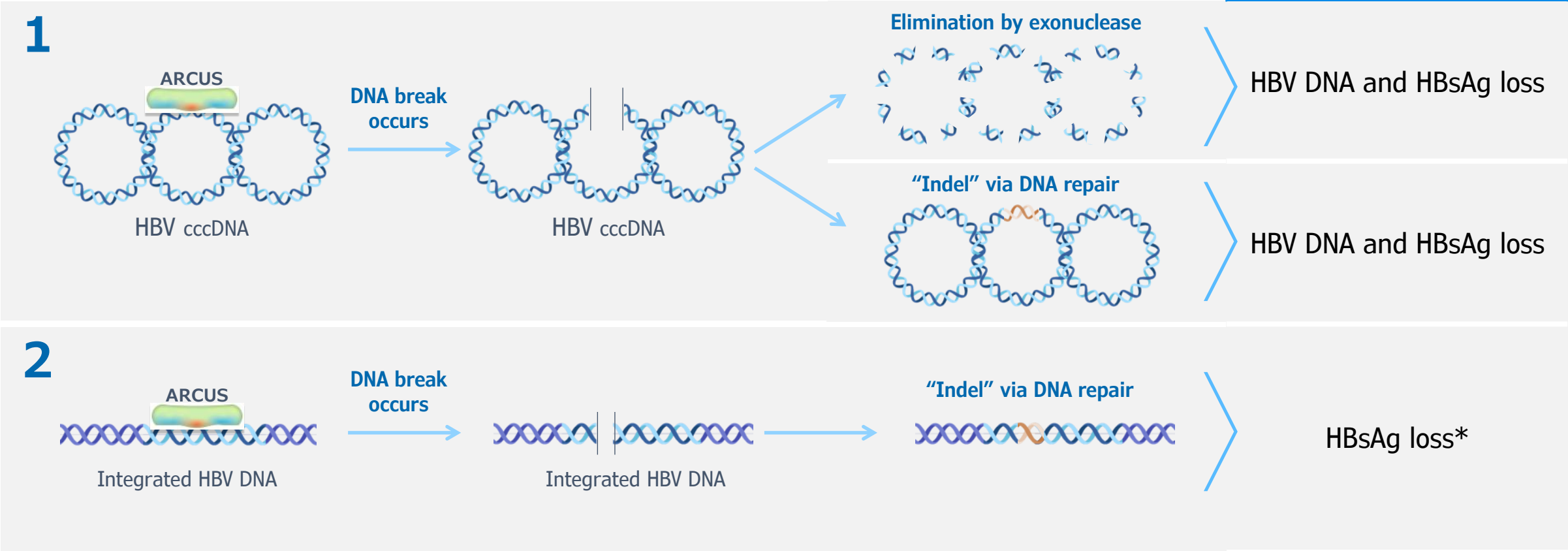
*on-track*  Submit IND/CTA in 2024

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



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

## Therapeutic Outcomes



\*Note: Integrated DNA does not produce HBV DNA

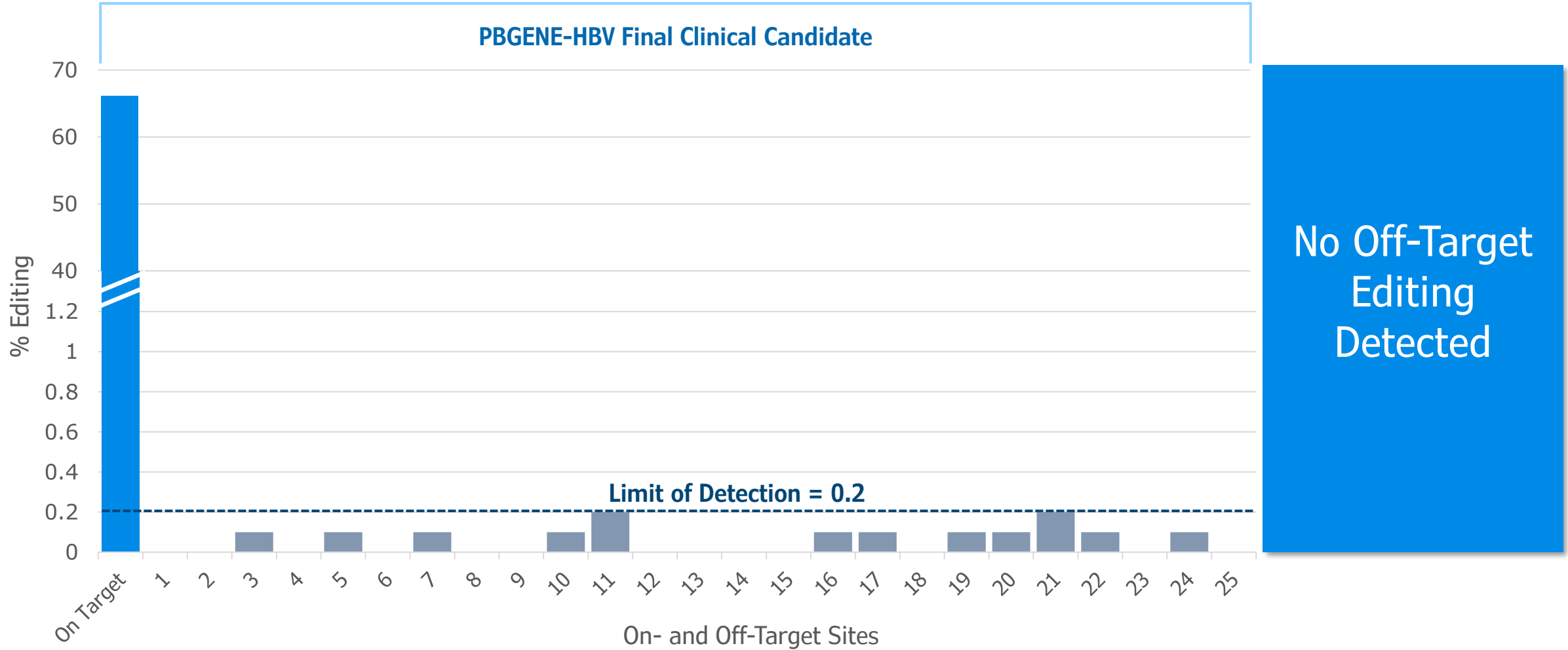
# AASLD 2023 Data Update

## Summary of New PBGENE-HBV Data Presented

- Enhanced Specificity With No Detectable Off-Target Editing at Maximal On-target Editing Dose
- NHP Study Demonstrates Up to 99% Viral Engagement
- Eliminates cccDNA and Inhibits Viral Markers in PHH
- ~95% Durable HBsAg Reduction Across Doses in Mouse Study
- Significant HBV DNA Reduction in Transgenic Mouse Supports Potential for Stopping NUC and Functional Cures in Future FIH Study



