AASLD 2026 Publication Number: 5002

Durable pgRNA loss in both HBeAg positive and negative patients treated with PBGENE-HBV supports path towards viral cure

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November 8, 2026

Man-Fung Yuen Disclosures

Advisory committee member:

- AiCuris
- Aligos Therapeutics
- Arbutus Biopharma
- Clear B Therapeutics
- Fujirebio Incorporation
- Gilead Sciences
- GlaxoSmithKline
- Immunocore
- Janssen
- Roche
- Sysmex Corporation
- Tune Therapeutics
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- Fujirebio Incorporation
- Gilead Sciences
- GlaxoSmithKline
- Roche
- Sysmex Corporation

Research grants:

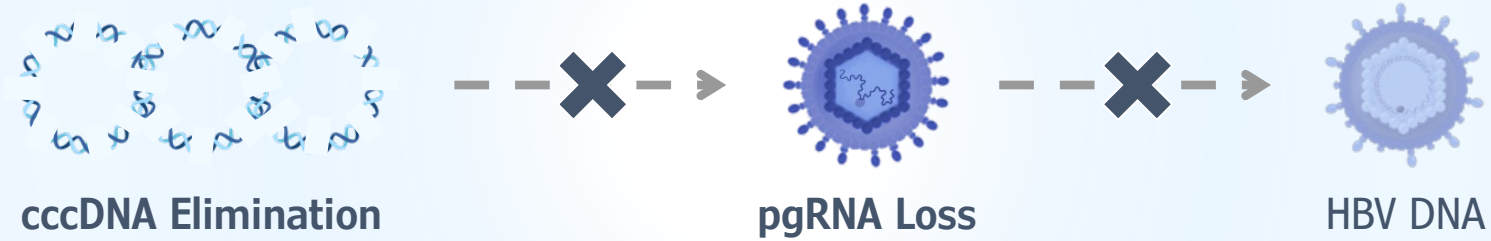
- AbbVie
- Arrowhead Pharmaceuticals
- Assembly Biosciences
- Fujirebio Incorporation
- Gilead Sciences
- Immunocore
- Precision BioSciences, Inc.
- Roche
- Sysmex Corporation

PBGENE-HBV: First-in-Class Gene Editor Designed to Eliminate cccDNA and Drive pgRNA Loss for a Potential Viral Cure

"True cure of HBV infection requires eradication, degradation…of cccDNA"[1]

—Dusheiko, et al. *NEJM,* 2023

PBGENE-HBV



PBGENE-HBV:
uniquely designed to achieve viral cure by eliminating cccDNA at the source of HBV

- PBGENE-HBV specifically recognizes a **highly conserved target** sequence within the Enhancer 1 element of both cccDNA and integrated HBV DNA
- **PBGENE-HBV preclinical safety:** specificity with no increased risks of translocations or integrations with multiple administrations in HBV-infected human cells

cccDNA, covalently closed circular DNA; HBV, hepatitis B virus; pgRNA, pregenomic RNA.

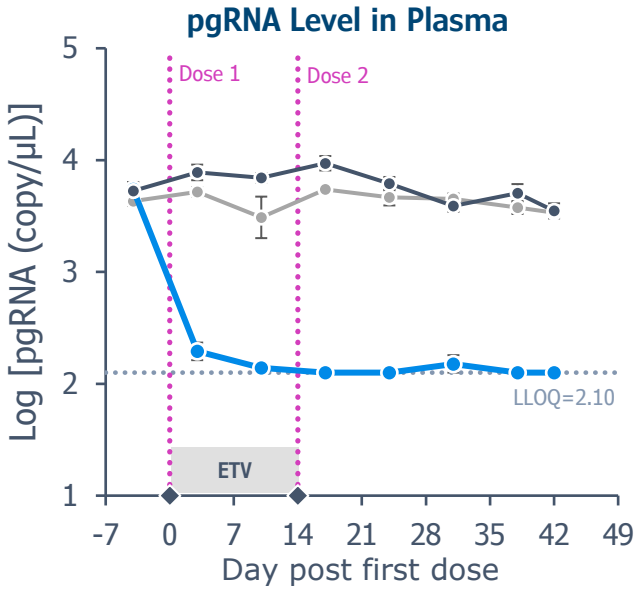
1. Dusheiko G, et al. *N Engl J Med*. 2023;388(1):55-69.

Preclinical Data Support Potential to Stop NUCs With pgRNA Loss and Detectable HBsAg

Study Design:

- HBV transgenic mouse model produces HBsAg and HBV DNA from full-length integrated HBV genome
- Treatment with PBGENE-HBV on Day 0 and 14, NUCs dosed daily from Day 0-14

PBGENE-HBV drove undetectable pgRNA



PBGENE-HBV + ETV Saline ETV Alone

ETV, entecavir; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; LLOQ, lower limit of quantification; NUC, nucleos(t)ide analog; pgRNA, pregenomic RNA.

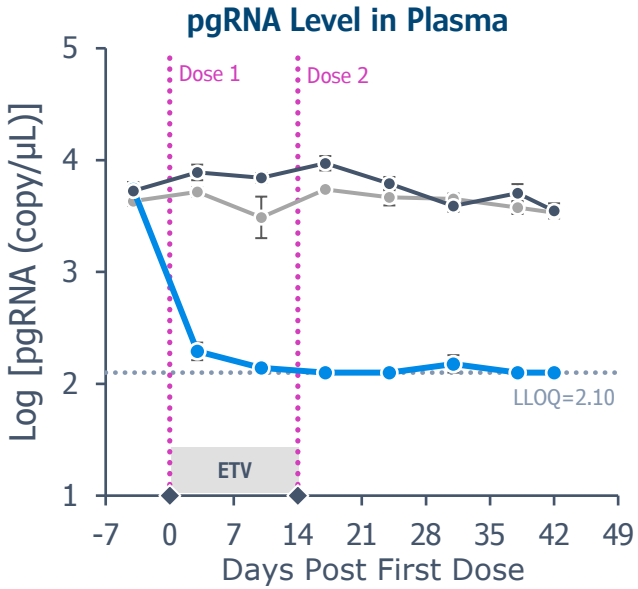
Precision BioSciences, Inc. Presented at: AASLD The Liver Meeting; November 10-14, 2023; Boston, MA.

