LBP-038

Initial safety data from ELIMINATE-B, the first clinical trial of a gene editing treatment for chronic hepatitis B

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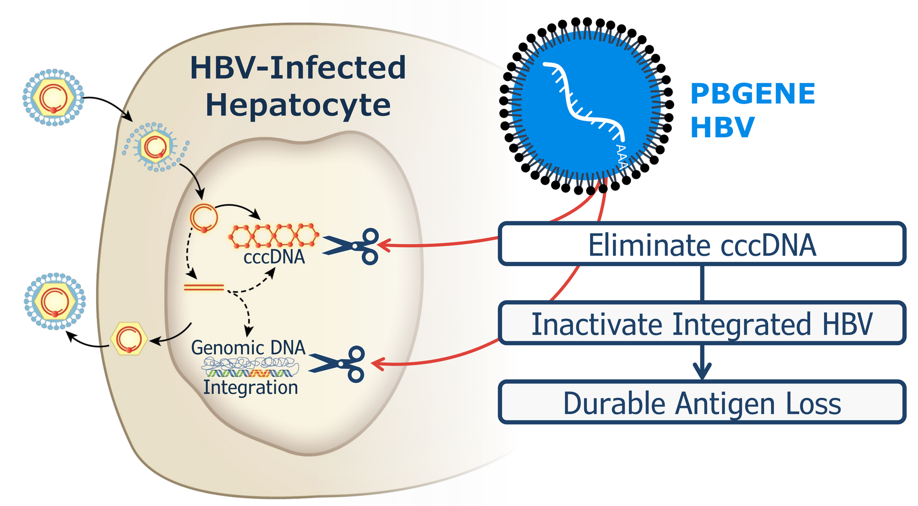
Introduction

Targeting the Root Cause of Chronic Hepatitis B

- Persistence of chronic hepatitis B virus (cHBV) is attributed to maintenance of the intrahepatic pool of the hepatitis B virus (HBV) covalently closed circular DNA (cccDNA).
- PBGENE-HBV is a lipid nanoparticle encapsulating (LNP) ARCUS mRNA that encodes an ARCUS nuclease. Once taken up into hepatocytes the mRNA is translated to an ARCUS protein that cuts a highly conserved target sequence in cccDNA and integrated HBV DNA.
- Cleavage of the target site leads to cccDNA elimination and inactivation of integrated HBV DNA (IntDNA) leading to a reduction of all viral products in preclinical models.



Preclinical Safety and Efficacy

Safety and Antiviral Effects in Multiple Models

Human HBV cell lines

IntDNA INACTIVATION: Dose-dependent editing and HBsAg reductions[1]

SAFETY: Comprehensive off-target analysis demonstrates high specificity[1]

Primary human hepatocytes

cccDNA ELIMINATION: Dose-dependent elimination of cccDNA and inhibition of viral markers[1]

SAFETY: Comprehensive off-target analysis demonstrates high specificity[2]

Transgenic Mouse Model

IntDNA INACTIVATION: Significant and sustainable reduction of HBV DNA in HBV transgenic mouse model[1]

Episomal AAV Mouse Model

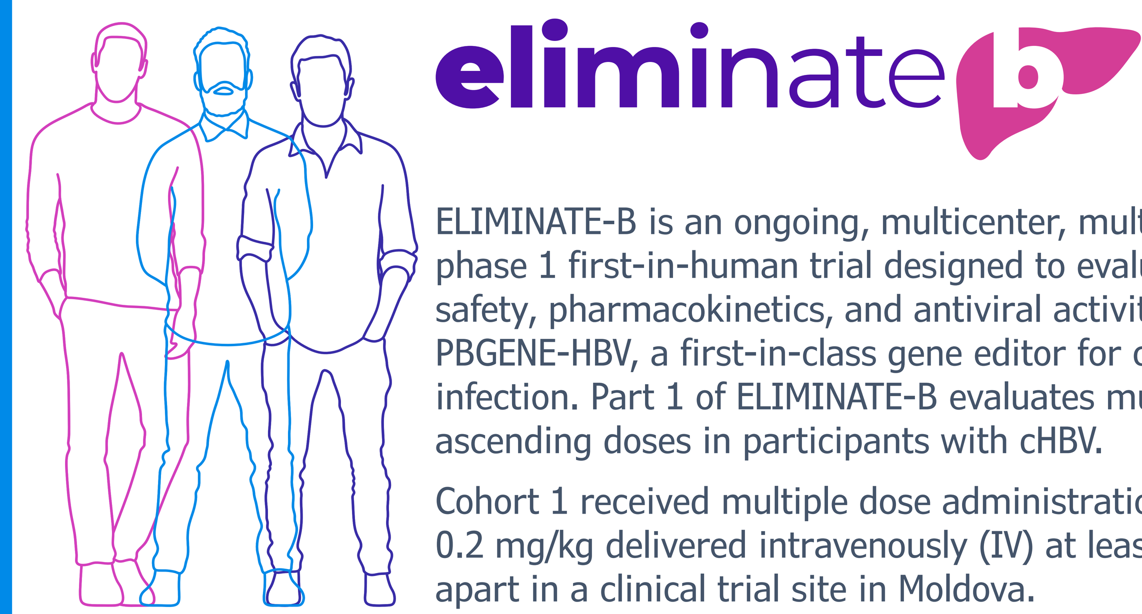
cccDNA ELIMINATION: >95% durable HBsAg reduction across multiple dose levels in AAV mouse model[1]

