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

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Global Hepatitis Summit

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VP Gene Therapy Discovery

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 and Section 21E of the Exchange Act. All statements contained in this herein and in any related presentation that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding research advancement, expected efficacy and benefit of our platform, programs, and product candidates, the approach and goal of providing a functional cure for genetic diseases, expectations regarding on-target activity and specificity of our gene editing approach, and application of novel HBV episomal in vivo models. In some cases, you can identify forward-looking statements by terms such as “aim,” “anticipate,” “approach,” “believe,” “contemplate,” “could,” “estimate,” “expect,” “goal,” “intend,” “look,” “may,” “mission,” “plan,” “possible,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would,” or the negative thereof and similar words and expressions.

Forward-looking statements are based on management’s current expectations, beliefs and assumptions and on information currently available to us. 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 and requirements under our current debt instruments and effects of restrictions thereunder; risks associated with raising additional capital; our operating expenses and our ability to predict what those expenses will be; our limited operating history; the success of our programs and product candidates in which we expend our resources; our limited ability or inability to assess the safety and efficacy of our product candidates; our dependence on our ARCUS technology; the 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 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; our ability to obtain an adequate supply of T cells from qualified donors; our ability to achieve our anticipated operating efficiencies at our manufacturing facility; delays or difficulties in our and our collaborators’ ability to enroll patients; changes in interim “top-line” and initial data that we announce or publish; if our product candidates do not work as intended or cause undesirable side effects; risks associated with applicable healthcare, data protection, privacy and security regulations and our compliance therewith; the rate and degree of market acceptance of any of our product candidates; the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements; our current and future relationships with and reliance on third parties including suppliers and manufacturers; our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates; potential litigation relating to infringement or misappropriation of intellectual property rights; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate key executives and personnel; market and economic conditions; effects of system failures and security breaches; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events; effects of COVID-19 pandemic and variants thereof, or any pandemic, epidemic or outbreak of an infectious disease; 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 Annual Report on Form 10-K for the annual period ended December 31, 2022, as any such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC’s website at www.sec.gov and the Investors page of our website under SEC Filings at investor.precisionbiosciences.com.

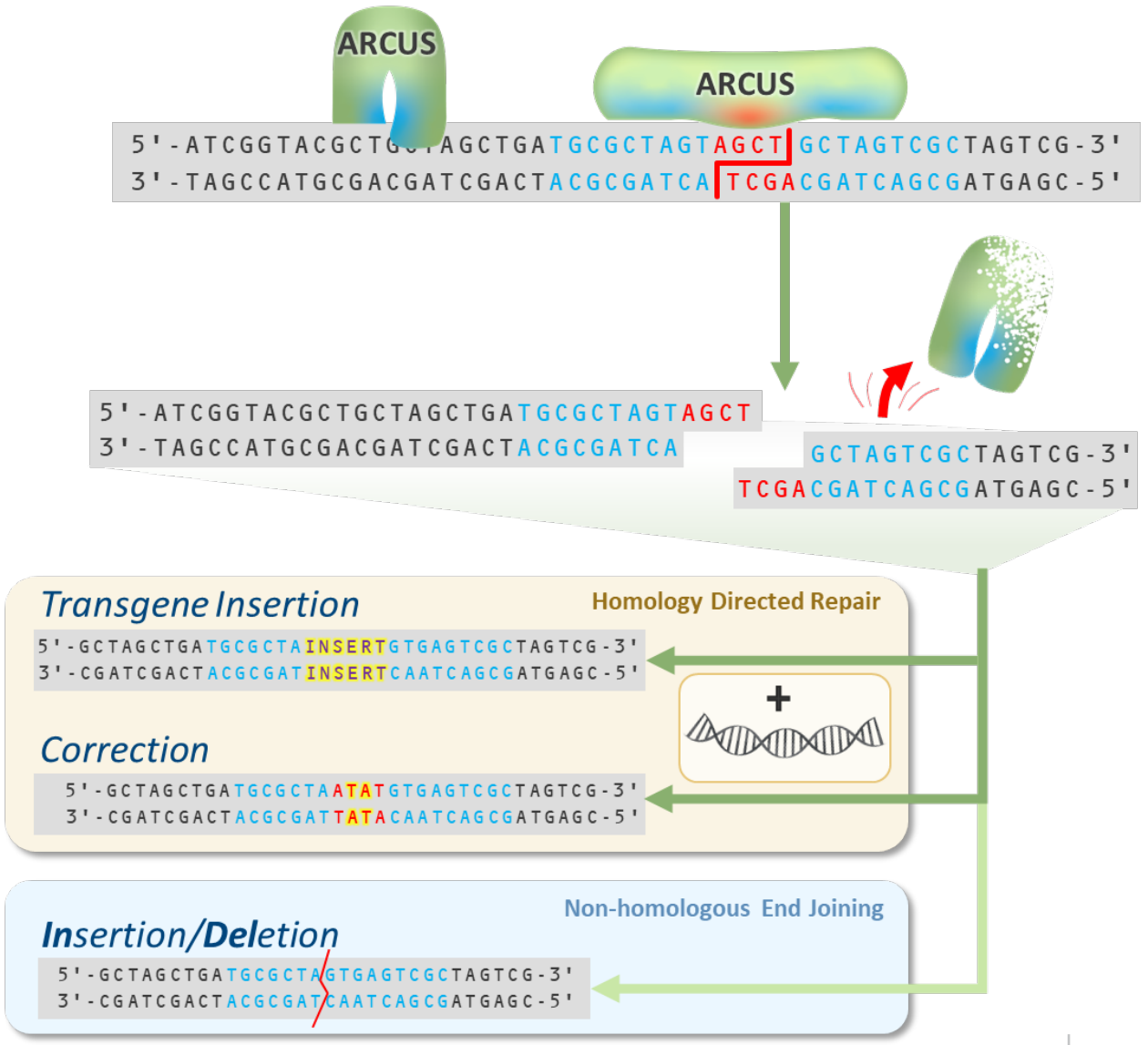
All forward-looking statements speak only as of the date of this presentation and, except as required by applicable law, we have no obligation to update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Disclosures