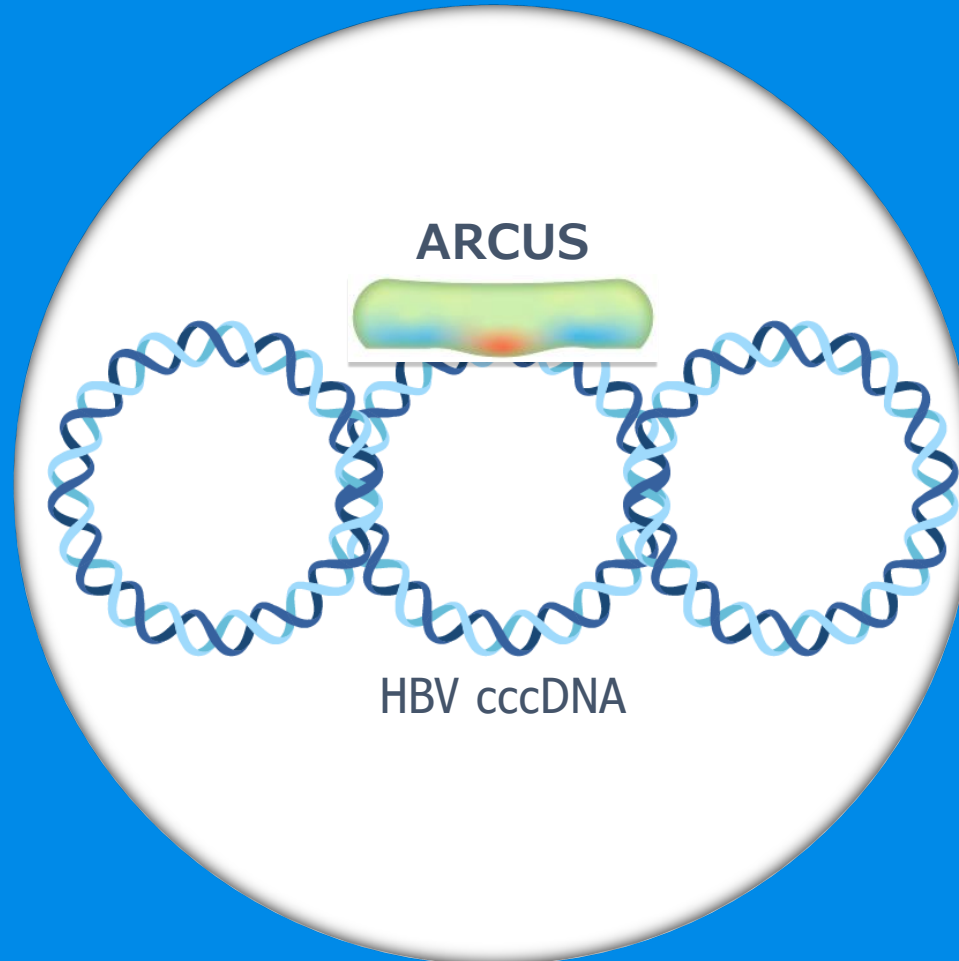
# Safety: PBGENE-HBV Final Clinical Candidate Shows Enhanced Specificity With No Detectable Off-Target Editing



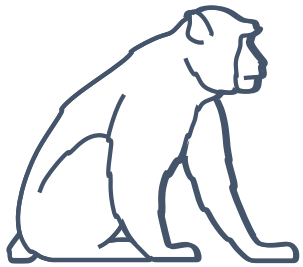
Notes:

- 1. The final optimized clinical candidate nuclease shows enhanced specificity from prior versions by eliminating off-target editing above LOD when examining 384 potential off-target sites

