HOPE-B Pivotal Trial: 3-Year Update

Health **O**utcomes with the **P**adua Gene: **E**valuation in Hemophilia **B**

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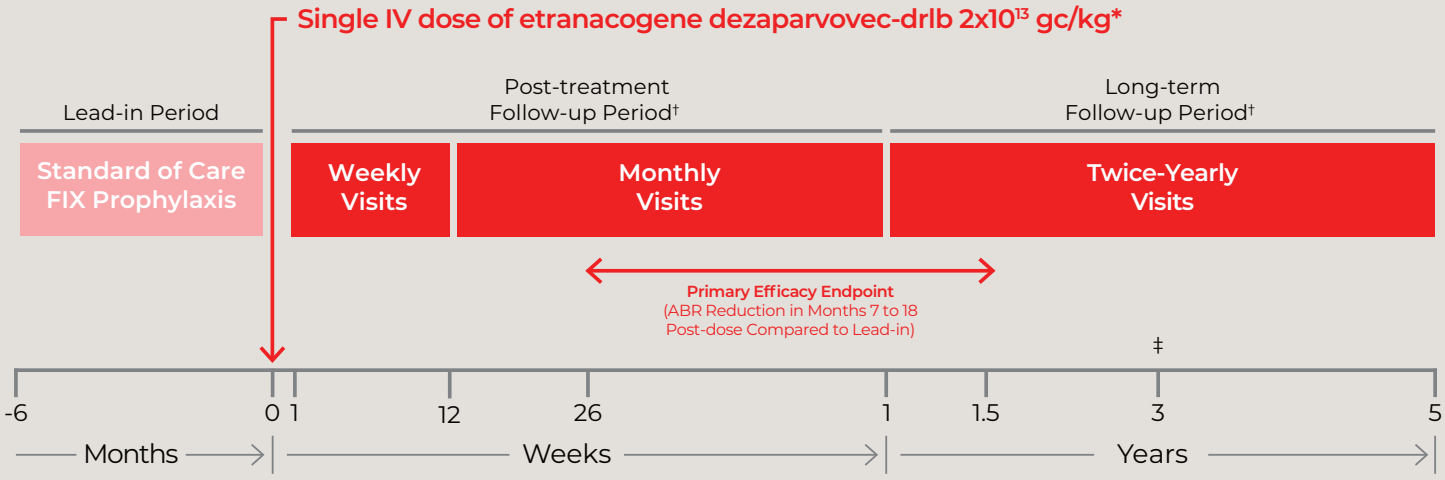
3 years following a single IV dose of etranacogene dezaparvovec-drlb, participants experienced[1]:

- Stable and durable increase in FIX activity
- Significant reductions in ABR compared to lead-in FIX prophylaxis period
- No new safety events; safety profile remained favorable

HOPE-B Clinical Trial Information[1,2]

HOPE-B Clinical Trial Design:

A phase 3, open-label, single-dose, multicenter study of etranacogene dezaparvovec-drlb, a liver-directed recombinant AAV5 vector expressing the Padua factor IX variant



* No prophylactic immunosuppression required. † At least quarterly contact (± 2 weeks) between site staff and participants to monitor occurrence of AEs. ‡ For this update, all patients had reached 3 years of follow-up.

Enrollment Criteria

Adult male
≥ 18 years

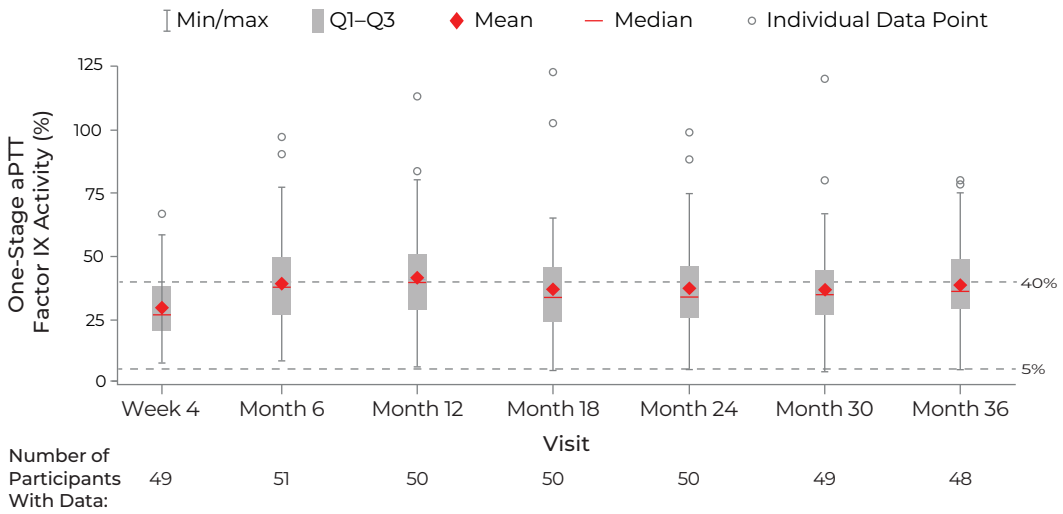
- Severe or moderately severe hemophilia B (FIX activity ≤ 2%)
- Receiving routine prophylaxis (≥ 2 months)
- With or without neutralizing antibodies to AAV5
- No FIX inhibitors, active HBV/HCV, uncontrolled HIV infection, advanced liver disease