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

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
- Can be optimized for high specificity
- Small size (364 amino acids) facilitates delivery



ARCUS Gene Editing: Rationale for HBV Cure

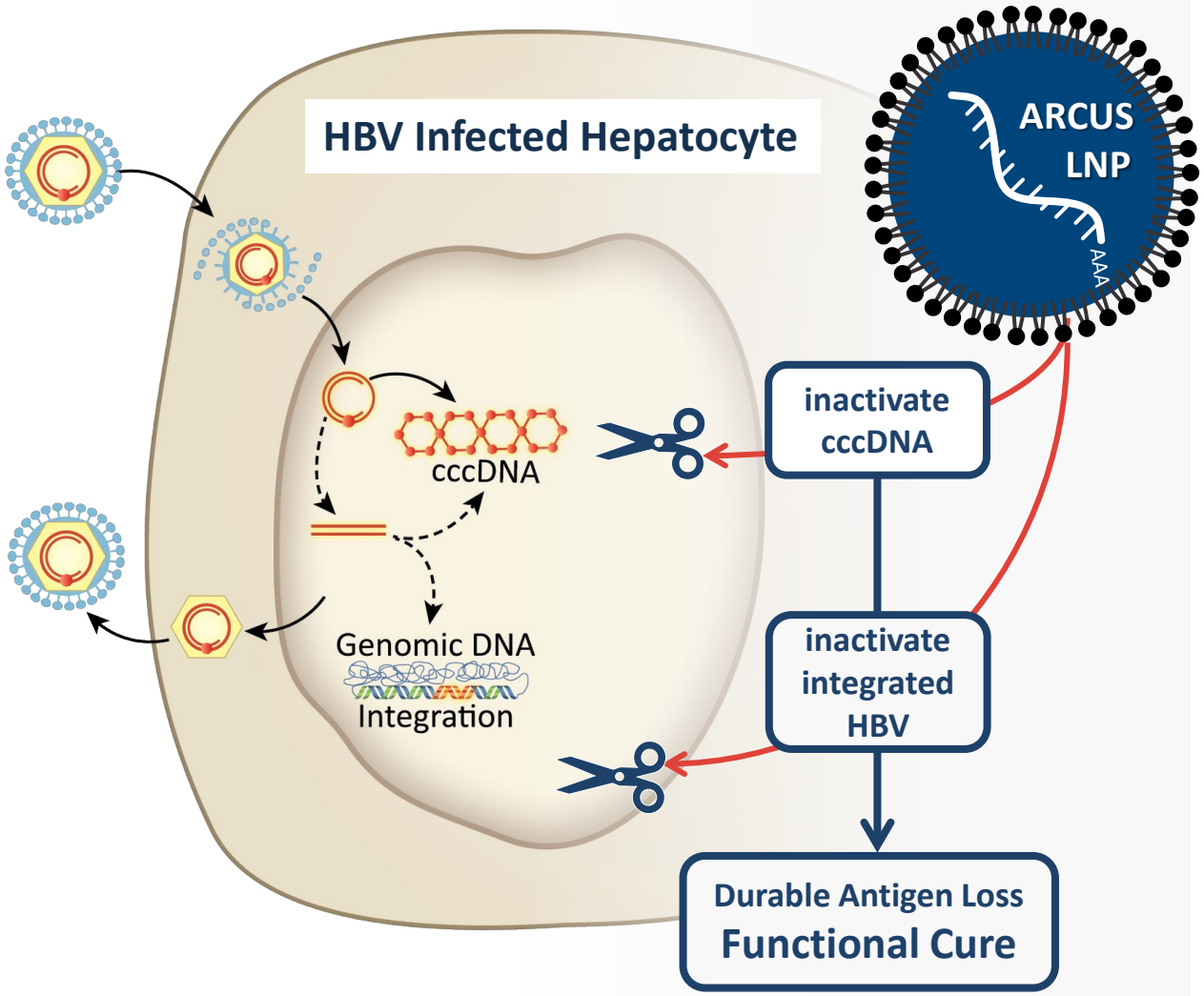
ARCUS-mediated inactivation of cccDNA and integrated HBV could result in a functional cure