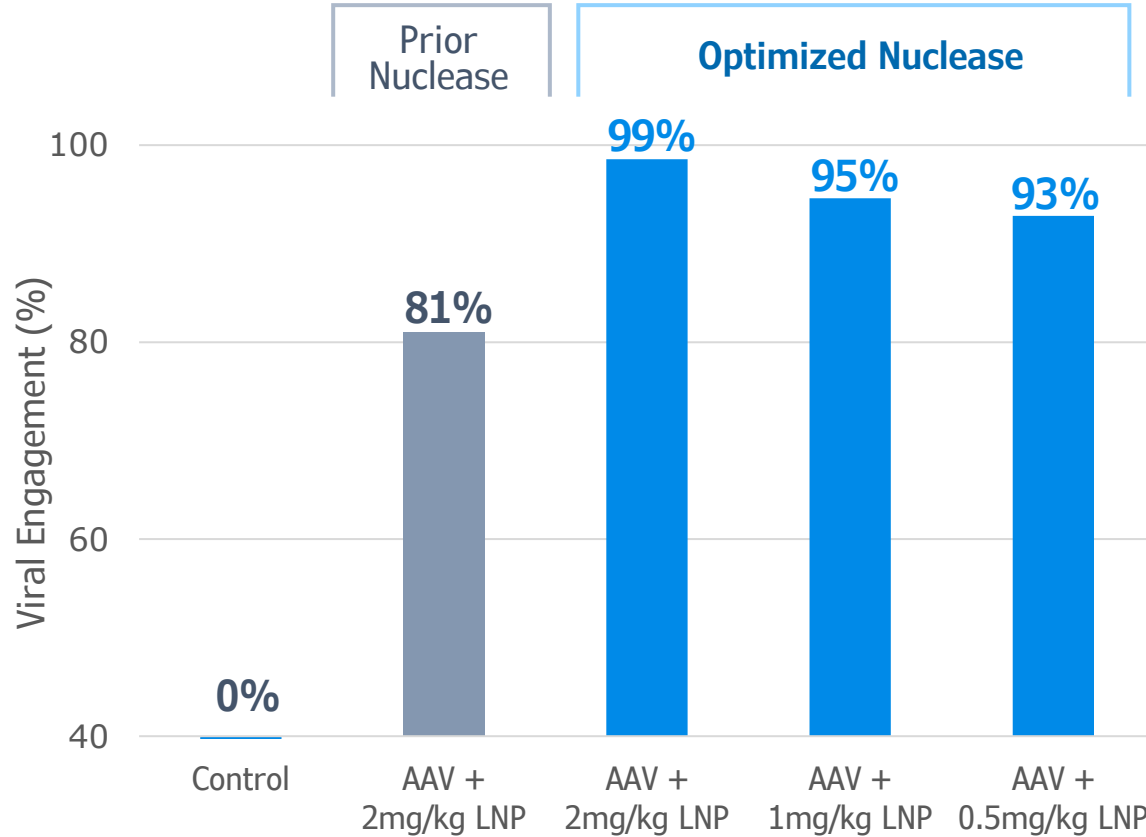
Eliminate  
cccDNA



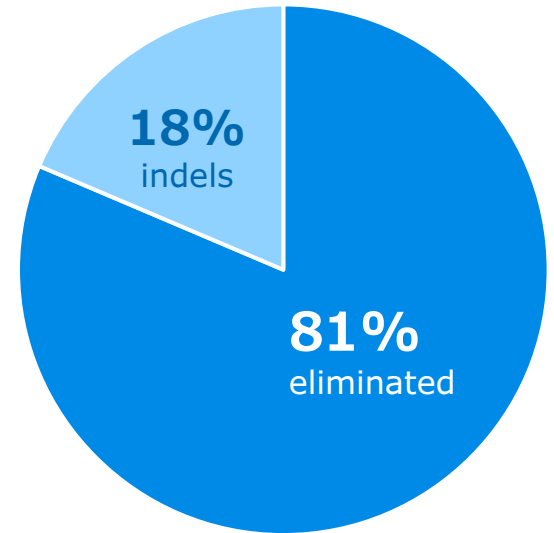
# Efficacy: Non-Human Primate (NHP) Study Demonstrates Up to 99% Viral Engagement, Suggestive of Strong Potential Efficacy Profile of PBGENE-HBV



ARCUS LNP



99% viral engagement at highest dose in NHP study



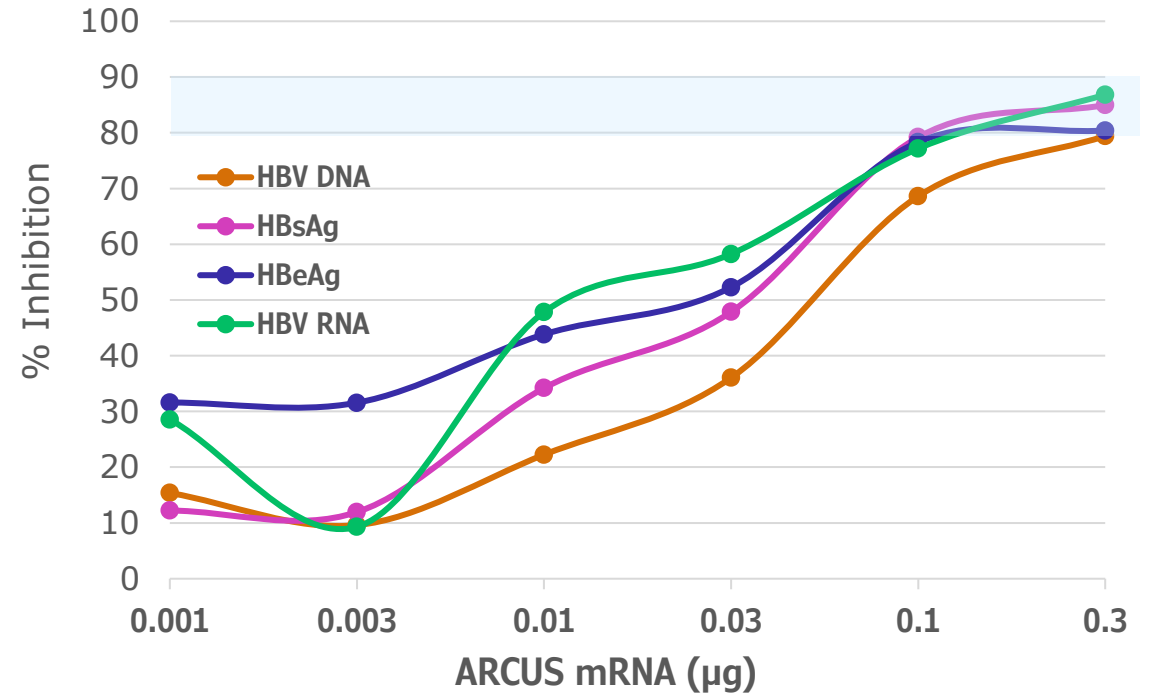
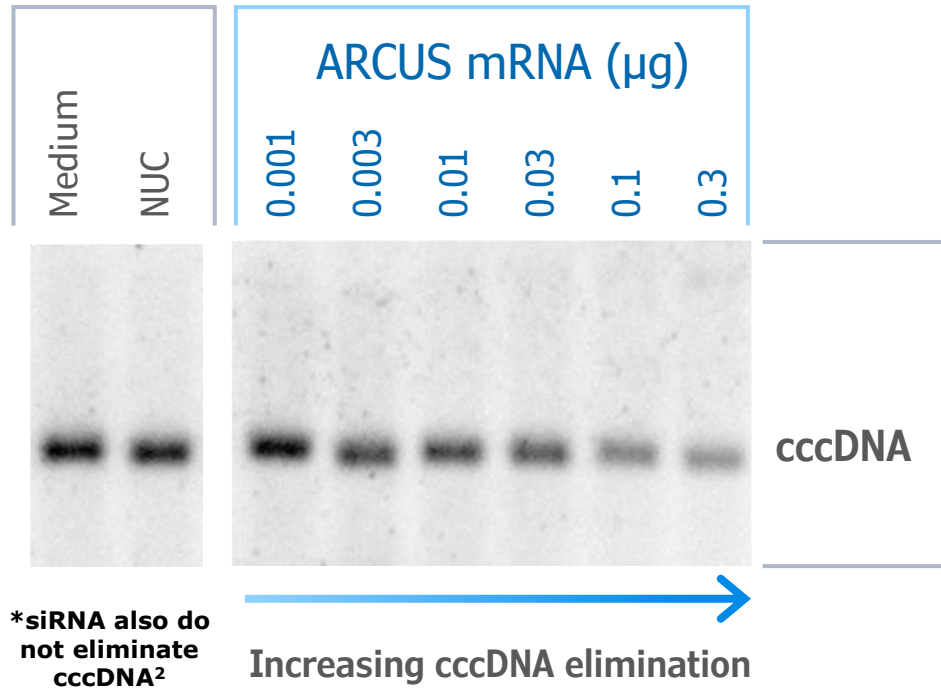
**★ Final clinical candidate expected to eliminate majority of cccDNA, this unique mechanism of action is critical to drive durable functional cures**

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: PBGENE-HBV Eliminates cccDNA and Inhibits Viral Markers in HBV-Infected Primary Human Hepatocytes (PHH)



