Targeting Hepatitis B cccDNA with a Sequence-Specific ARCUS Nuclease to Eliminate Hepatitis B Virus *In Vivo*

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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.

Disclosures

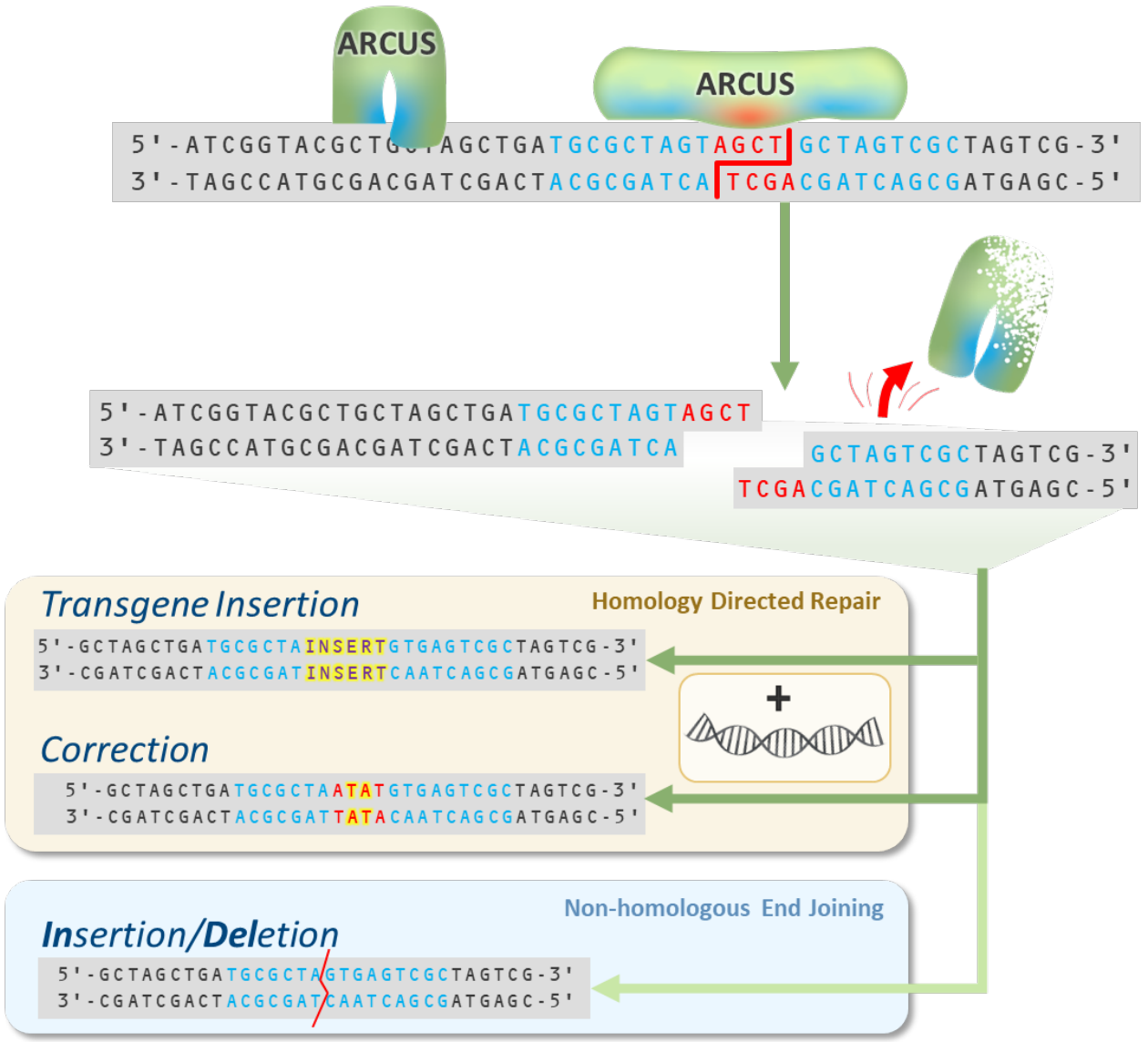
- I am an employee of Precision BioSciences, Inc. (Nasdaq: DTIL)

Overview

- Introduction to ARCUS and a HBV gene editing therapeutic approach
- Targeting HBV cccDNA in primary human hepatocytes (PHH)
- Novel HBV episomal mouse and non-human primate (NHP) models

ARCUS: Engineering Nature's Genome Editing System

- ARCUS is derived from I-CreI, a naturally-occurring green algae homing endonuclease
- Single protein of two linked monomers, which recognize a 22 bp DNA target site
- Target site recognition and cleavage rely solely on an extensive DNA-protein interface
- DNA cleavage results in 3' sticky ends
- Small size (364 amino acids) facilitates delivery