Chronic HBV (cHBV) unmet need is massive

US >860,000 cHBV infections

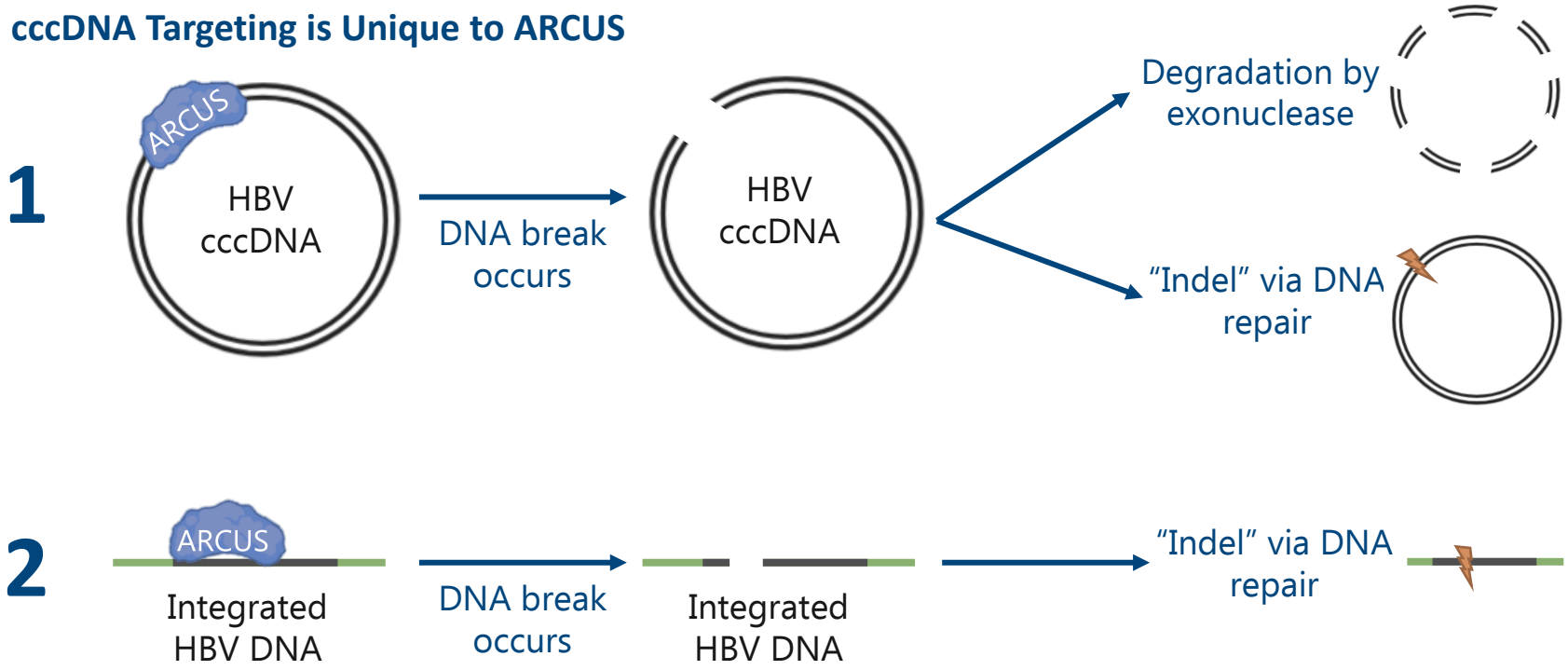
Globally >200 million cHBV infections

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



Dual Action Therapeutic Strategy for HBV-Targeting ARCUS Nucleases

cccDNA Targeting is Unique to ARCUS



Outcomes

Loss of cccDNA
Loss of HBsAg

Mutated cccDNA
Loss of HBsAg

Mutated HBV DNA
Loss of HBsAg

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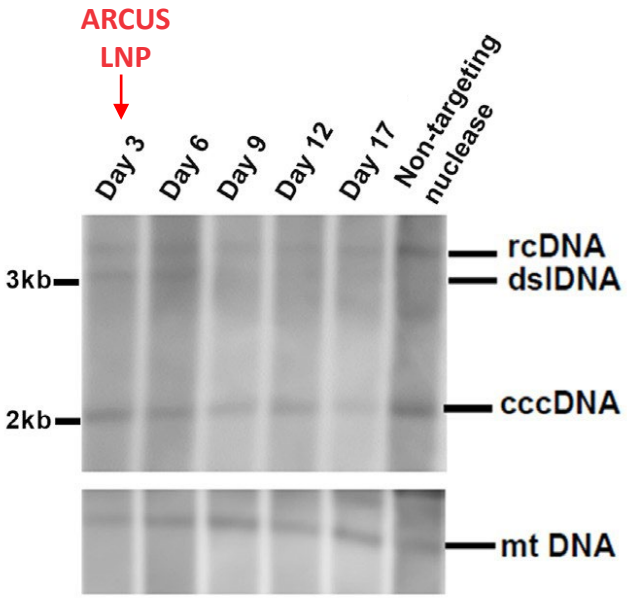
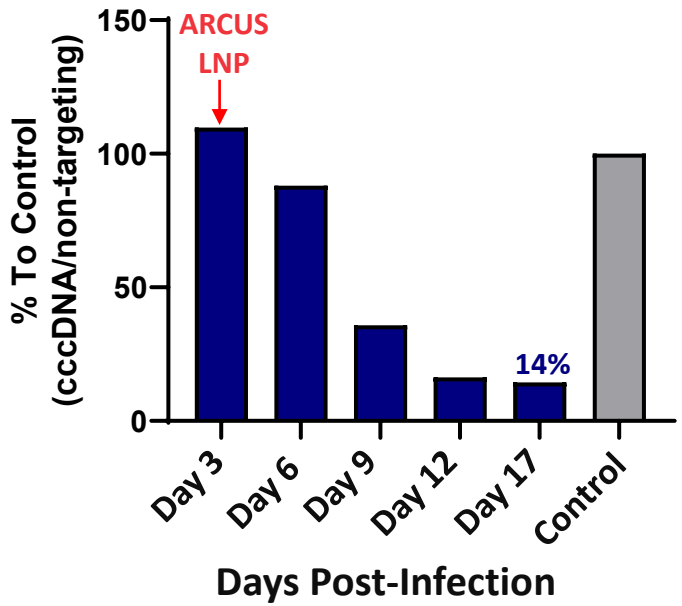
ARCUS Nuclease Activity in HBV-Infected Primary Human Hepatocytes