**Proof of principle: Final clinical candidate nuclease demonstrates a dose-dependent elimination of cccDNA**

**Final clinical candidate reduces HBsAg, HBeAg, HBV DNA, and HBV RNA by 80-90% (vs. 77% HBsAg and 80% HBV DNA reduction in prior nuclease)**



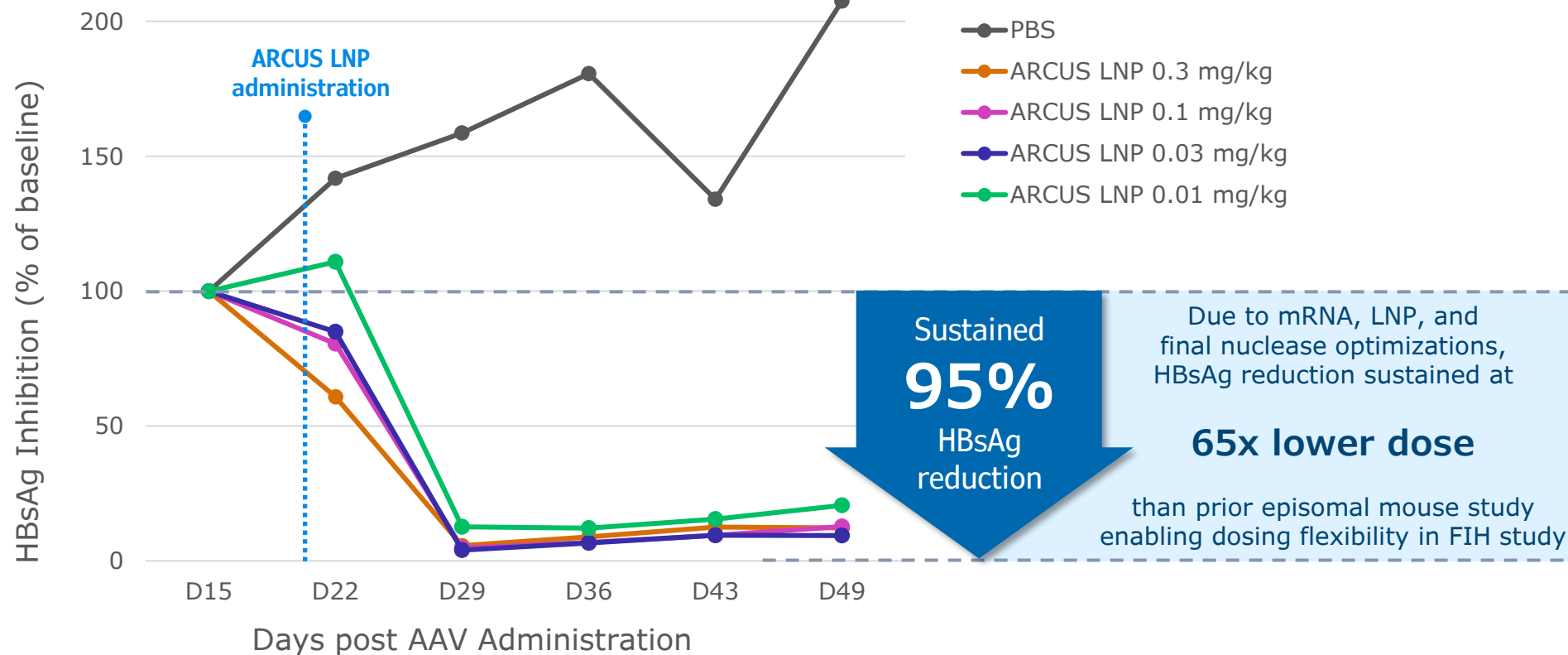
Notes:

1. NUC is nucleos(t)ide analog and in this experiment, lamivudine (LAM) was used
2. Therapeutic shutdown of HBV transcripts promotes reappearance of the SMC5/6 complex and silencing of the viral genome in vivo; Allweiss L., et al. 2022

# Efficacy: PBGENE-HBV Demonstrates Up to 95% Durable HBsAg Reduction Across Dose Levels in Episomal Mouse Study



Prior Nuclease	Final Clinical Candidate
90% viral engagement	95% viral engagement



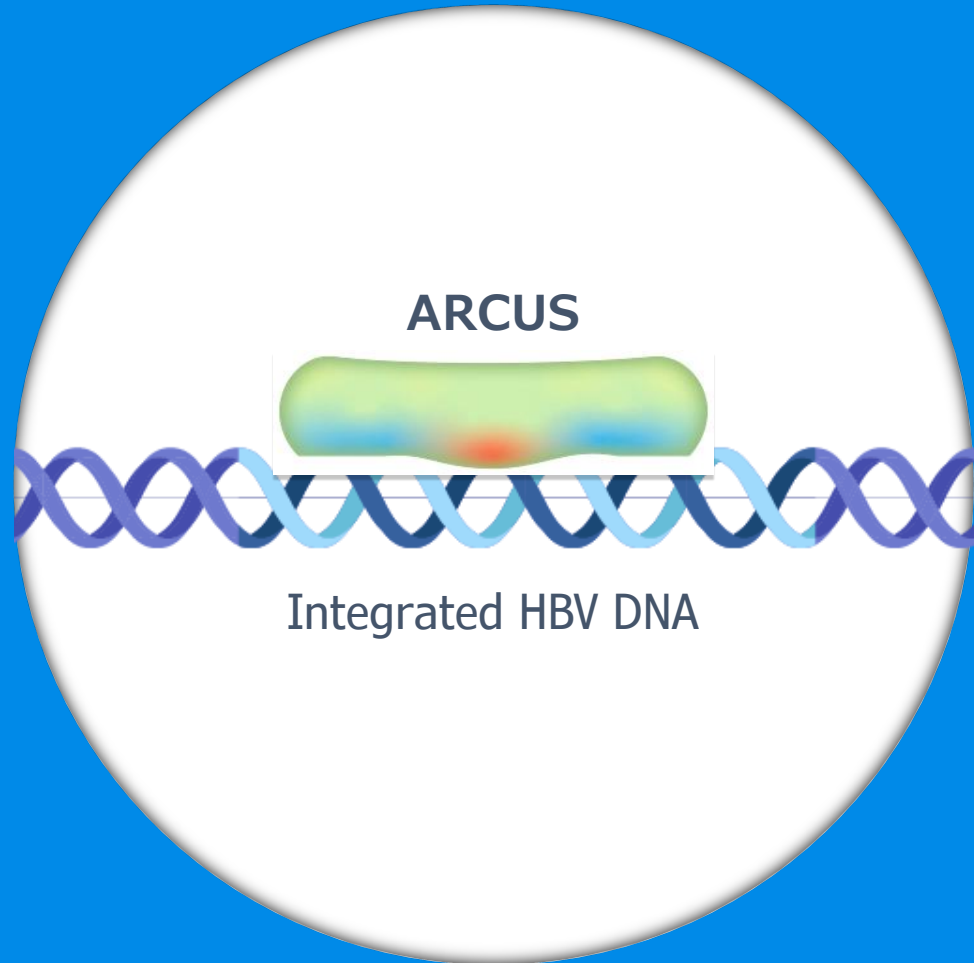
★ Final clinical candidate nuclease offers dosing flexibility while continuing to demonstrate high viral engagement resulting in significant and durable HBsAg reduction necessary to drive functional cures