ARCUS Gene Editing: Rationale for HBV Cure

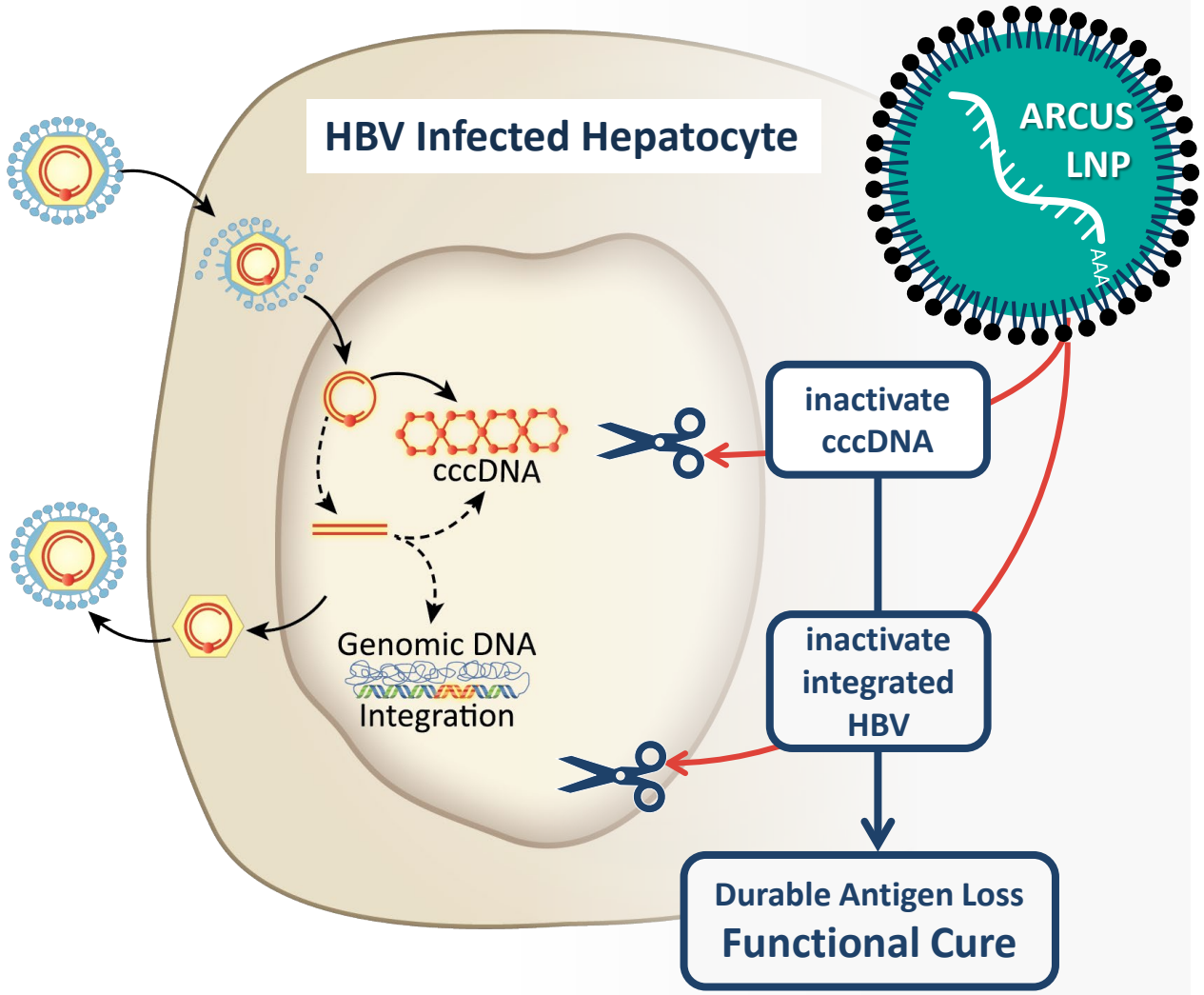
ARCUS-mediated inactivation of cccDNA and integrated HBV could result in a functional cure