Preclinical Data Support Potential to Stop NUCs With pgRNA Loss and Detectable HBsAg

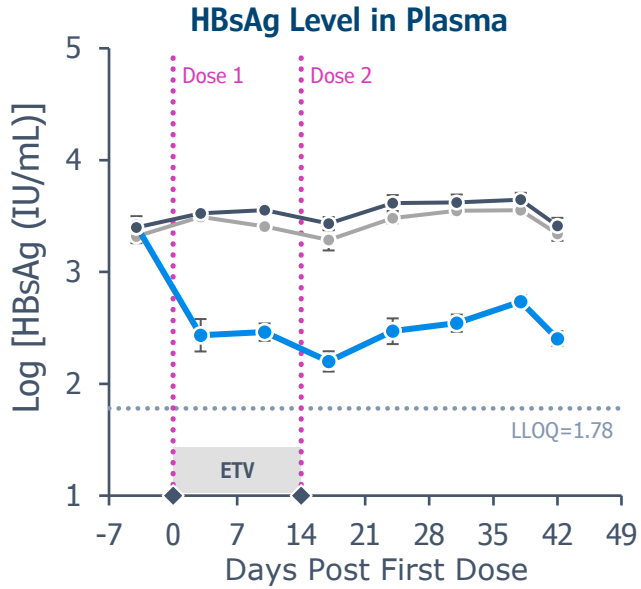
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HBsAg was detectable in all PBGENE-HBV–treated groups



PBGENE-HBV + ETV Saline ETV Alone

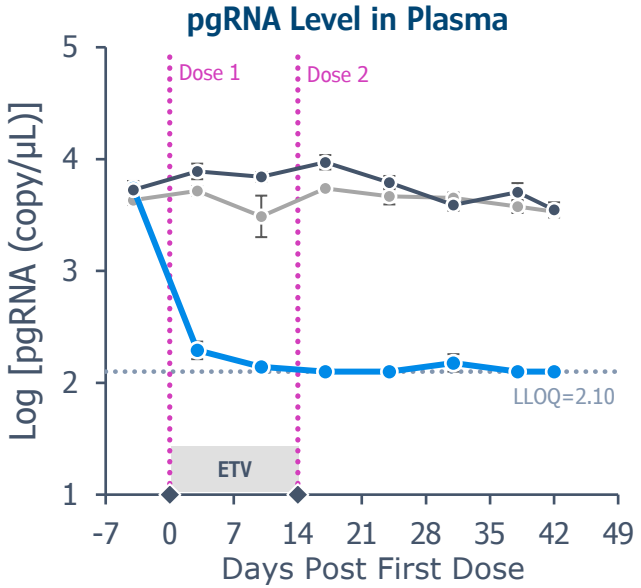
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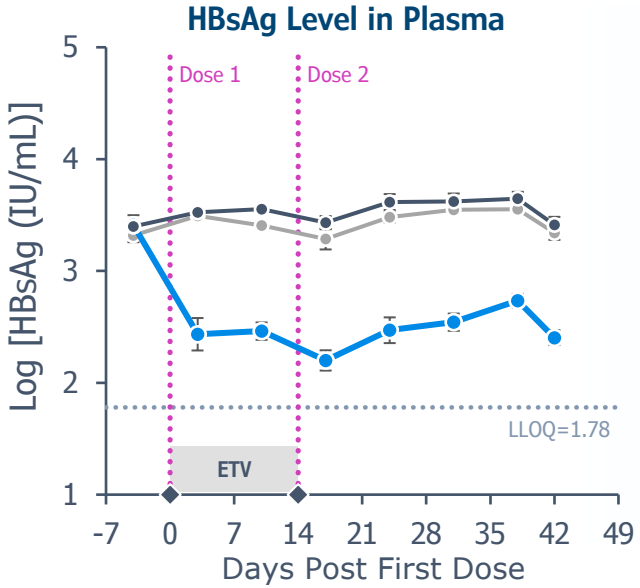
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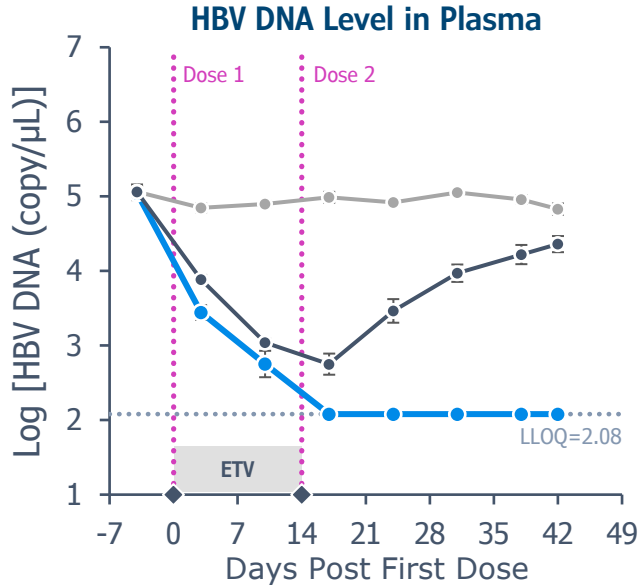