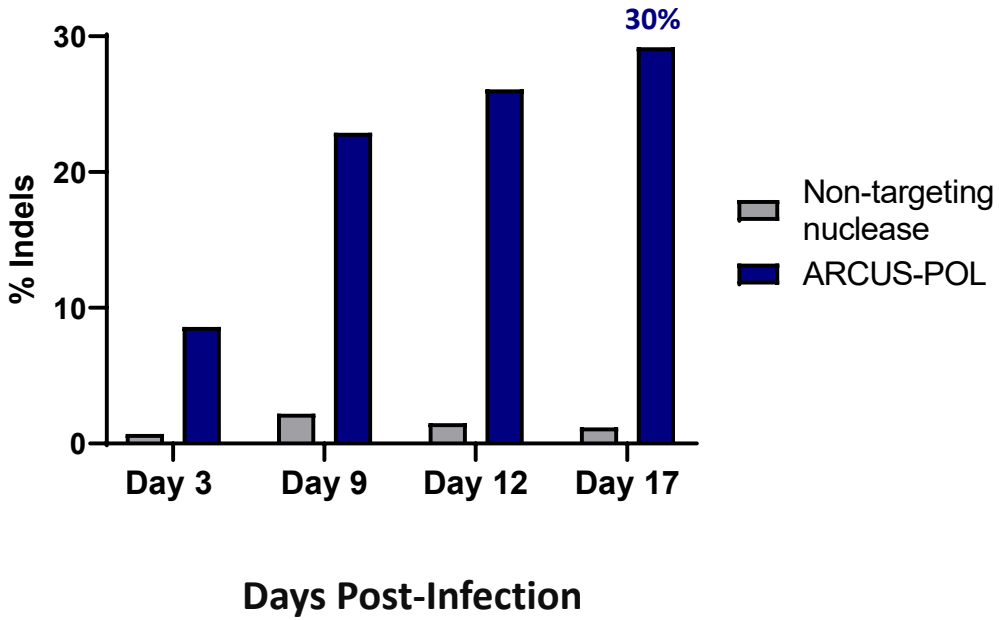
- In HBV-infected primary human hepatocytes (PHH), ARCUS-POL showed an 85% reduction in cccDNA and 30% of the remaining cccDNA contained indels.

cccDNA Degradation





cccDNA Indels



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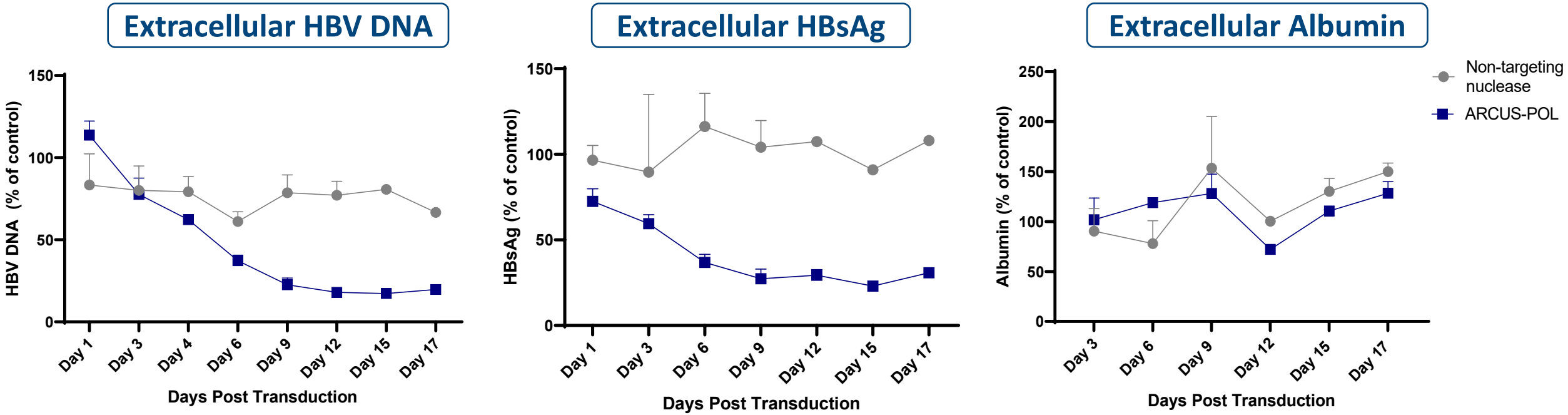
ARCUS Nuclease Activity in HBV-Infected Primary Human Hepatocytes