Baseline Characteristics

Characteristic	Full Analysis Set (N = 54)
Average age, y (range)	41.5 (19–75)
NAb status at baseline, n (%)	
Negative	33 (61)
Positive	21 (39)
HIV+, n (%)	3 (6)
Previous HBV, n (%)	9 (17)
Previous HCV, n (%)	31 (57)

Clinical Study Results After 3 Years[1]

FIX activity was sustained over 3 years post-treatment[3]



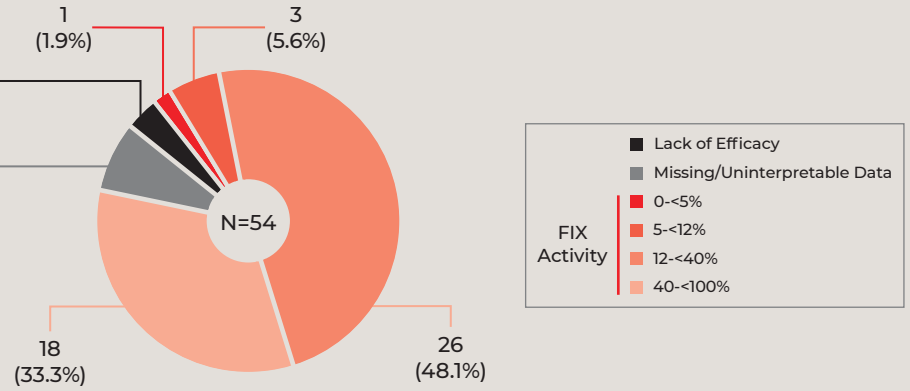
Endogenous FIX Activity Levels	At Year 3
Mean ± SD	38.6 ± 17.8%
Median	36.0%
IQR	29.5 – 48.1%
Min – Max	4.8 – 80.3%

Mild-normal FIX activity was achieved for the majority of participants

2 (3.7%) Lack of Efficacy
- Participant with highest NAb titer
- Participant who received ~10% of the planned dose

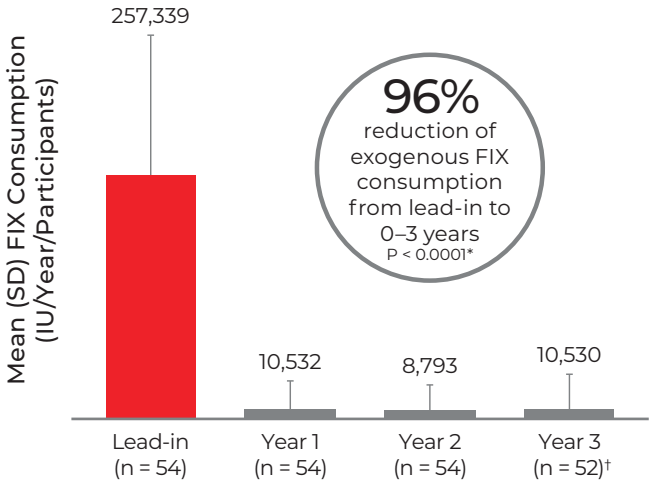
4 (7.4%) Missing/Uninterpretable Data

Reason for Missing/ Uninterpretable Data	Last FIX Activity Levels*
Death at month 15 (unrelated to treatment)	43.7%
Liver transplant (HCC unrelated to treatment)	36.7%
Return to FIX prophylaxis at month 30	3.6%
Non-analyzable sample (hemolysis)	33.5%