HBsAg was detectable in all PBGENE-HBV–treated groups



NUCs stopped with undetectable pgRNA and stable HBsAg decline

PBGENE-HBV–treated mice sustain HBV DNA reduction/loss after ETV withdrawal



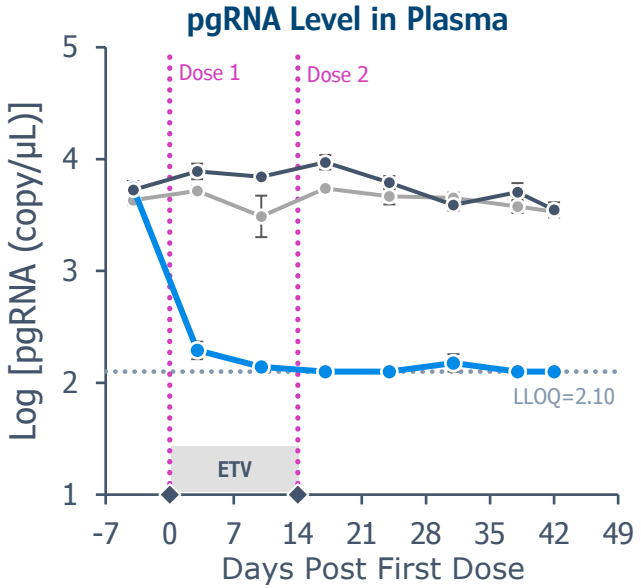
PBGENE-HBV + ETV — Saline — ETV Alone

ETV, entecavir; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IU/mL, international units per milliliter; LLOQ, lower limit of quantification; NUC, nucleos(t)ide analog; pgRNA, pregenomic RNA.
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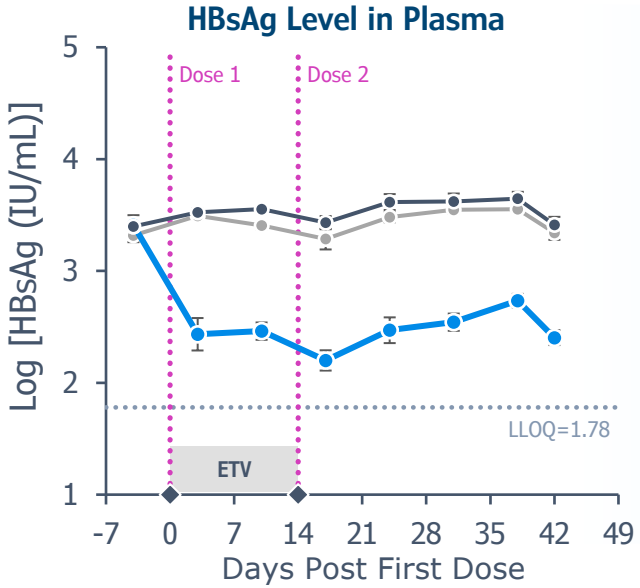
Preclinical Data Support Potential to Stop NUCs With pgRNA Loss and Detectable HBsAg

GOAL: For PBGENE-HBV, sustained undetectable HBV DNA off all treatment for potential **viral cure**[1]

PBGENE-HBV drove undetectable pgRNA

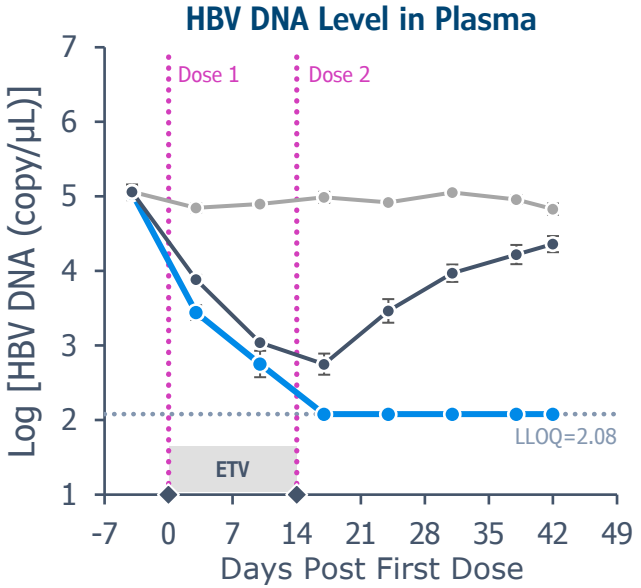


HBsAg was detectable in all PBGENE-HBV–treated groups



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Precision BioSciences. AASLD The Liver Meeting, Boston, November 10–14, 2023.
1. FDA. Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment. April 2022. Accessed November 2, 2026.

Phase 1 Study Design (NCT06680232)

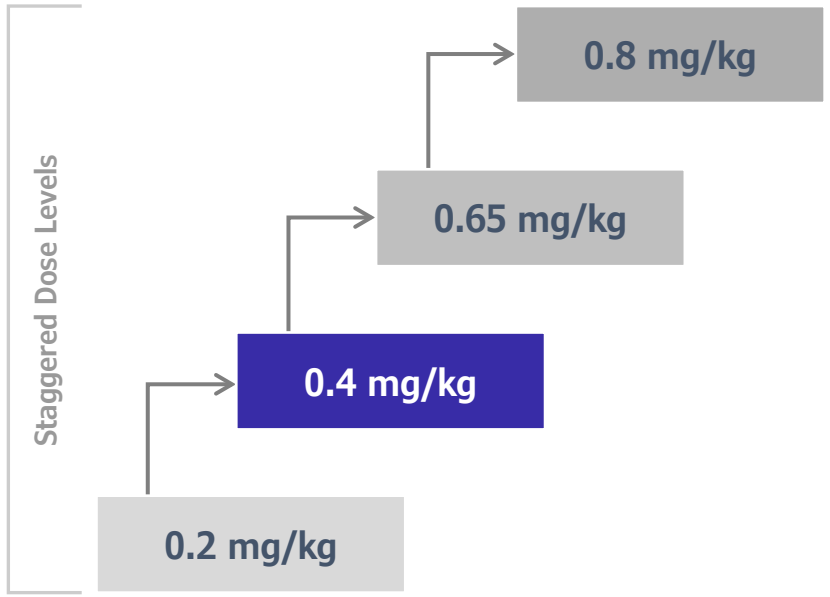
Key Inclusion Criteria

- HBeAg-negative or -positive CHB
- CHB infection documented by serum HBsAg-positivity for ≥12 months
- Serum HBsAg ≥100 IU/mL at screening with no upper limit
- Virologically suppressed and currently on NUC treatment