Nonhuman primates

cccDNA ELIMINATION: 99% viral engagement at highest dose[1]

SAFETY AND PHARMACOKINETICS: Multiple doses were well-tolerated in NHP[2,3]

ELIMINATE-B Methods



ELIMINATE-B is an ongoing, multicenter, multinational, phase 1 first-in-human trial designed to evaluate the safety, pharmacokinetics, and antiviral activity of PBGENE-HBV, a first-in-class gene editor for cHBV infection. Part 1 of ELIMINATE-B evaluates multiple ascending doses in participants with cHBV.

Cohort 1 received multiple dose administrations of 0.2 mg/kg delivered intravenously (IV) at least 8 weeks apart in a clinical trial site in Moldova.

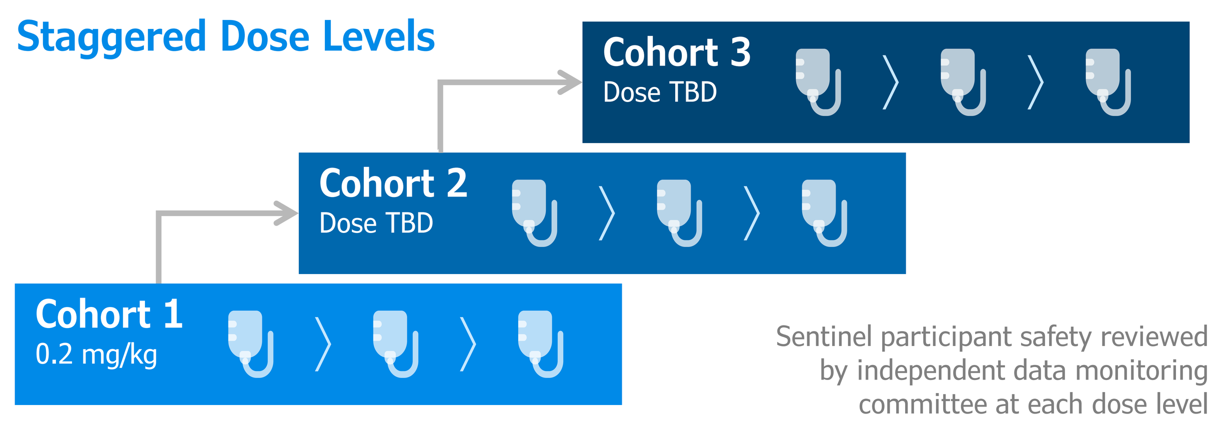
Inclusion Criteria

- HBeAg-negative cHBV
- cHBV infection documented by serum HBsAg-positivity for ≥ 12 months
- Serum HBsAg ≥200 IU/mL at screening
- Virologically suppressed and currently on nucleos(t)ide analog (NA) treatment; HBV DNA < 20 IU/mL
- Serum ALT ≤ 1.5× ULN
- FibroScan™ ≤ 8.5kPa within 6 months

Exclusion Criteria

- History of liver cirrhosis, regardless of any subsequent improvement in histology
- Hepatitis A, D, or E virus infection, HIV type 1 or type 2 infection, or history of hepatitis C infection
- Evidence of liver decompensation at any time
- Signs of hepatocellular carcinoma

Staggered Dose Levels



Sentinel participant safety reviewed by independent data monitoring committee at each dose level

Participant Demographics

Characteristic	Cohort 1
Number of Participants	3
Mean Age in years (range)	41 (39-44)
Male sex (%)	(100%)
Ethnicity/Race	Caucasian
Duration of CHB Infection (range)	18 years (7.5-39)
Type of NA (%)	TDF (100%)
Mean Years on NA (range)	6.6 (5.9-7.2)
Mean Baseline HBsAg (range)	4387 IU/mL (561-11813)
ALT≤ULN* (%)	3 (100%)

Primary Endpoint

Frequency and Severity of dose-limiting toxicities (DLT)

A DLT is any clinically significant, organ-specific, treatment-emergent adverse event (AE) ≥ Grade 3 that does not decrease to ≤ Grade 2 within 7 days and is related to study medication. DLT Period: 28 days post dose administration.