Chronic HBV (cHBV) unmet need is massive

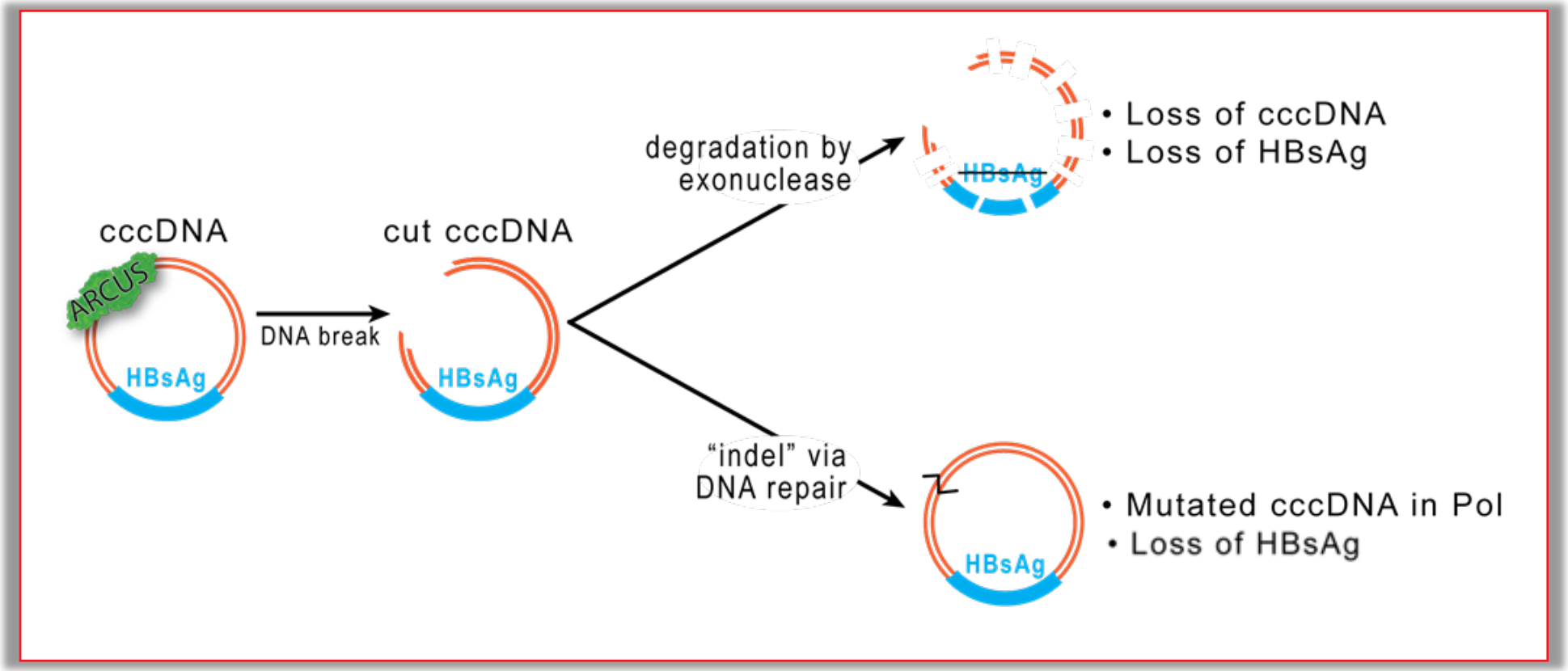
US >860,000 cHBV infections

Globally >200 million cHBV infections

- >90% of infected infants develop cHBV
- ≤50% of infected children 1-5 years develop cHBV
- 5-10% of infected healthy adults develop cHBV



cccDNA Fate After ARCUS Cleavage

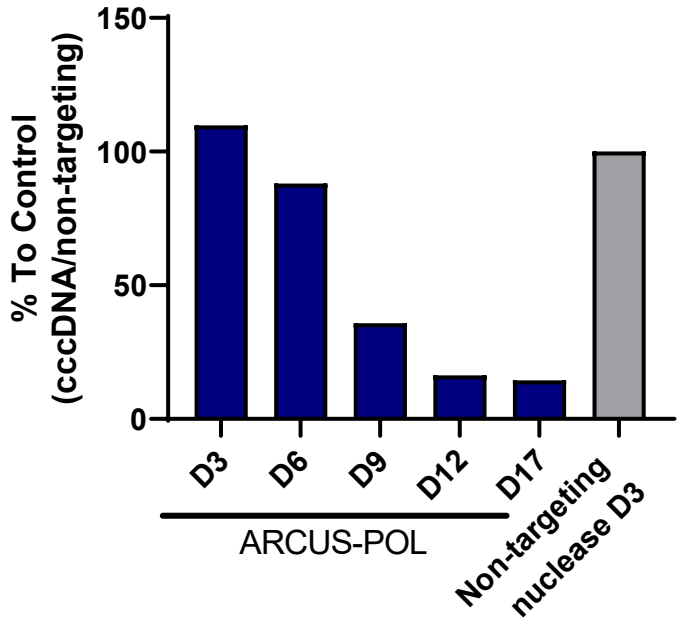


ARCUS-POL targets a highly conserved site in the HBV polymerase gene

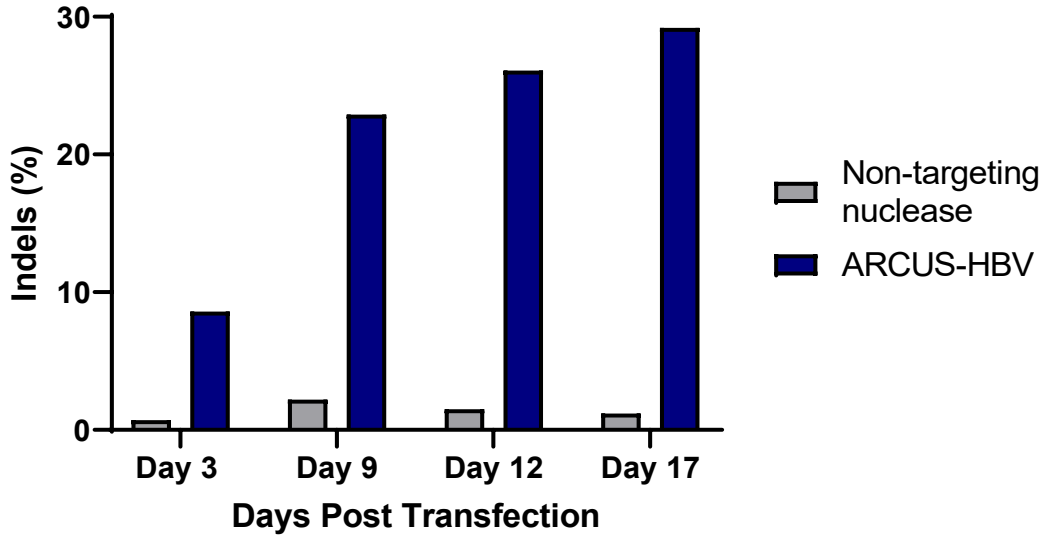
ARCUS Nuclease Activity in HBV-Infected Primary Human Hepatocytes