Key Exclusion Criteria

- No history of liver cirrhosis or signs of HCC
- No current HAV, HDV, HEV, or HIV infections and no history of or current HCV infection
- No prior investigational agents within 6 months of screening

Multiple Ascending Dose Escalation



59 Administrations in 25 Participants

Endpoints

Primary

Safety:

- Frequency and severity of DLTs

Secondary

Additional safety:

- Frequency and severity of AEs and changes in physical examinations, vital signs, and safety labs
- PK parameters: AUC, Tmax, Cmax, Cmin, and t1/2

Efficacy:

- Change from baseline in:
  - HBsAg and anti-HBs levels
  - HBV DNA and HBV RNA levels
- Proportion of participants who:
  - Can discontinue NUC therapy
  - Sustained HBV DNA control off all therapies[1]

GOAL: Identify a safe and efficacious dose for Phase 2 – **0.4 mg/kg**

AE, adverse event; anti-HBs, hepatitis B surface antibody; AUC, area under the curve; CHB, chronic hepatitis B virus; Cmax, maximum concentration; Cmin, minimum concentration; DLT, dose-limiting toxicity; HAV, hepatitis A virus; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis D virus; HEV, hepatitis E virus; HIV, human immunodeficiency virus; IU/mL, international units per milliliter; NUC, nucleos(t)ide analog; PK, pharmacokinetic; t1/2, half-life; Tmax, time to maximum concentration.

1. US Food and Drug Administration. Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment. Published April 2022. Accessed November 2, 2026.

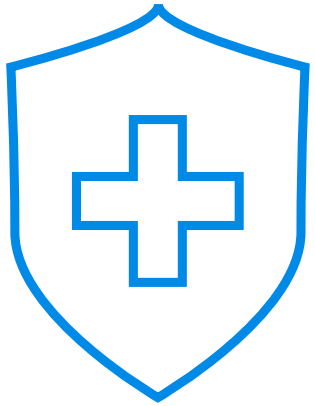
Demographics and Baseline Characteristics

Demographics		Number (%)
Sex	Male	20 (80)
	Female	5 (20)
Ethnicity/ Race	Caucasian	7 (28)
	Asian	16 (64)
	Native Hawaiian or Other Pacific Islander	2 (8)

Baseline Characteristics	Mean	Range
Age (years)	48	34-64
Time on NUCs (years)	11.8	1.2-29.1
Baseline pgRNA (C/mL)	257	TND-5,750
Baseline HBsAg (IU/mL)	4,203	178-34,489

C/mL, copies per milliliter; HBsAg, hepatitis B surface antigen; IU/mL, international units per milliliter; NUC, nucleos(t)ide analog; pgRNA, pregenomic RNA; TND, target not detected.

PBGENE-HBV Safety Profile Executive Summary



- 59 doses administered across 25 evaluable participants
- Primary endpoint: No dose-limiting toxicities observed
- Most common adverse events are infusion-related reactions consistent with LNP effects, with onset and resolution within 24 hours of infusion
- Consistent with LNP effects, transient, reversible ALT/AST lab abnormalities have been observed. All were asymptomatic with no elevated bilirubin, and no cases of Hy's Law
- No Grade ≥3 hypotension has been observed at the go-forward dose of 0.4 mg/kg since implementing modified infusion protocol (n=15 administrations in 8 participants)
- Safety at 0.4 and 0.65 mg/kg is the focus of today's presentation
- Repeat doses at 0.8 mg/kg without current infusion protocol were not continued[1]

Safety profile of PBGENE-HBV at 0.4 mg/kg supports further evaluation in Phase 2

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; LNP, lipid nanoparticle.
Data cutoff: September 28, 2026.
1. All data from 0.8 mg/kg dose level presented in May 2026 Investor Presentation. No additional doses or safety events at 0.8 mg/kg.
https://investor.precisionbiosciences.com/events/event-details/precision-biosciences-host-investor-webcast-discuss-late-breaking-pbgene-hbv

PBGENE-HBV Safety Profile: Clear Evidence of Therapeutic Window at 0.4 mg/kg

Number of participants with AEs[a]:		0.65 mg/kg n=6	0.4 mg/kg n=13	0.4 mg/kg with current infusion protocol n=8 of 13
Grade 3	Hypotension	4	3[b]	-
Grade 3 and 4	ALT/AST lab abnormality	4	2	1
SAEs		-	-	-