Notes:

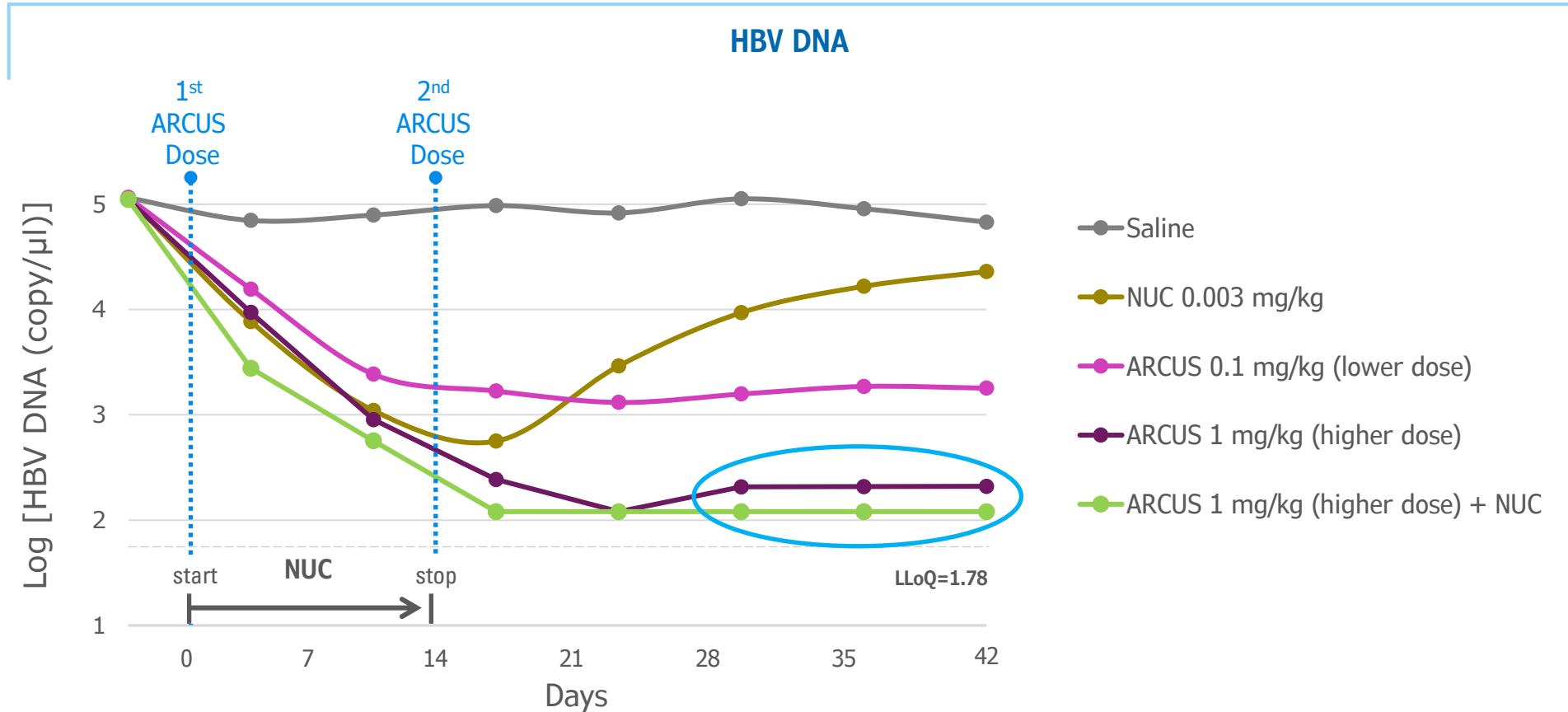
1. Prior nuclease data shared at R&D Day in September '23, and prior nuclease tested at a higher 2mg/kg dose
2. Viral engagement (elimination +/- inactivation through indels); ARCUS LNP administration at D21



# Inactivate Integrated HBV DNA



# 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

Notes:  
1. NUC = nucleos(t)ide analog, entecavir used in this study  
2. HBV DNA levels measured in plasma

# ARCUS

## Potential Curative Strategy for HBV

- › Eliminate cccDNA
- › Inactivate HBV DNA

- **Simplicity of ARCUS:** single component editor offers advantages when applied to HBV elimination
- **mRNA Sequence Optimization:** 8x improvement in protein expression permitting dosing flexibility
- **ARCUS Dual Mechanism:** eliminates cccDNA and inactivates integrated HBV DNA across models in robust preclinical package
- **First Gene Editor in HBV:** ARCUS is engineered to benefit wide-range of patients by targeting >92% of isolates across genotypes



# *The Quest for a Functional Cure Through ARCUS HBV Elimination Strategy*



**Dr. Geoffrey Dusheiko, MD, FCP(SA), FRCS**  
*Emeritus Professor of Medicine  
King's College Hospital & University College London*