In HBV-infected primary human hepatocytes (PHH), ARCUS-POL showed an 85% reduction in cccDNA and 30% of the remaining cccDNA contained indels.

cccDNA Degradation



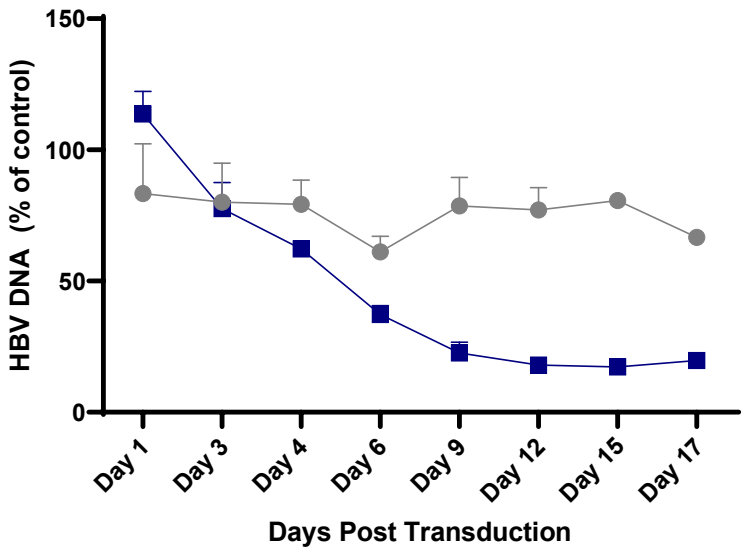
cccDNA Indels



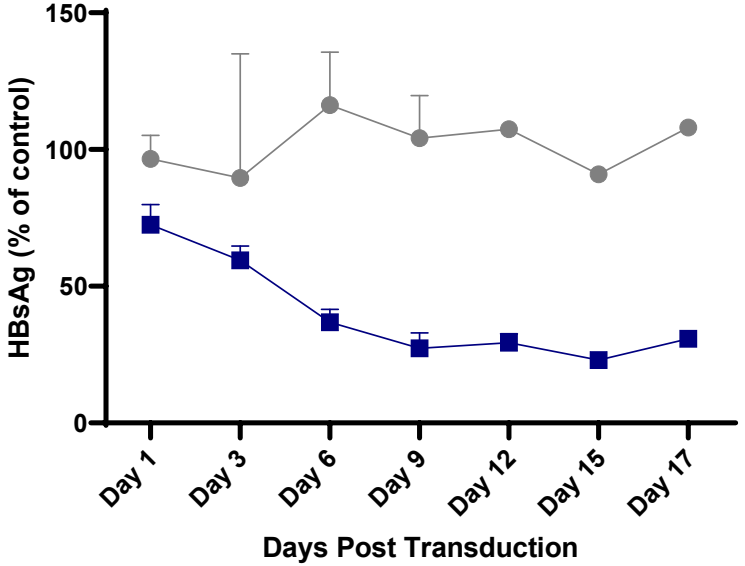
ARCUS Nuclease Activity in HBV-Infected Primary Human Hepatocytes

ARCUS-POL treated cells demonstrated an 80% reduction in extracellular HBV DNA and a 77% reduction in secreted sAg, and no change in albumin.