Secondary Endpoints

- Frequency & severity of AEs
- Changes in clinical laboratory data
- PK parameters of PBGENE-HBV
- Antiviral activity of PBGENE-HBV — HBsAg levels over time

Results

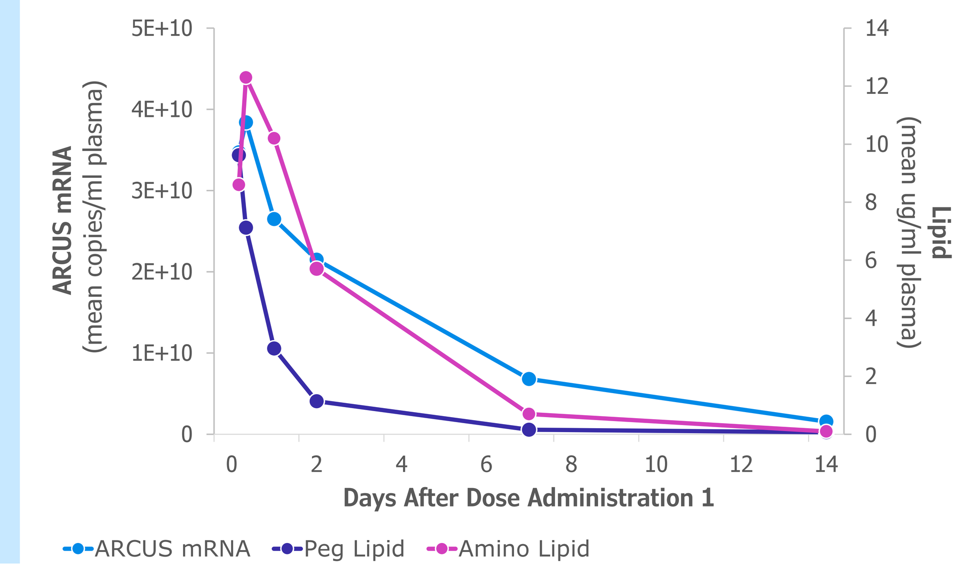
Cohort 1 Treatment-Related / Possibly Treatment-Related Adverse Events (AEs)

No Serious Adverse Events (SAE) or Dose Limiting Toxicities (DLT)

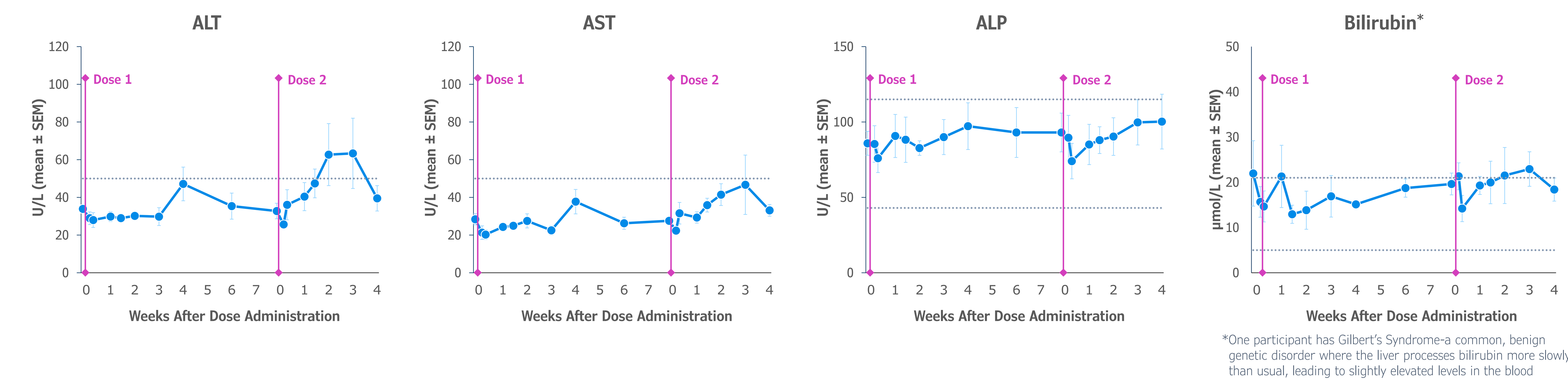
Number of participants experiencing:	0.2 mg/kg, (n=3) Two dose administrations
Grade 1 AEs	
Arthralgia	1
Chills	1
Fever	1
Myalgia	2
Sinus Tachycardia	1
Grade 2 AEs	
Fever	1
Headache	1
No Grade ≥3 AEs / SAEs	
No DLTs	