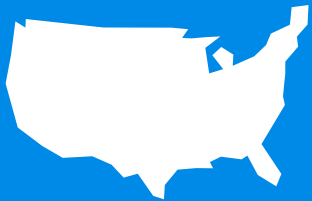


# HBV Currently Lacks a Curative Treatment

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

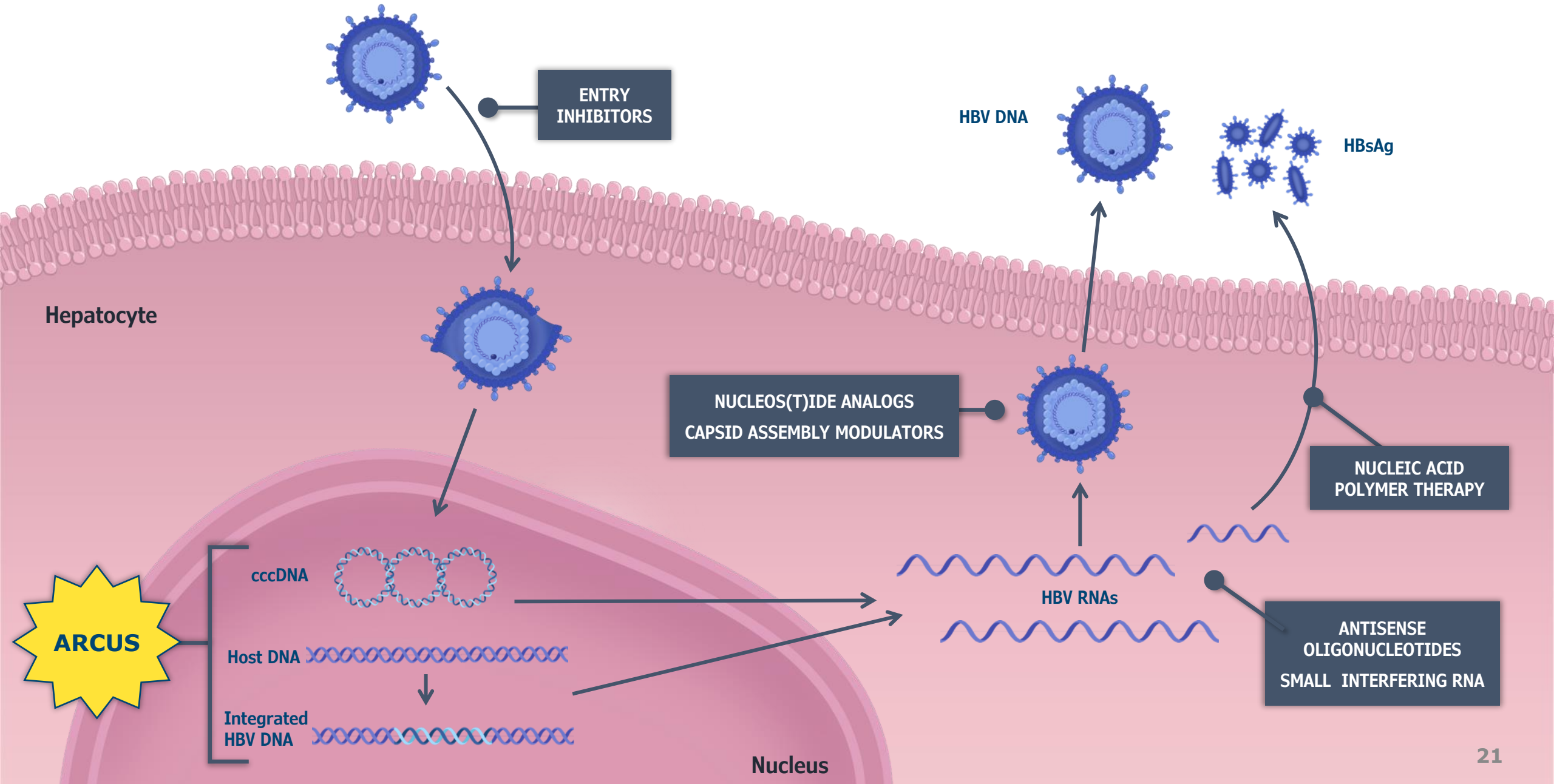


with HBV infections may develop complications, such as cirrhosis, liver failure, or liver cancer, which account for the majority of HBV-related deaths.

Current HBV treatments require life-long chronic treatment that may result in viral suppression by reducing circulating HBV DNA, but **these therapies do not eliminate HBV cccDNA and inactivate integrated HBV DNA.**



# Hepatitis B – ARCUS is Differentiated Versus Other Approaches

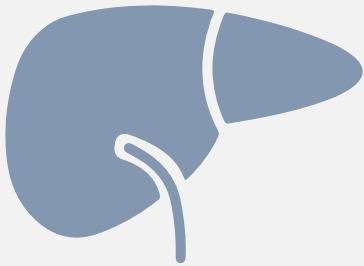


# The Quest for a Functional Cure Through HBV Elimination Strategy

**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



# Q&A



**Cassie Gorsuch, PhD**

Vice President, Head of Gene Therapy Discovery  
Precision BioSciences, Inc.



**Dr. Geoffrey Dusheiko, MD**

Emeritus Professor of Medicine  
Royal Free Hospital & University College





# Near-Term Catalysts Include Filing CTA/IND for PBGENE-HBV in 2024

1

## Drive Organic Development

Focus on Eliminations, Excisions and Insertions

Lead programs

PBGENE-HBV  
(Elimination)

PBGENE-PMM  
(Elimination)