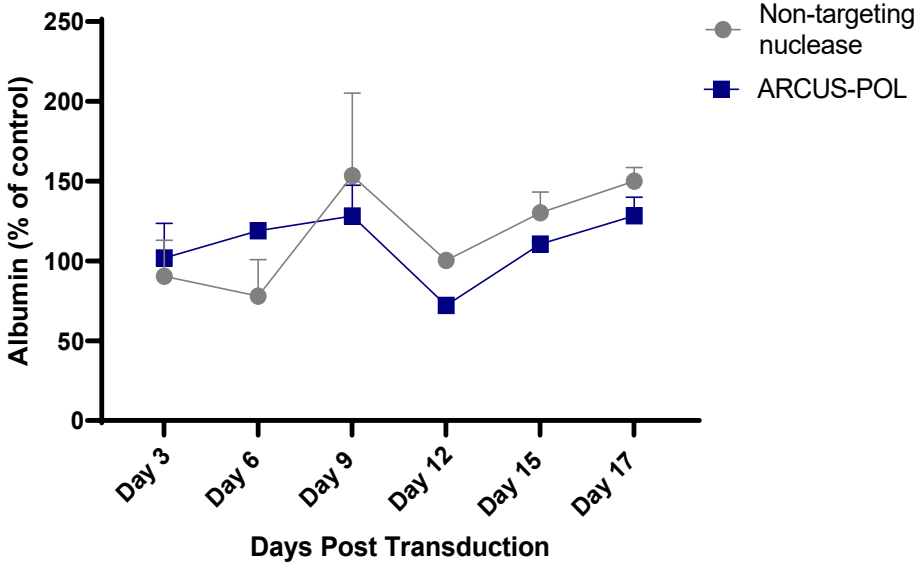
Extracellular HBV DNA



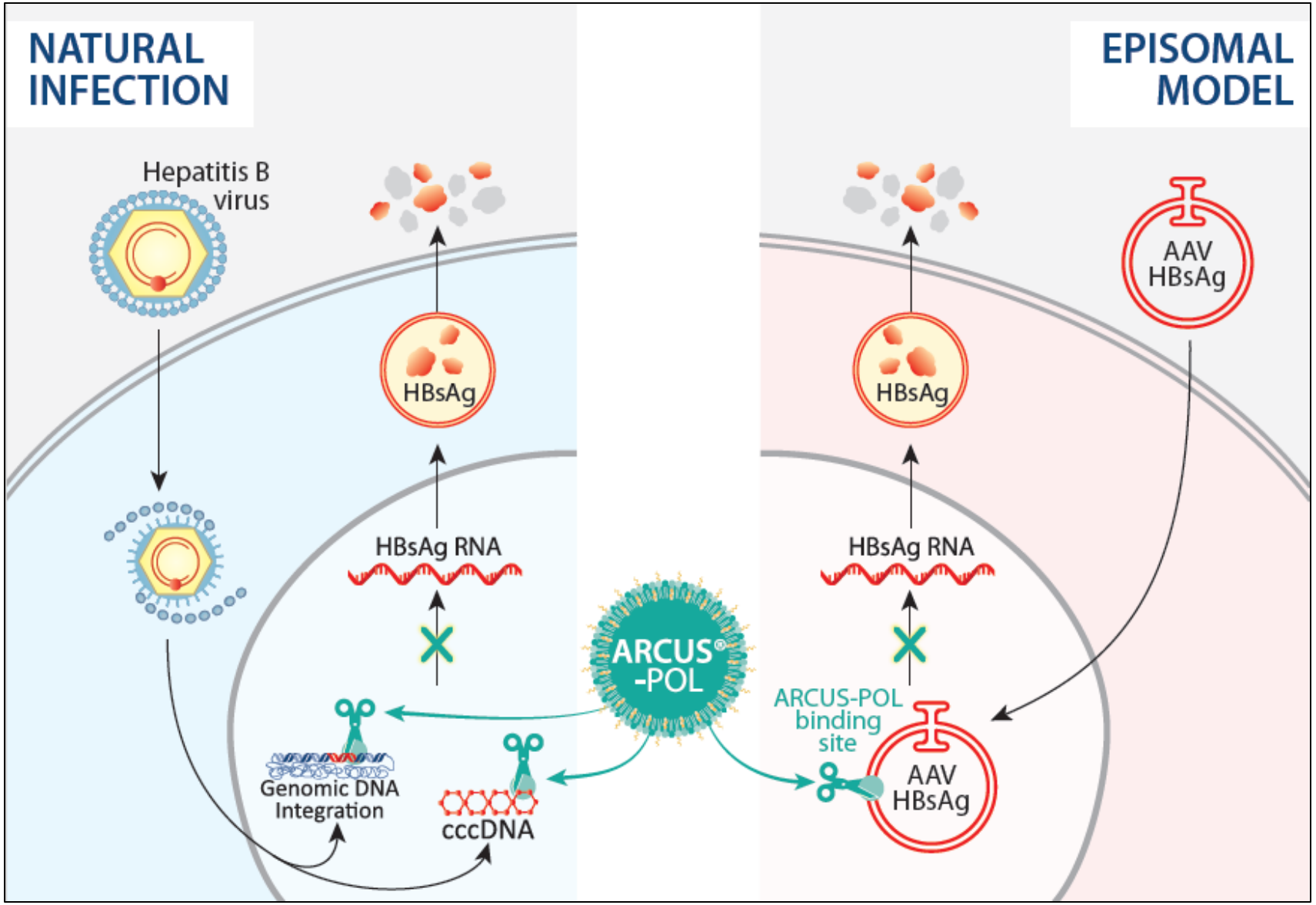
Extracellular HBsAg



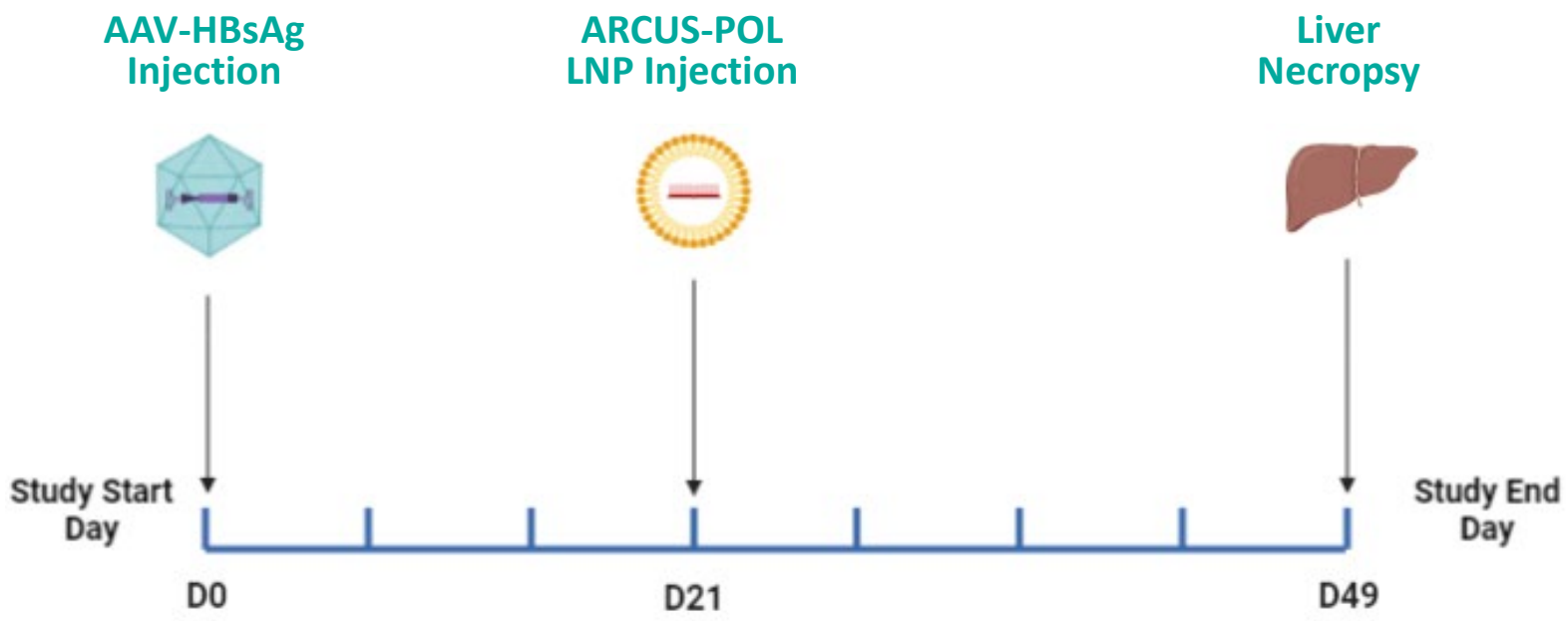
Extracellular Albumin



HBV Episomal *In Vivo* Model



Episomal Mouse Model—Outline

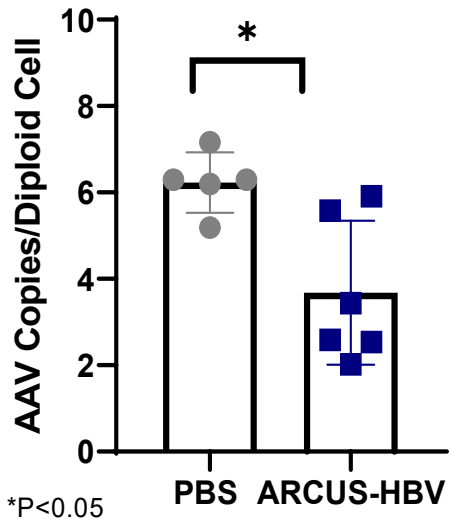


- AAV HBsAg Dose: 5e11vg
- ARCUS-POL LNP Dose: 2 mg/kg
- Weekly blood draws for HBsAg

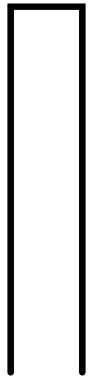
Episomal Mouse Model—Molecular Analyses

- The ARCUS-POL nuclease significantly reduced AAV copies in the liver compared to the PBS control group.
- The remaining AAV had an average of 86% indels in the ARCUS-POL treated group.
- The AAV degradation and indel formation resulting from ARCUS-POL cutting resulted in a 96% sustained reduction in HBsAg from one week post ARCUS-POL administration until necropsy at week seven.