Cohort 1 Pharmacokinetics

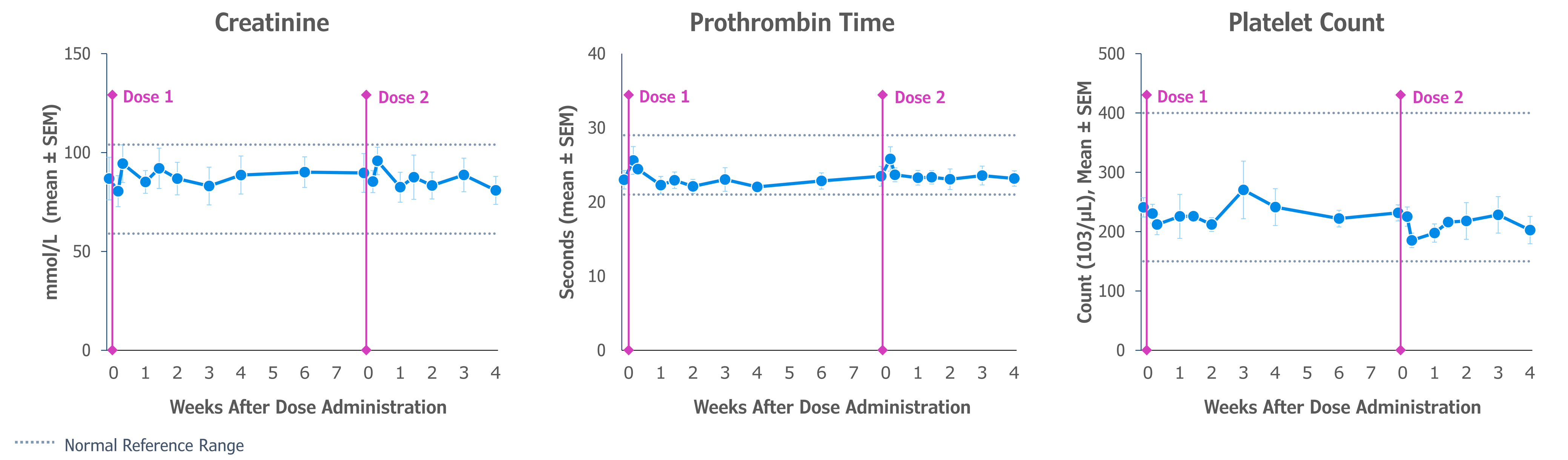
Majority of PBGENE-HBV exposure is complete within 7 days, consistent with nonclinical NHP data



Cohort 1 Clinical Safety



*One participant has Gilbert's Syndrome-a common, benign genetic disorder where the liver processes bilirubin more slowly than usual, leading to slightly elevated levels in the blood



Key Safety Summarized

- No clinically significant laboratory abnormalities after 2 dose administrations at 0.2 mg/kg.
- Transient ALT elevations were considered clinically insignificant.
- Platelets remained within normal limits.

Conclusions

- Clinical safety data demonstrates that PBGENE-HBV was well tolerated with no DLTs and no serious adverse events after multiple dose administrations.
- These data support the continued evaluation of multiple dose administrations per dose cohort and higher dose level cohorts of PBGENE-HBV, with the goal of achieving HBV cure.
- Safety and PK data validates the translation of the NHP model to the clinic.

PRECISION BIOSCIENCES

REFERENCES:
[1]Harrison, E.B. et al. Preclinical efficacy and safety of ARCUS-POL Nucleases for chronic hepatitis B: A potentially curative strategy. AASLD. Boston, MA. 2023, 5040-C
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[3]Van Cott, A. et al. PBGENE-HBV Definitive preclinical toxicokinetic and toxicology data enables advancement to clinical trials for a potentially curative gene editing treatment for chronic hepatitis B. GHS. LA, CA. 2025, 30267

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