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



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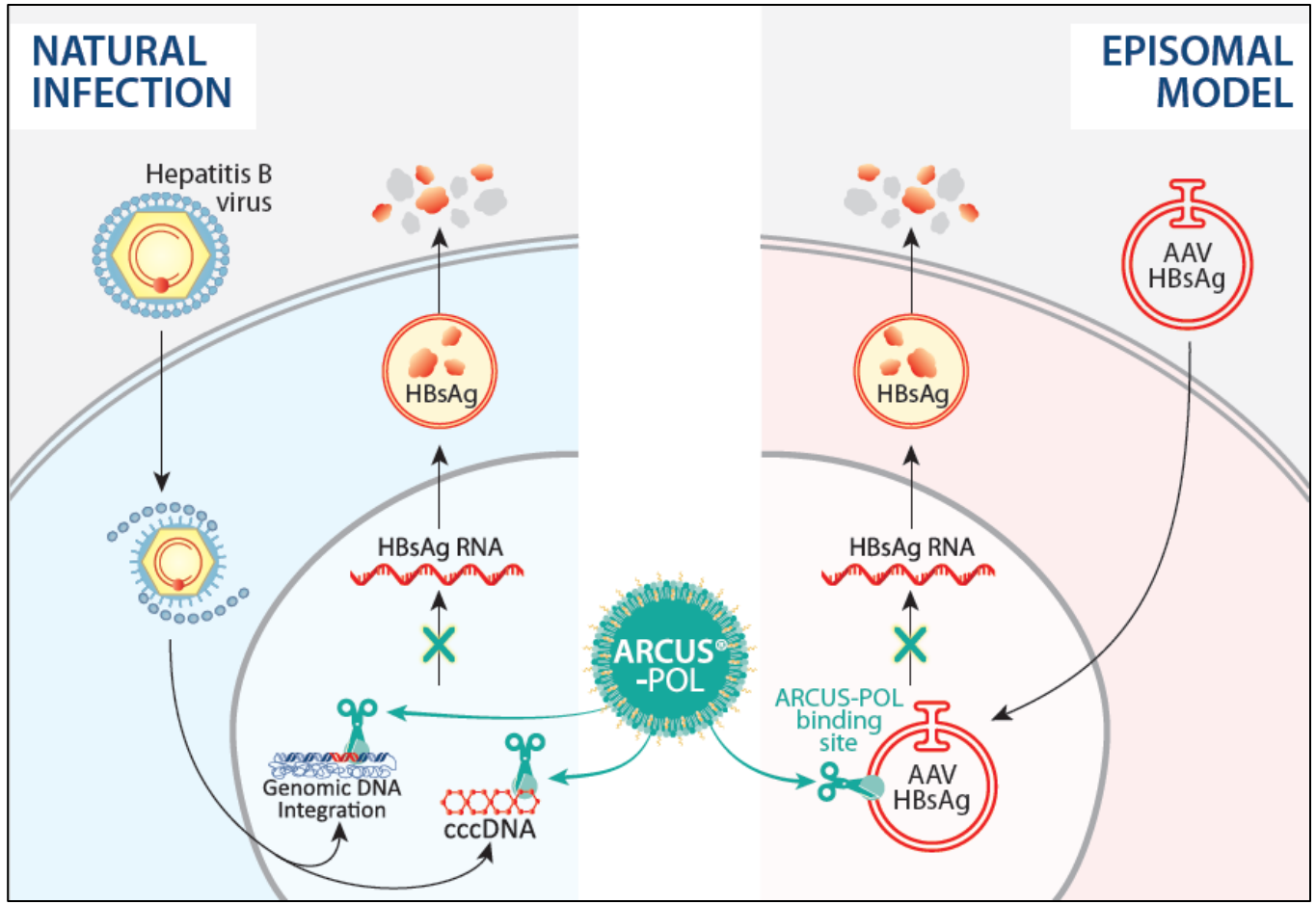
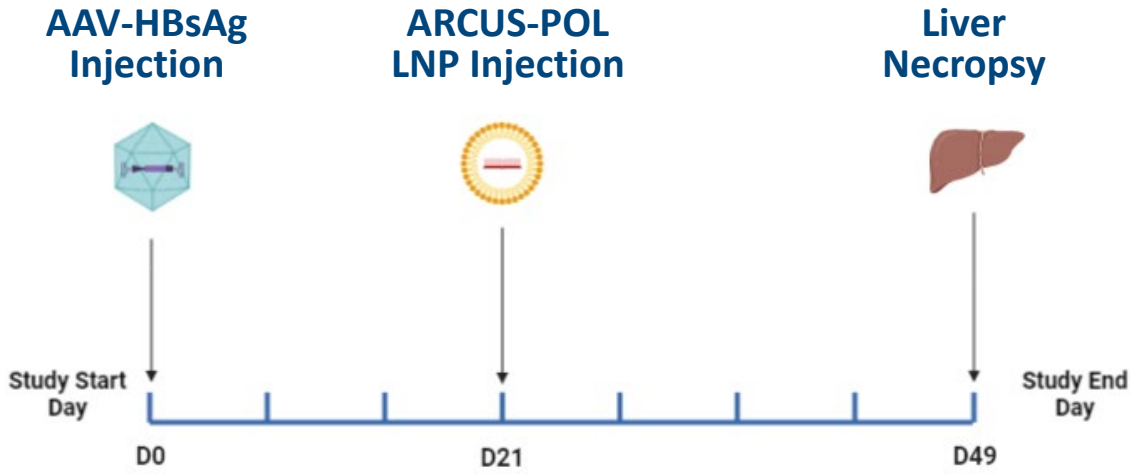
HBV Episomal *In Vivo* Model



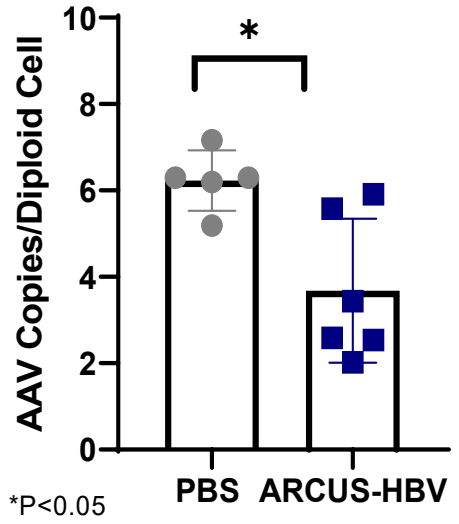


- AAV HBsAg Dose: 5e11vg
- ARCUS-POL LNP Dose: 2 mg/kg
- Weekly blood draws for HBsAg

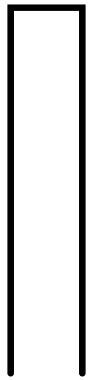
Episomal Mouse Model—Molecular Analyses

- 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.