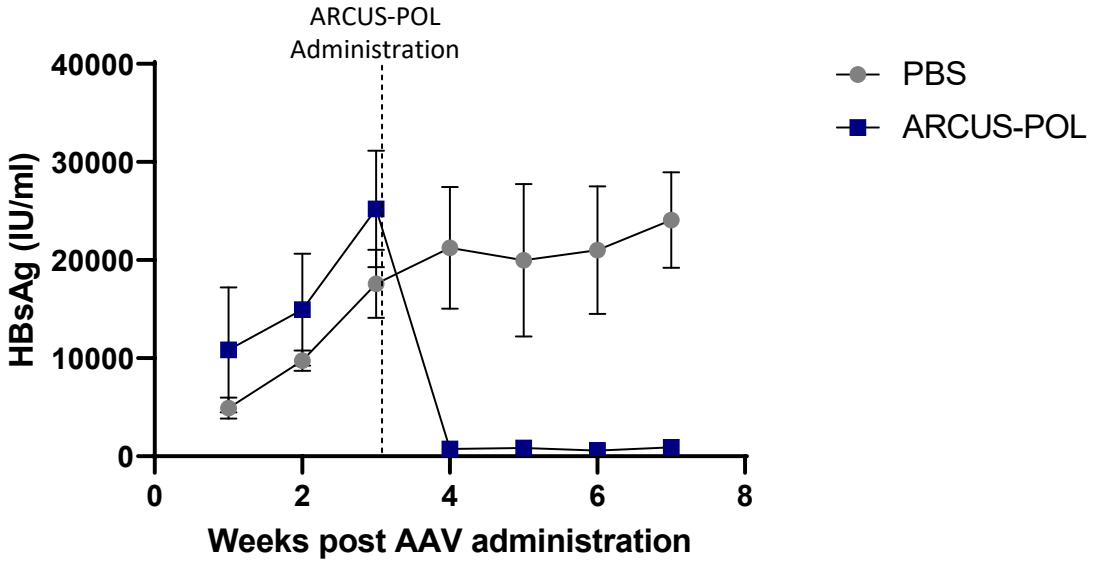
AAV Copy Number



AAV Indels



Secreted HBsAg

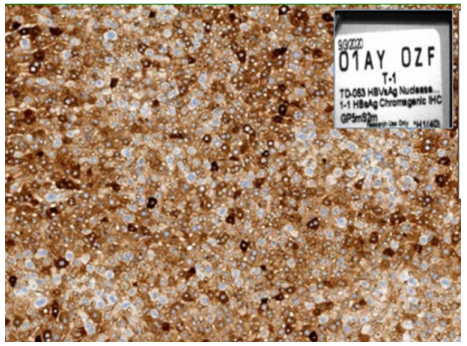
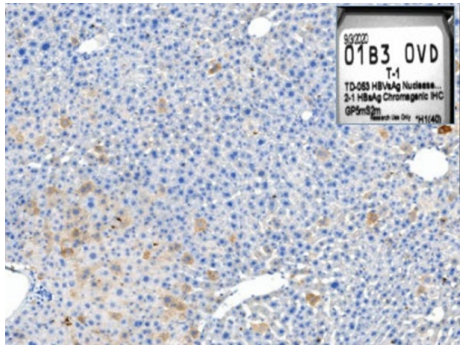
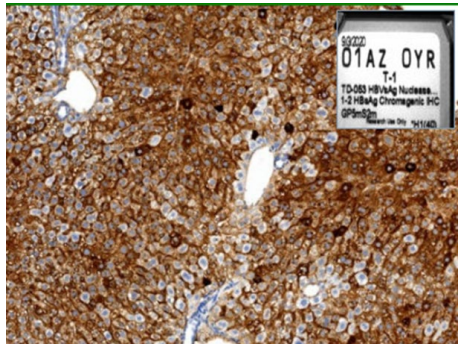
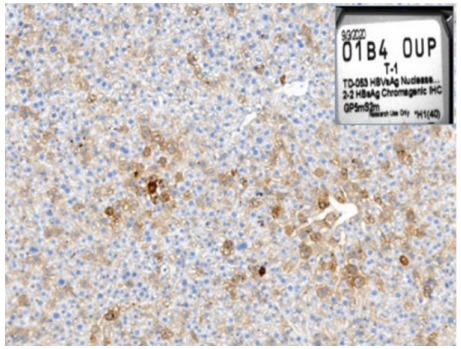


Episomal Mouse Study—Liver HBsAg Immunohistochemistry

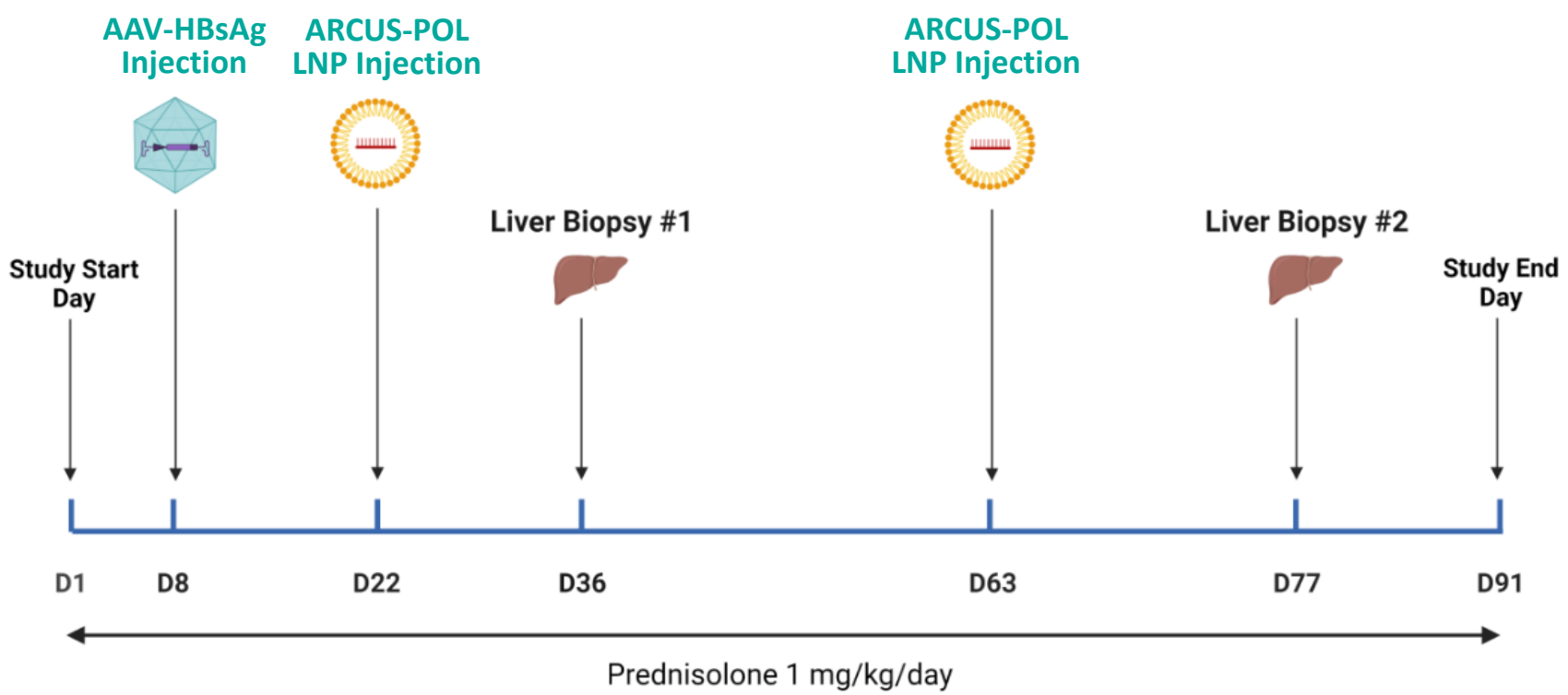
Mice treated with ARCUS-POL showed a significant loss in HBsAg in the liver compared to non-nuclease treated mice.