Targeted  
CTA/IND

2024

2025

Lead Program

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\*

in partnership with

in partnership with

**Prevail**  
THERAPEUTICS

A Wholly Owned Subsidiary  
of Eli Lilly and Company

**NOVARTIS**

**ECURE**

CTA/IND filing expected  
before end of 2023

Near Term  
Catalyst



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

# *Appendix*

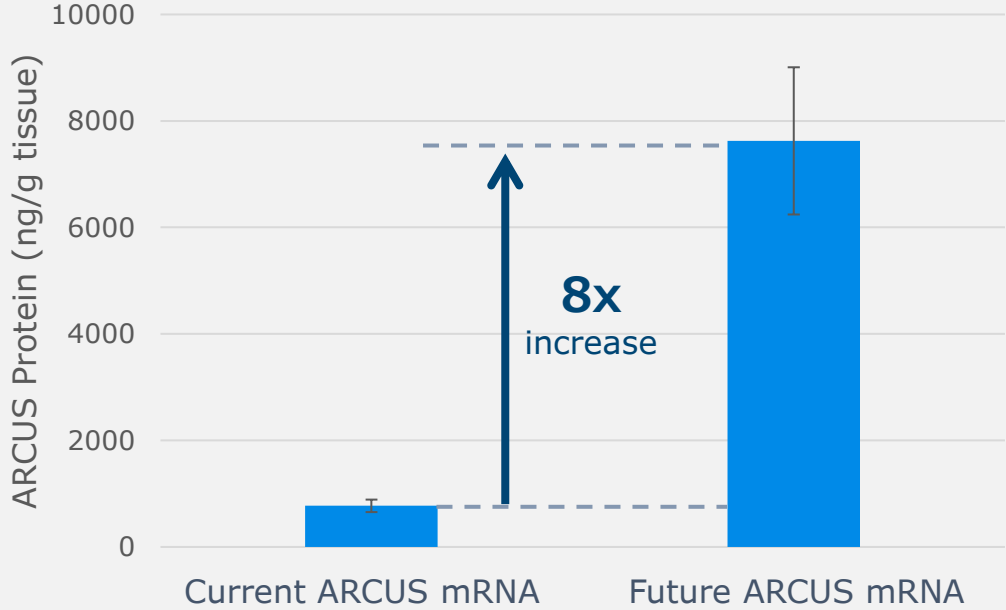


# Through Our PBGENE-HBV Program Enhancements, We Have Conducted mRNA Optimization



**mRNA Sequence Optimization**

ARCUS Protein Expression in Mice

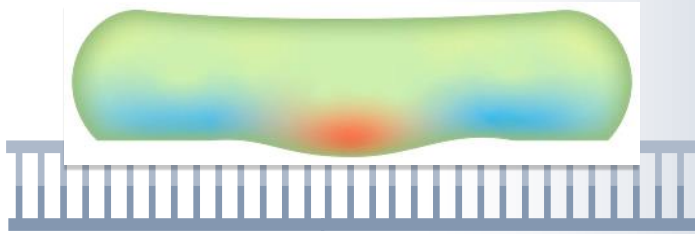