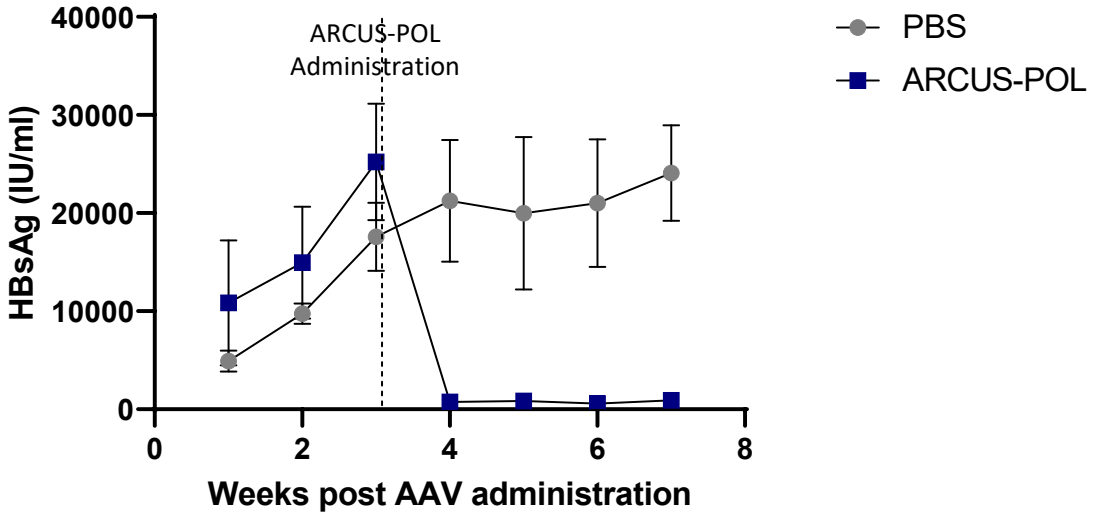
AAV Copy Number



AAV Indels



Secreted HBsAg



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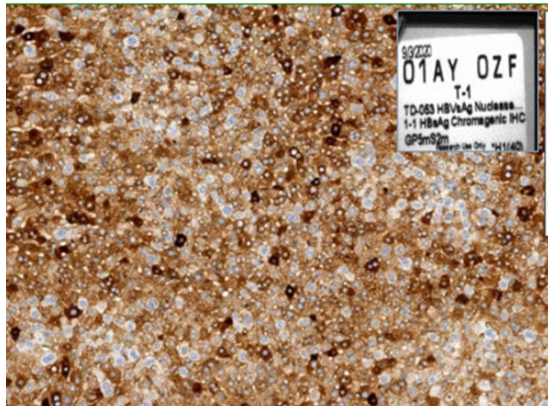
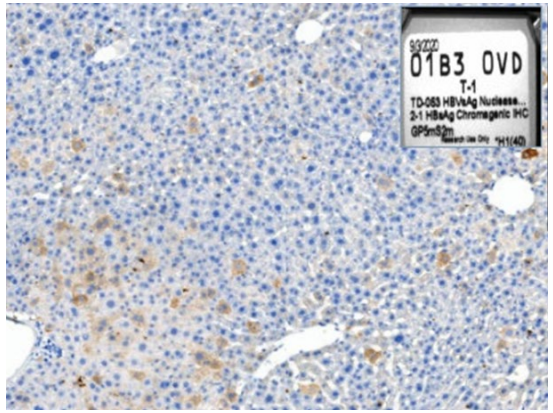
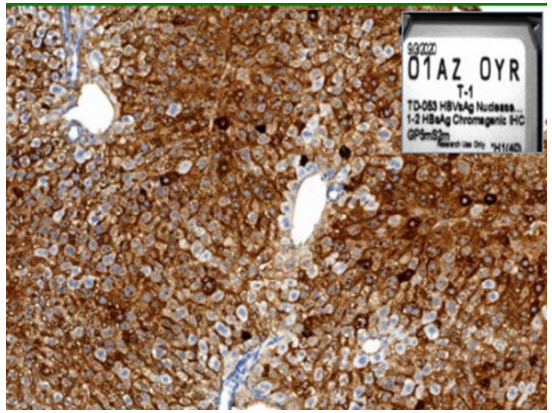
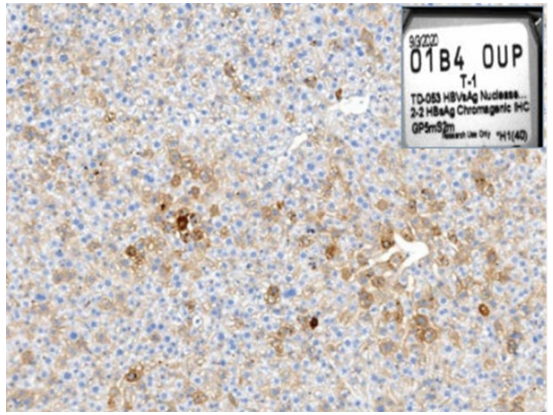
Episomal Mouse Study—Liver HBsAg Immunohistochemistry

- 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
	
	