Blue = Nucleus

Brown = HBsAg

Group 1: No Nuclease	Group 2: ARCUS-POL
	
	

NHP HBV Episomal Study—Outline

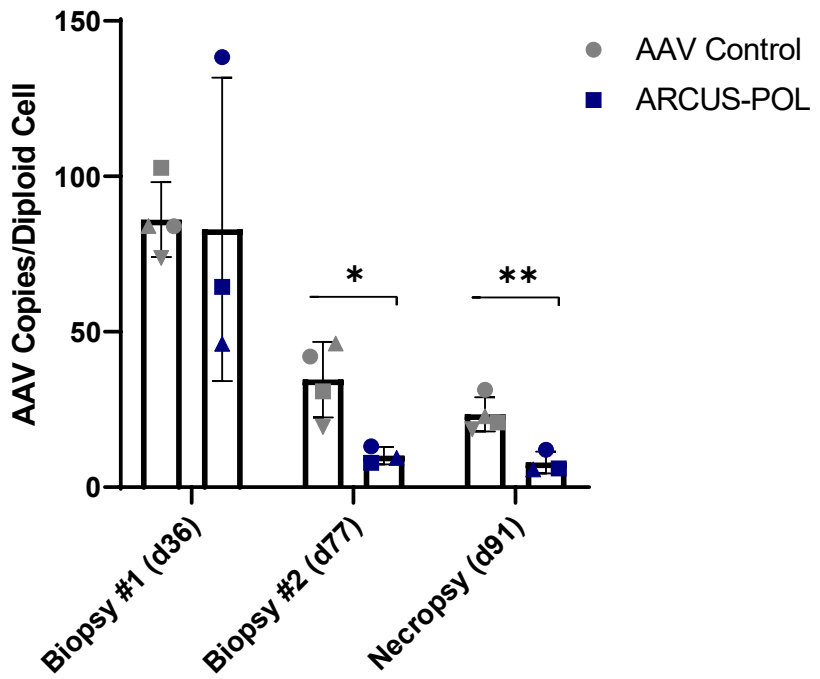


- AAV HBsAg Dose: 6e12 vg/kg
- ARCUS-POL LNP Dose: 2 mg/kg
- Weekly blood draws for HBsAg

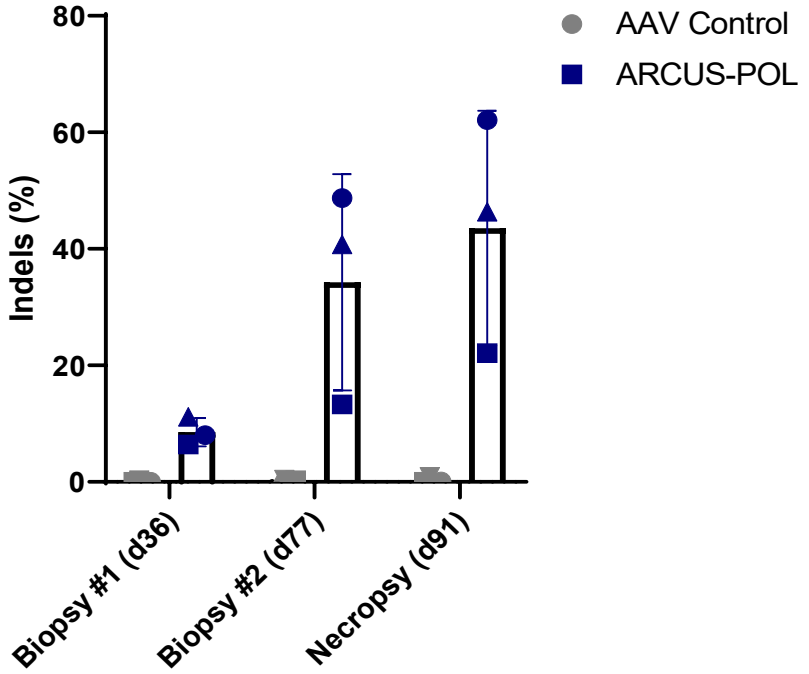
NHP HBV Episomal Study—AAV Copy Number and Indels

- AAV copies were significantly decreased following a second dose of ARCUS-POL.
- The remaining AAV had an average of 44% indels at necropsy.
- Despite immunosuppression, NHPs were unable to maintain secreted HBsAg to use as a biomarker.

AAV Copy Number



AAV Indels



Conclusions

- ARCUS-POL demonstrated high levels of editing against cccDNA with subsequent reduction of HBsAg levels in PHHs.
- We have developed a novel HBV model in mice and NHPs, which demonstrated high levels of editing and HBsAg reductions.
- Our gene editing approach demonstrated high on-target activity and specificity against the HBV polymerase gene and is a promising therapeutic approach for an HBV cure.
- Precision will pursue clinical development of its PBGENE-HBV candidate using LNP delivery and expects to submit an IND/CTA in 2024.

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