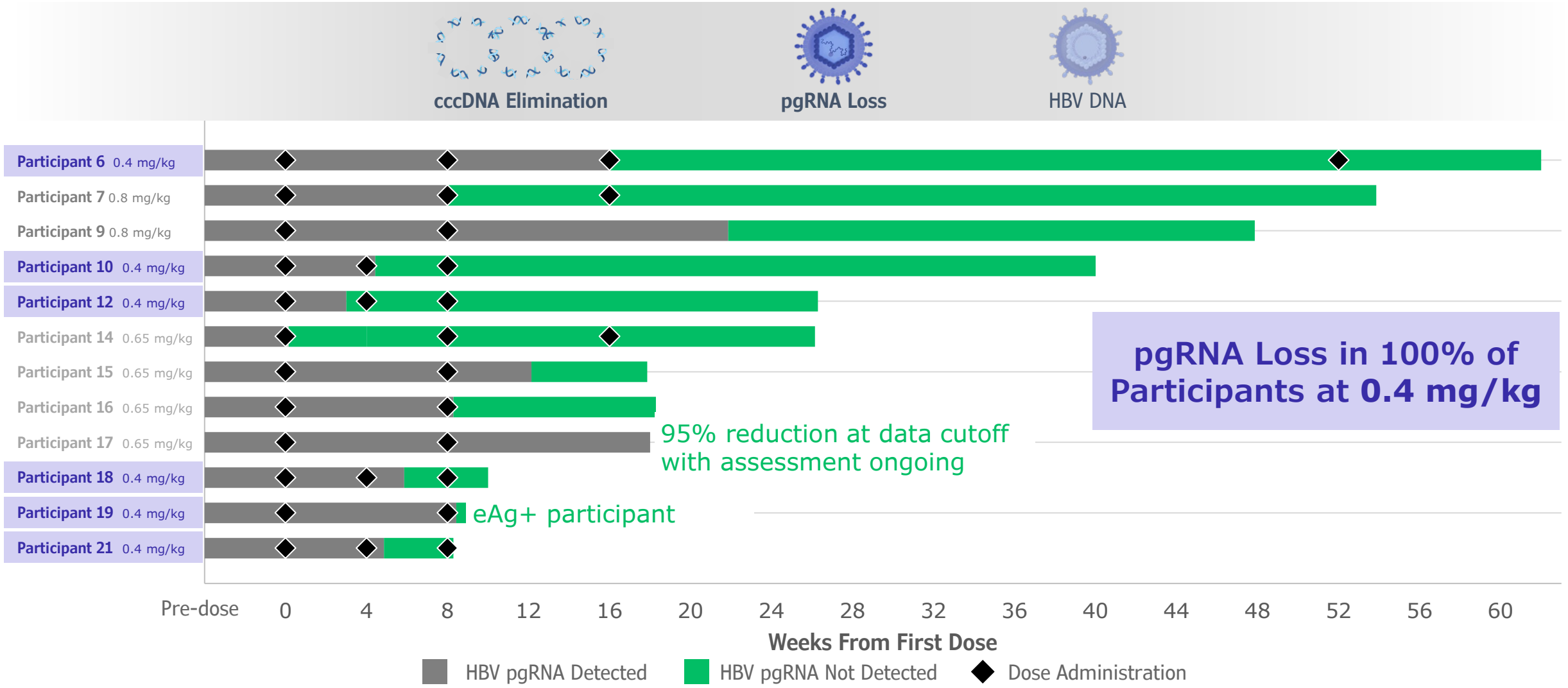
- **Key Safety Learnings:** LNP-related inflammatory response on repeat doses was mitigated through adjusting original infusion protocol (2-hour infusion, 10 mg dexamethasone) to current infusion protocol (5-hour, 20 mg dexamethasone [split across 2 doses], prophylactic saline infusion)
- **With Current Infusion Protocol:**
  - **No Grade ≥3 hypotension** has been observed at 0.4 mg/kg since implementing a simple modified infusion protocol to blunt LNP-related inflammatory response
  - **One delayed ALT/AST lab abnormality** was observed after third dose, with peak ALT at 306 U/L and AST at 278 U/L. No intervention was required, no changes in bilirubin were observed, and no cases of Hy's Law
- Repeat administrations at 0.65 mg/kg resulted in a higher number of participants with transient Grade 3 hypotension and ALT/AST lab abnormalities. No changes in bilirubin and no Hy's Law. These lab abnormalities were transient; 3/4 participants fully resolved on their own, 1 participant received steroid intervention and has resolved

Favorable safety profile for PBGENE-HBV at 0.4 mg/kg

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; LNP, lipid nanoparticle; SAE, serious adverse event; U/L, units per liter.
Data cutoff: September 28, 2026.
[a]AEs shown are treatment-related and possibly treatment-related. [b]Grade 3 hypotension was observed at 0.4 mg/kg prior to current infusion protocol.
1. Safety profiles at 0.2 and 0.8 mg/kg were previously presented in May 2026, and no additional administrations at these doses were planned. Two SAEs were observed in the same participant dosed at the discontinued dose of 0.8 mg/kg. https://investor.precisionbiosciences.com/events/event-details/precision-biosciences-host-investor-webcast-discuss-late-breaking-pbgene-hbv

Phase 1 ELIMINATE-B Efficacy Data Support Advancement to Phase 2

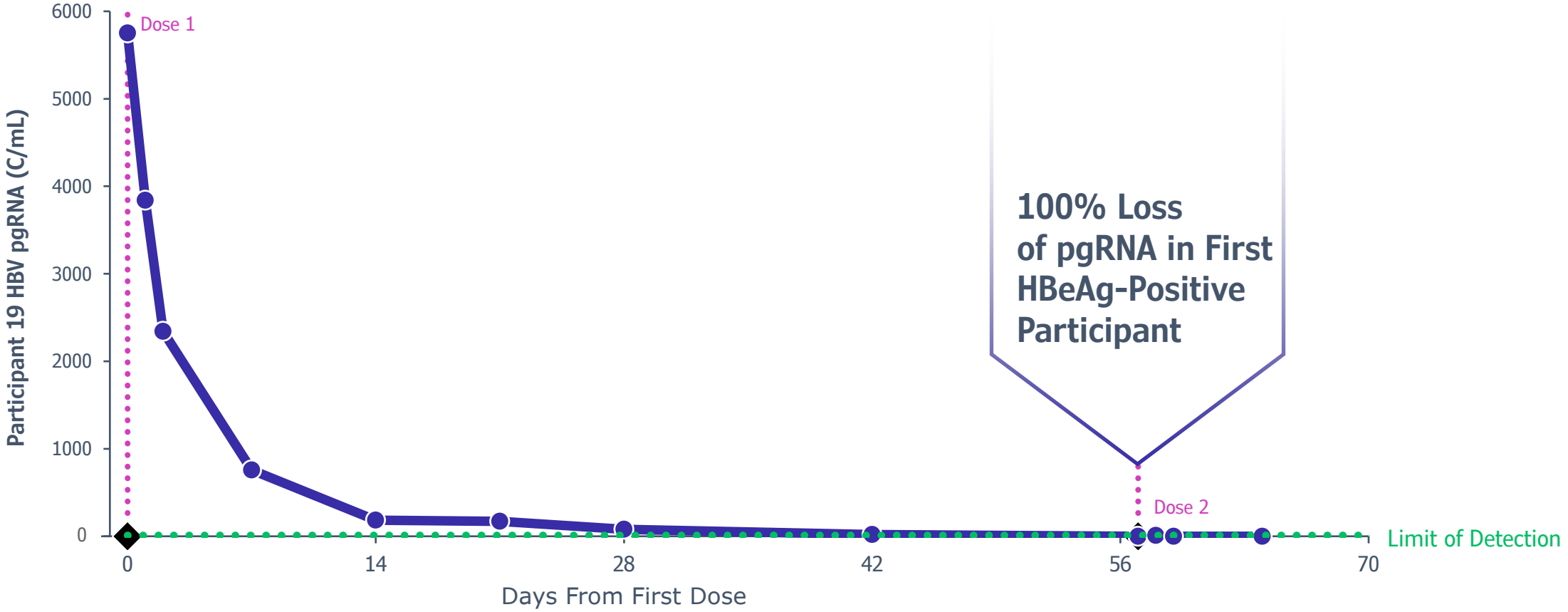
PBGENE-HBV Drove Ongoing Durable pgRNA Undetectable Through cccDNA Elimination