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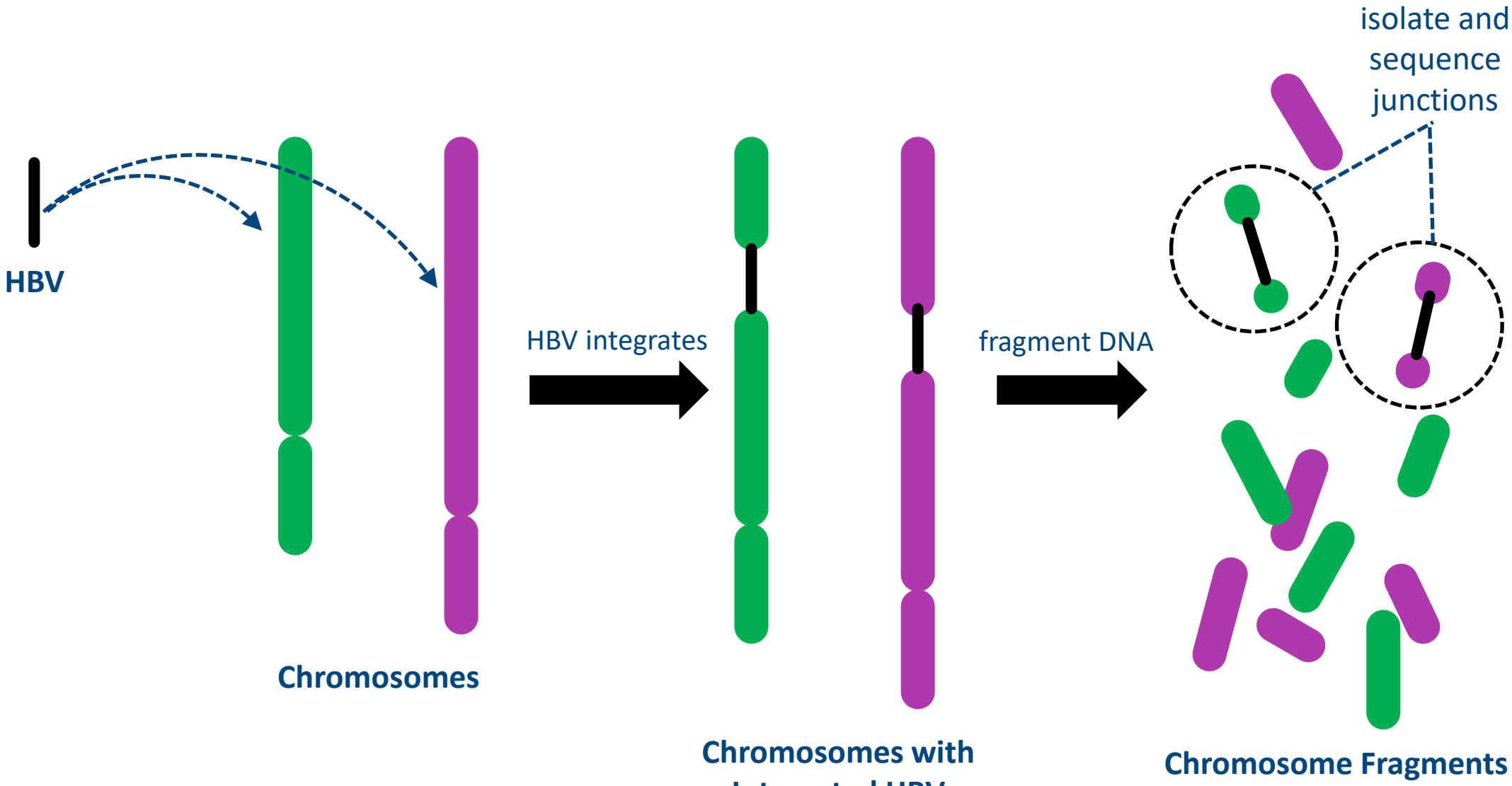
cccDNA Integration into the Genome of HBV Infected PHHs



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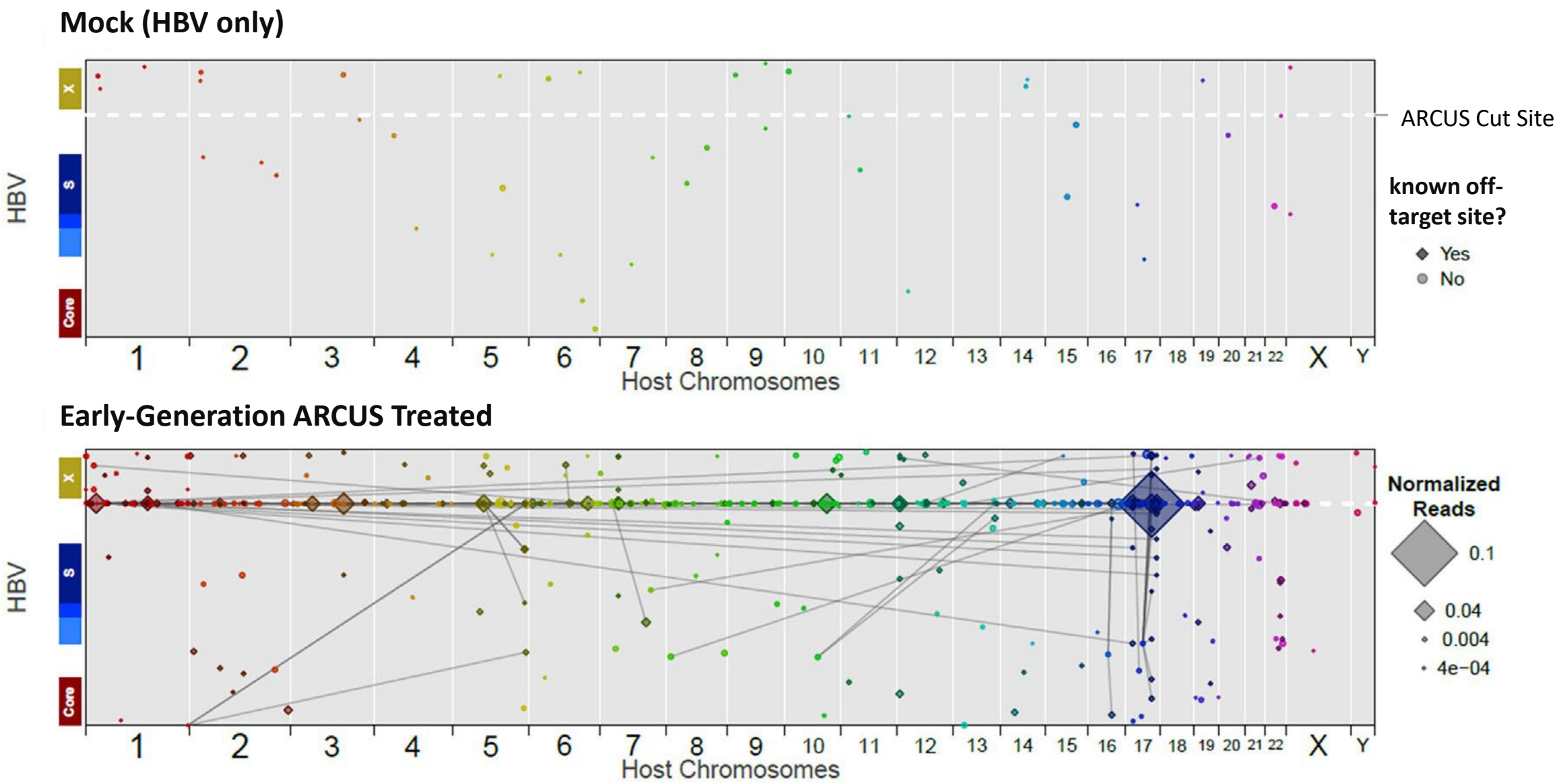