# Taking Advantage of ARCUS Simplicity for HBV

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

› Easy to deliver

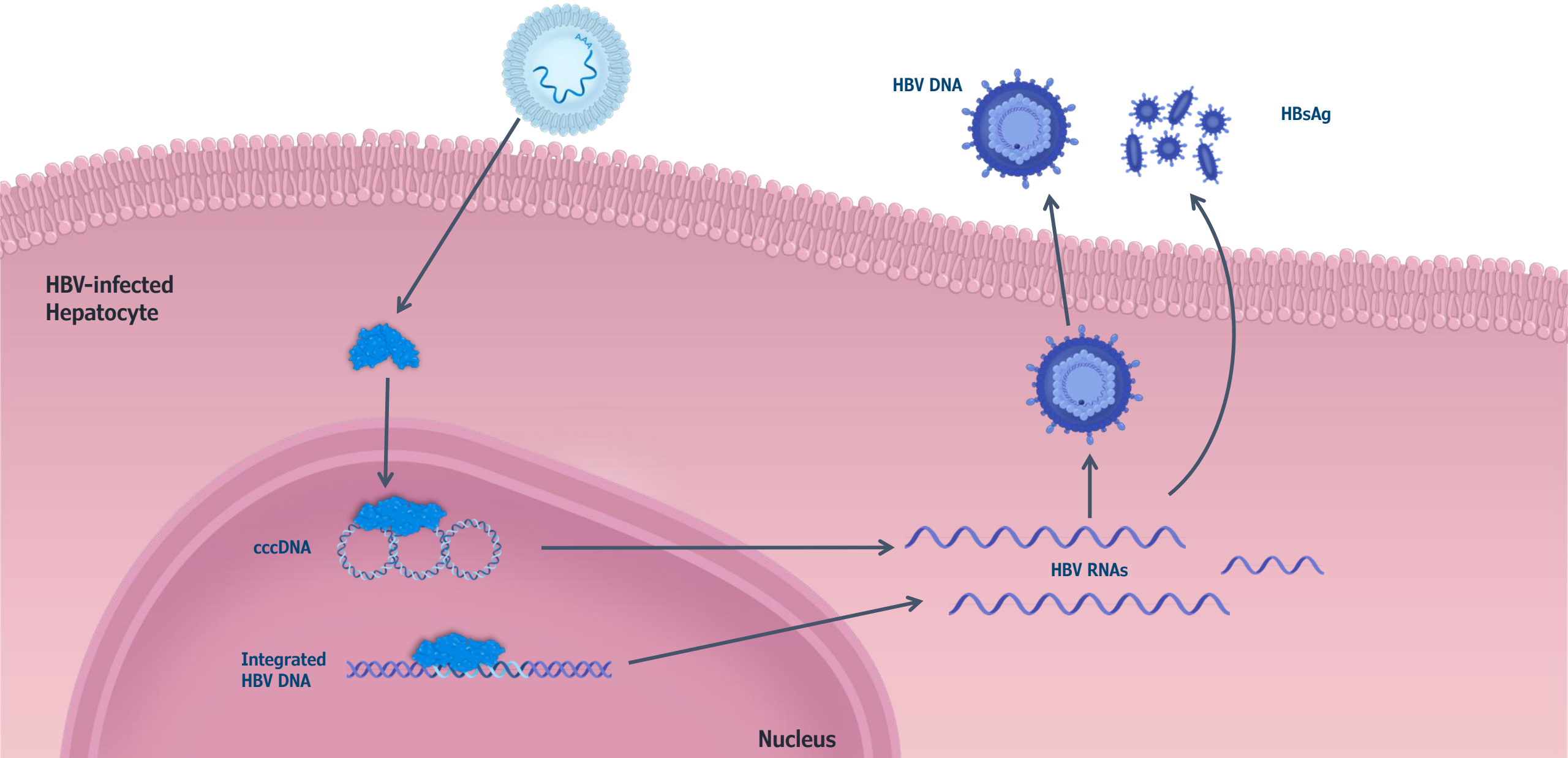
› High efficiency

› Low dose improves safety



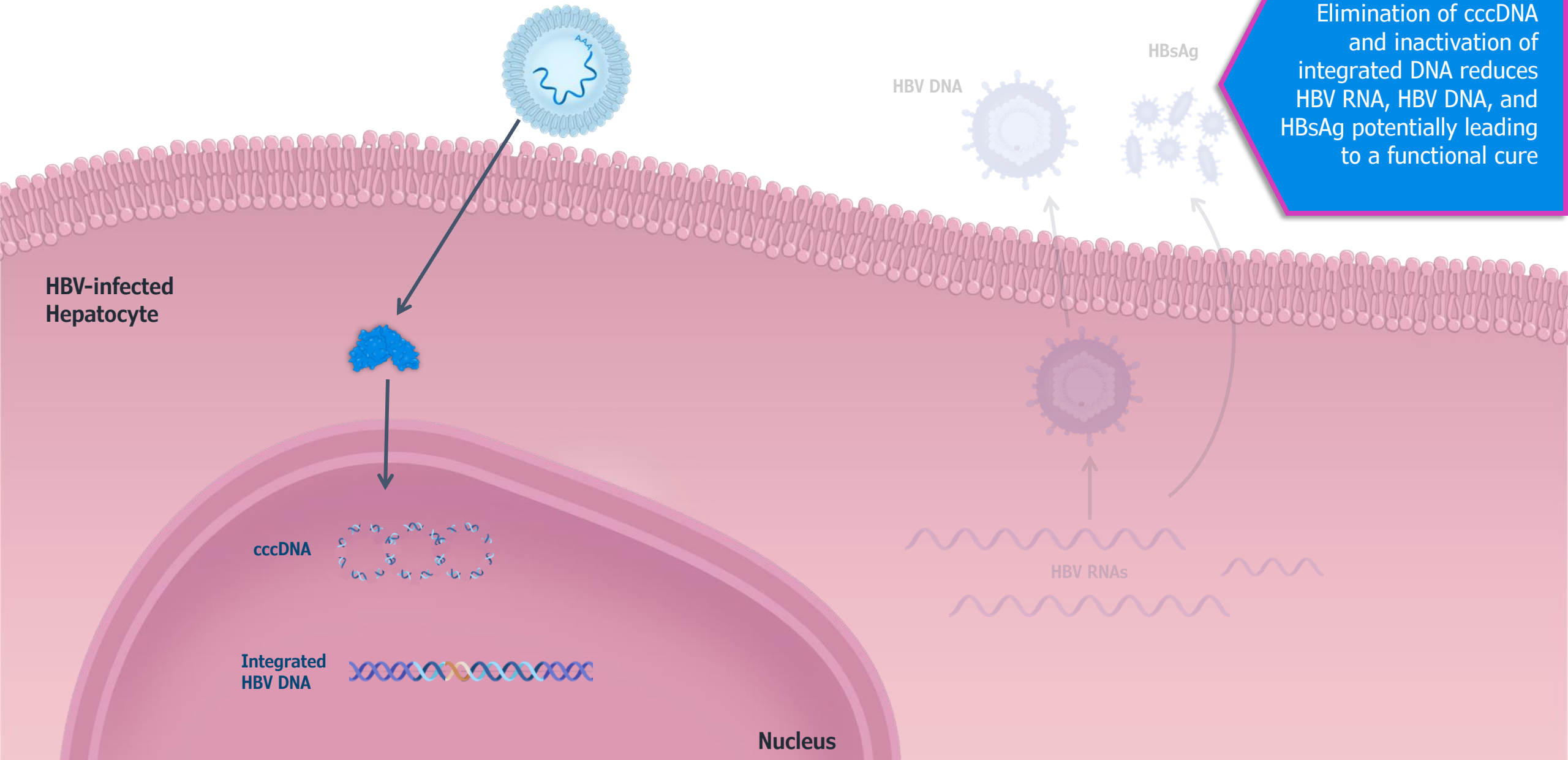
# ARCUS Approach for a Functional Cure

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



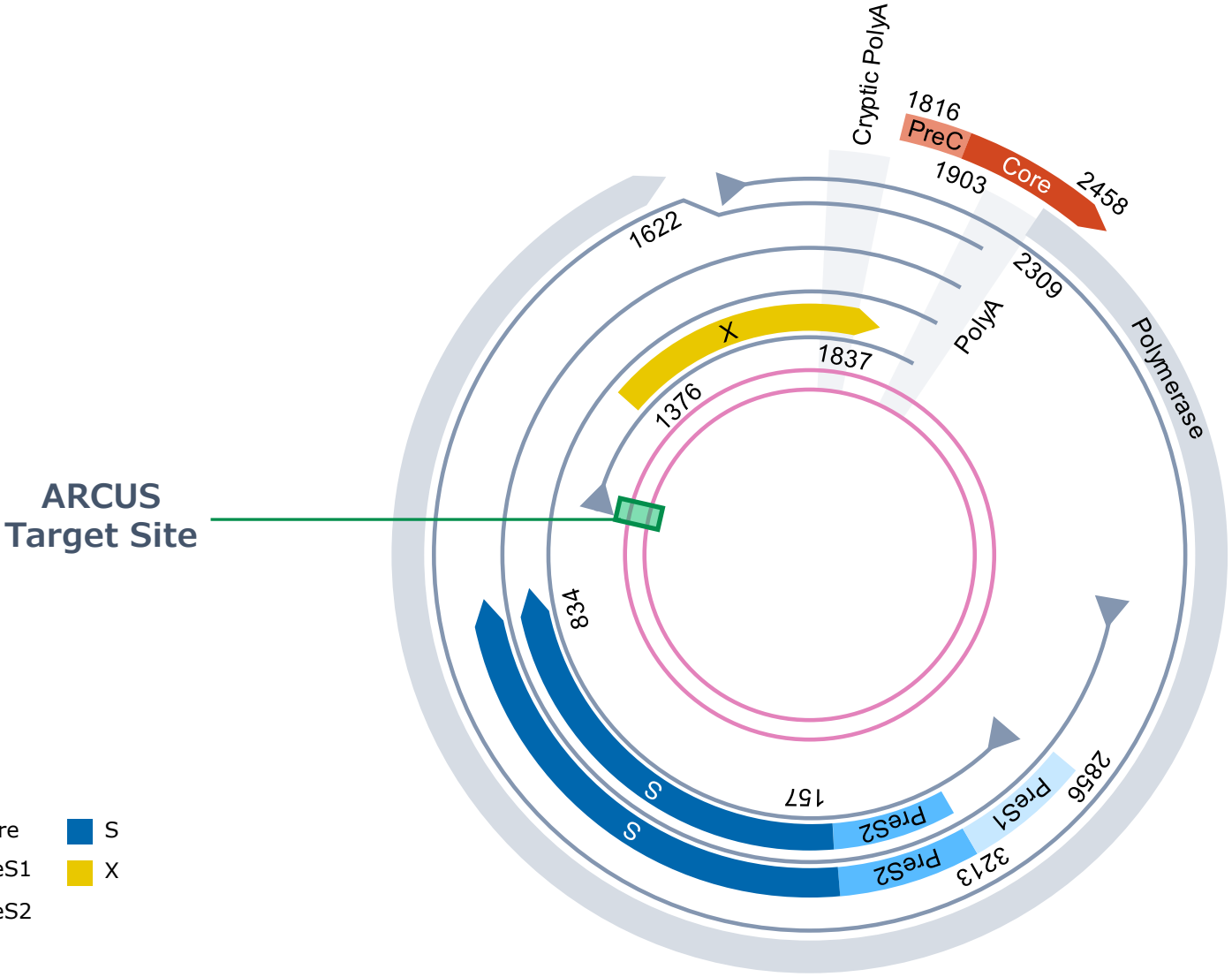
# ARCUS Approach for a Functional Cure

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

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



Target site conserved in **92%** of isolates across genotypes<sup>1,2</sup>

- Core
- S
- PreS1
- X
- PreS2



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