Evaluable participants defined as those who have 28 days of data from initial dose. pgRNA was measured by the Roche HBV RNA that is specific to cccDNA transcripts.[1] Green indicates repeated measurements below the LLOD (<5 copies/mL) at each timepoint maintained until the most recent follow-up visit.
cccDNA, covalently closed circular DNA; eAg, hepatitis B e antigen; HBV, hepatitis B virus; LLOD, lower limit of detection; pgRNA, pregenomic RNA.
Data cutoff: September 28, 2026.

1. Testoni B, et al. *Gut*. 2024;73(4):659-667.

Eliminating cccDNA at 0.4 mg/kg Leads to 100% Loss of pgRNA in First HBeAg+ Participant



pgRNA loss in HBeAg-positive participant with 3.7-log baseline pgRNA demonstrates PBGENE-HBV potently eliminated cccDNA in the highest viral burden population

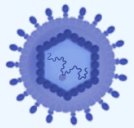
pgRNA was measured by the Roche HBV RNA that is specific to cccDNA transcripts.[1] Dotted green line indicates measurements below the LLOD (<5 copies/mL).
C/mL, copies per milliliter; cccDNA, covalently closed circular DNA; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; LLOD, lower limit of detection; pgRNA, pregenomic RNA.

1. Testoni B, et al. Gut. 2024;73(4):659-667.

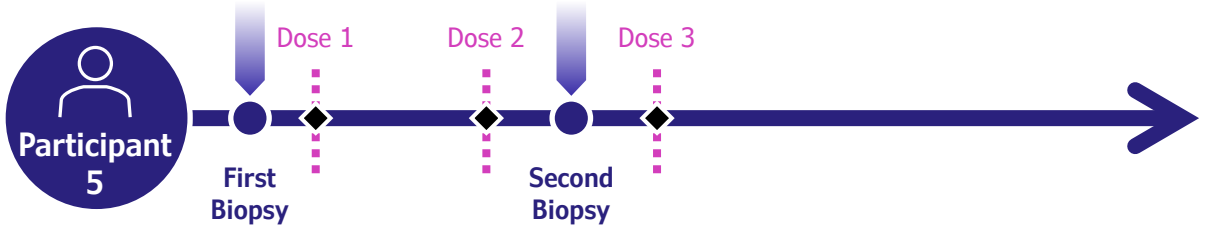
Biopsy Data Support Substantial cccDNA Elimination at 0.4 mg/kg