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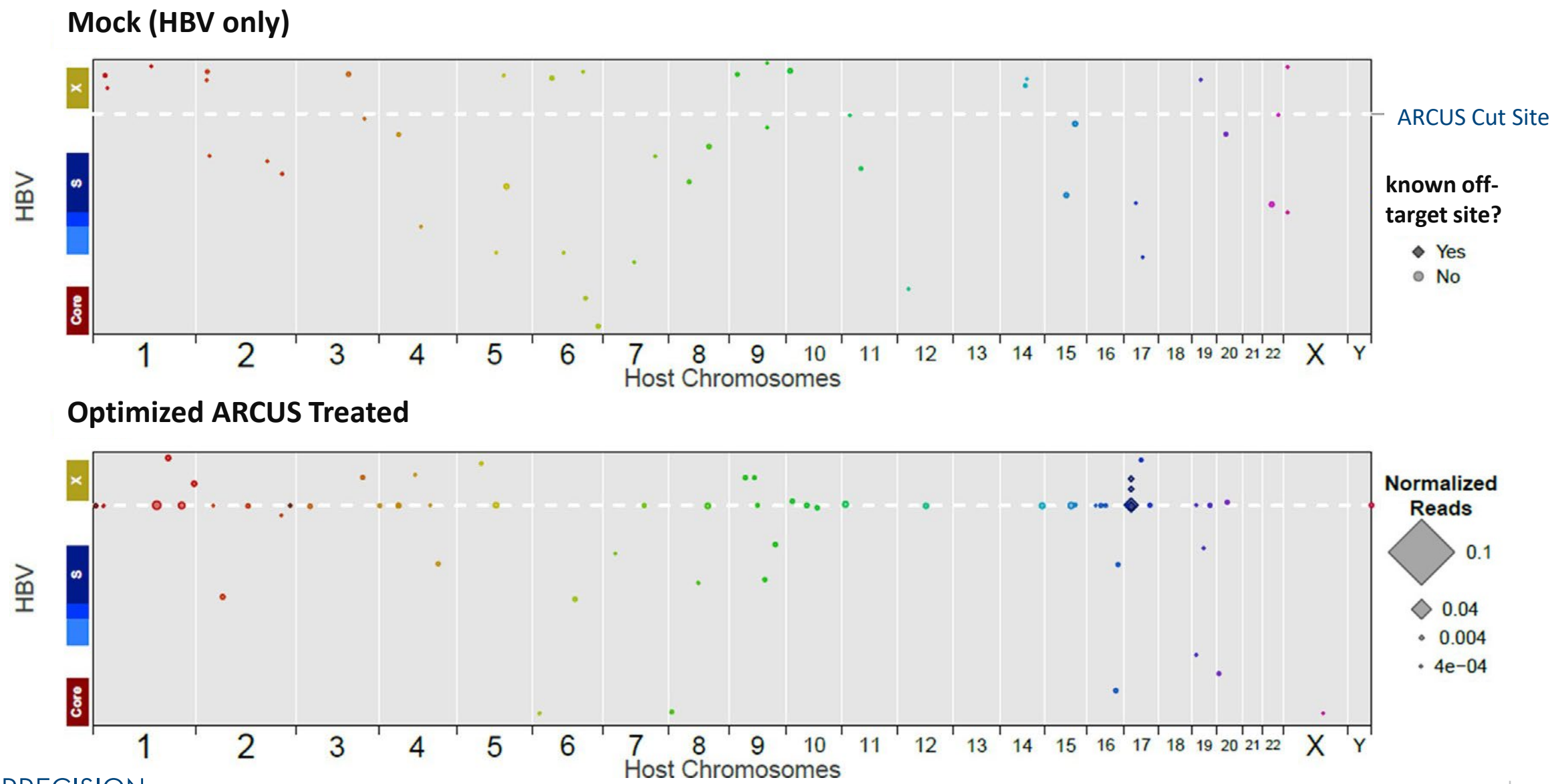

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Conclusions

- ARCUS demonstrates high levels of editing against cccDNA with subsequent reduction of HBsAg and HBV DNA in PHHs.
- We have demonstrated durable HBsAg reductions after a single LNP administration in an AAV mouse model of HBV.
- Our gene editing approach demonstrates high on-target activity and specificity against the HBV polymerase gene and could be a promising therapeutic approach for an HBV cure.

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