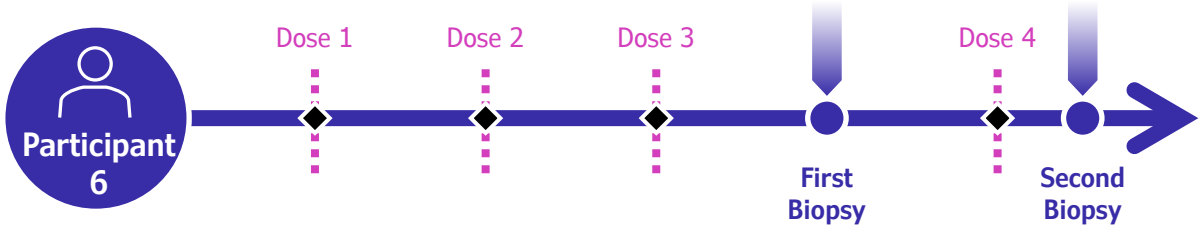
cccDNA elimination is nuclease mediated

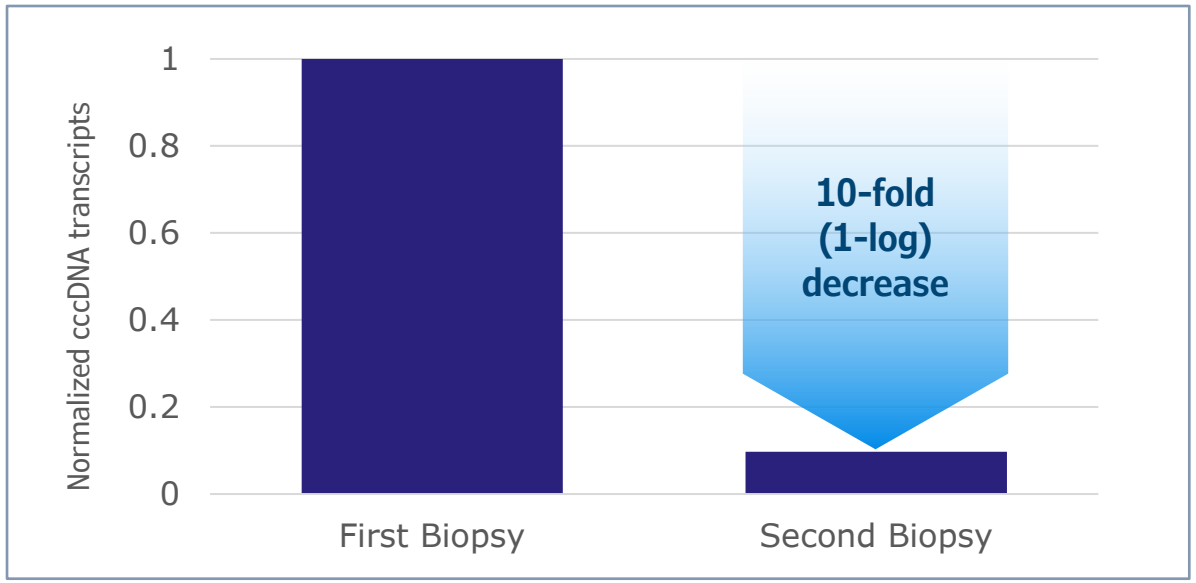

cccDNA Elimination

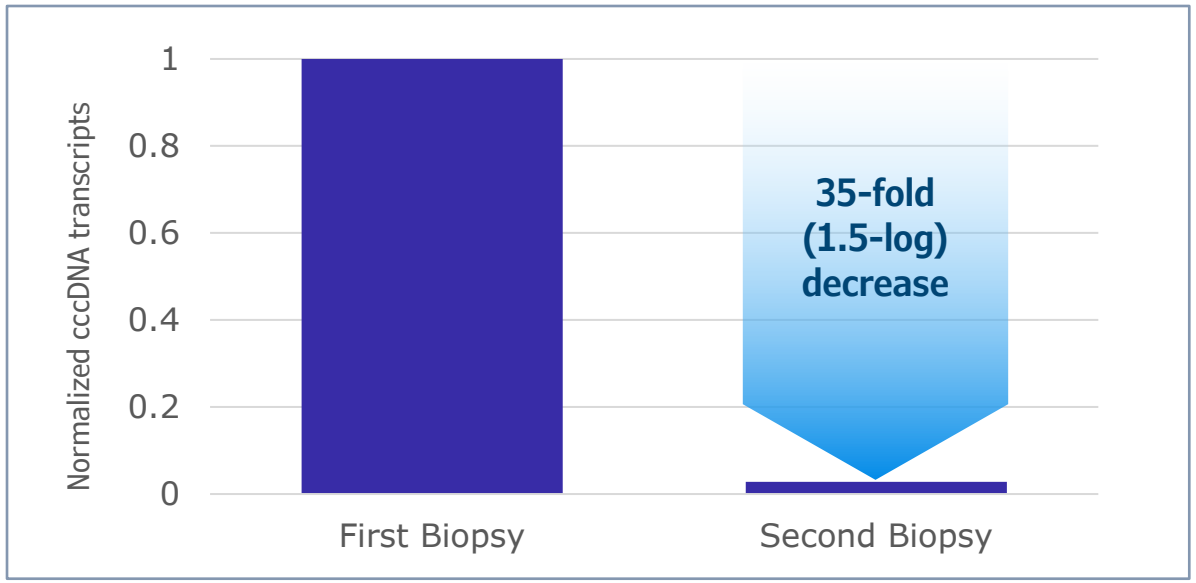

pgRNA loss


HBV DNA









cccDNA, covalently closed circular DNA; HBV, hepatitis B virus; pgRNA, pregenomic RNA.
Data cutoff: September 28, 2026.

Substantial HBsAg Declines in All Participants Supportive of cccDNA Elimination Across a Heterogeneous Population

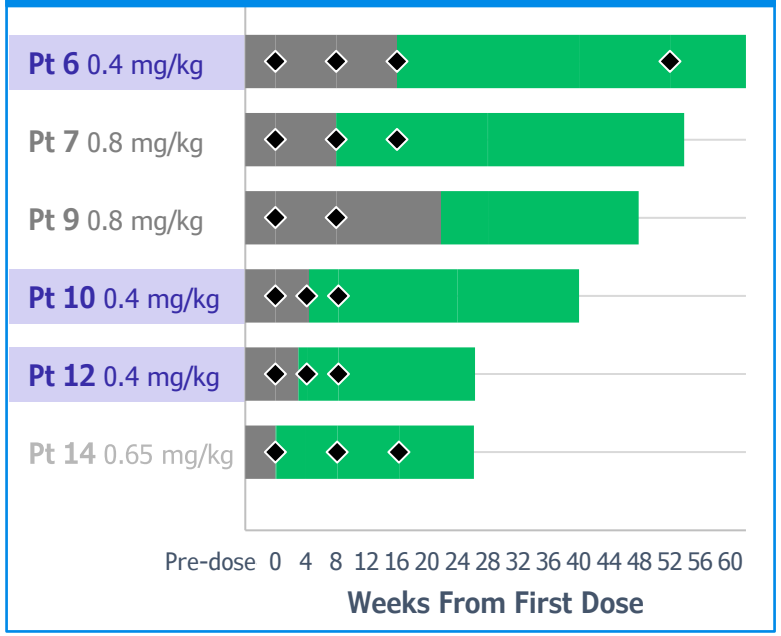


0.4 mg/kg was sufficient to drive maximal efficacy

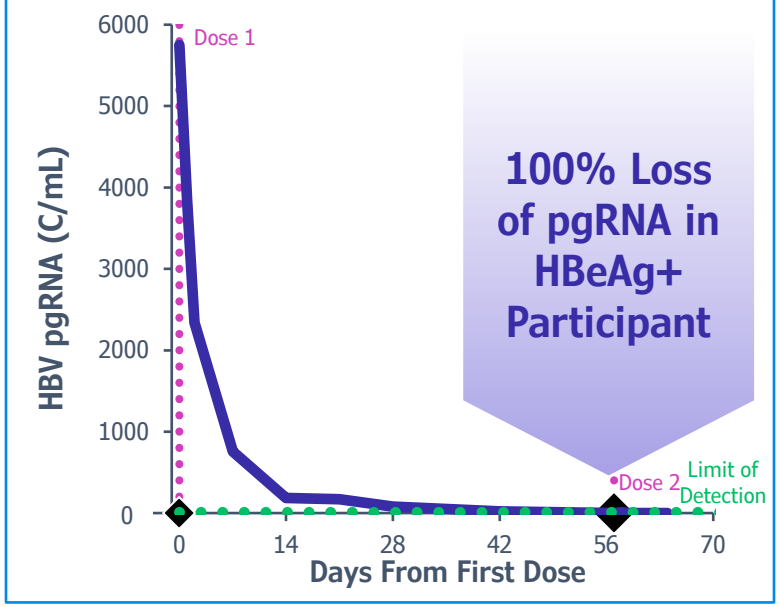
Participant 25 is not yet evaluable for efficacy.
cccDNA, covalently closed circular DNA; HBsAg, hepatitis B surface antigen.
Data cutoff: September 28, 2026.

Compelling Efficacy Data Support 0.4 mg/kg as Go-Forward Dose for Phase 2

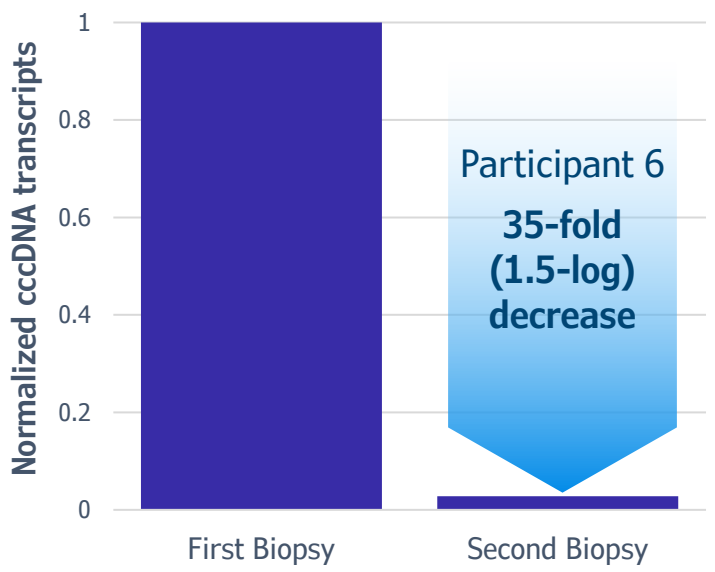
Durable pgRNA Loss >6 Months



100% pgRNA Loss in HBeAg+ Participant

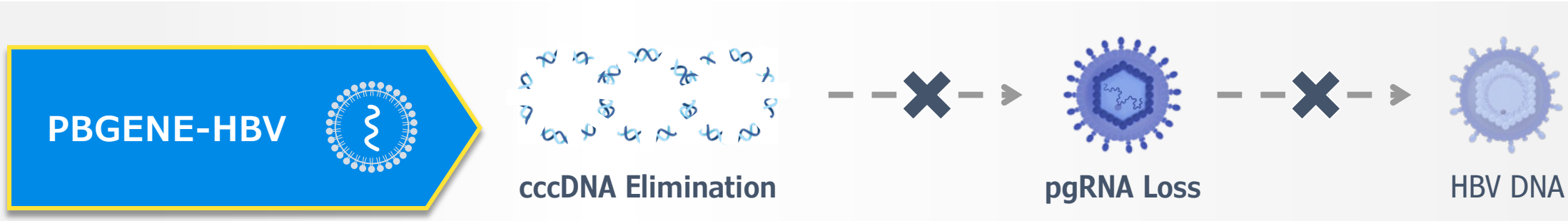


Liver Biopsies with ≥1-log cccDNA Elimination



C/mL, copies per milliliter; cccDNA, covalently closed circular DNA; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; pgRNA, pregenomic RNA; Pt, participant.
Data cutoff: September 28, 2026.

SUMMARY: Durable pgRNA Loss in Both HBeAg-Positive and -Negative Participants Treated With PBGENE-HBV Supports a Path Toward Viral Cure



Safety:

- PBGENE-HBV was well-tolerated with **no DLTs** across 59 doses in 25 participants, at levels ranging up to 0.8 mg/kg
- Manageable safety profile with no SAEs, with all participants completing planned doses at 0.4 mg/kg with new infusion protocol
- No Grade ≥3 hypotension at 0.4 mg/kg with new infusion protocol
- In the global Phase 1 ELIMINATE-B trial, there were no cases of elevated bilirubin, Hy's Law, or evidence of synthetic liver dysfunction

Efficacy:

cccDNA Elimination:

Biopsies in 2 participants at **0.4 mg/kg** showed **1-log and 1.5-log reduction** in transcripts from cccDNA

Durable pgRNA Loss:

- 92% (11/12) of participants achieved pgRNA loss
- **pgRNA loss in 100% of participants at 0.4 mg/kg**
- All participants with **≥6-month** follow-up have maintained durable pgRNA loss
- **In an HBeAg-positive participant**, loss of pgRNA after treatment with PBGENE-HBV at **0.4 mg/kg** showed elimination of cccDNA is not limited to participants with lower cccDNA burden

Next Steps:

Safety and efficacy data at **0.4 mg/kg support Phase 2a global expansion** to evaluate PBGENE-HBV as monotherapy and combination therapy for **potential viral cure** and functional cure[1,2]

AASLD 2026 Publication Number: 5002

cccDNA, covalently closed circular DNA; DLT, dose-limiting toxicity; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; pgRNA, pregenomic RNA; SAE, serious adverse event.

1. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol*. 2025;83(2):502-583. 2. US Food and Drug Administration. Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment. Published April 2022. Accessed November 2, 2026.

We thank the study **participants**, **investigators**, and **clinical site staff** for their participation and support in the ELIMINATE-B study. We also acknowledge the important contributions of the clinical operations and other functional teams, as well as our partners in the HBV field who have shared valuable insights on the trial design.