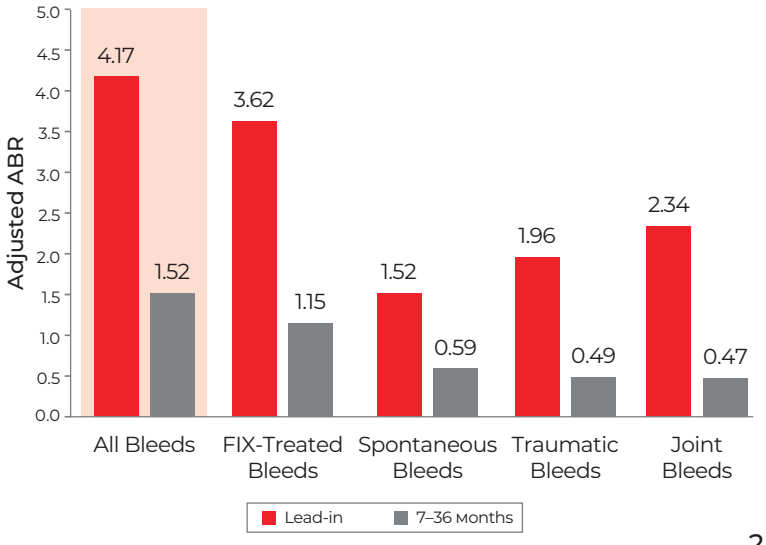
* Based on One-stage FIX activity levels from central laboratory results. Only "uncontaminated" samples were included in analysis; that is, blood sampling did not occur within five half-lives of exogenous FIX use.

94% of participants discontinued FIX prophylaxis and remained prophylaxis free



* P value is calculated using a paired *t*-test comparing post-treatment and lead-in periods.
† 1 patient died (prophylaxis-free) and 1 patient who remained on prophylaxis withdrew consent for efficacy assessment.

Bleed protection shown at 7–18 months was maintained at 3 years: Lead-in versus Months 7–36



Clinical Study Results After 3 Years[1] *(continued)*

Etranacogene dezaparvovec-drlb remains safe and well-tolerated

TRAEs by MedDRA PT*	Participants, n (%)	Events, n
At least 1 TRAE	38 (70.4)	93
ALT increased	9 (16.7)	10
Headache	8 (14.8)	9
Influenza-like illness	7 (13.0)	8
AST increased	5 (9.3)	6
CPK increased	4 (7.4)	6
Dizziness	4 (7.4)	4
Fatigue	4 (7.4)	4
Nausea	4 (7.4)	4
Arthralgia	3 (5.6)	3

- 91 of 93 (97.8%) TRAEs occurred in the first 6 months
- IRR† occurred in 7 (13.0%) participants
- No treatment related SAE
- 1 death and 1 instance of hepatocellular carcinoma, reported, unrelated to treatment
- No FIX inhibitors, no thrombotic events

* MedDRA Version 26.0 was used for coding. † IRR: Infusion-related reaction were defined as any adverse events related to the investigation medical product administration procedure or unexpected reactions. They were infusion any treatment-emergent adverse event occurring within 24 hours of infusion, qualifying for special notification, assessed as related or possibly related by the investigator and considered as an infusion-related reaction during the safety assessment. They were infusion site reaction, hypersensitivity (i.e., urticaria), facial flushing, itching, also headache, dizziness, etc.

Abbreviations: AAV5, adeno associated virus serotype 5; ABR, annualized bleed rate; AE, adverse event; ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; CPK, creatinine phosphokinase; FIX, factor IX; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; IRR, infusion-related reaction; IU, international unit; IV, intravenous; MedDRA PT, Medical Dictionary for Regulatory Activities Preferred Term; NAb, neutralizing antibodies; Q, quartile; SAE, serious adverse event; SD, standard deviation; TRAE, treatment-related adverse event.

References: 1. Pipe SW, et al. Oral Presentation at ASH Annual Meeting, December 11, 2023. 2. Pipe SW, et al. *N Engl J Med* 2023;388:706–18. 3. Data on file. Available from CSL Behring as DOF HGX-005.

Information provided is based on the oral presentation on December 11, 2023 at ASH 2023 Annual meeting. Please scan this QR code for more information:

IMPORTANT SAFETY INFORMATION

Warning and Precautions

Infusion Reactions

Infusion reactions, including hypersensitivity reactions and anaphylaxis, may occur. Monitor during administration and for at least 3 hours after end of infusion. If symptoms occur, slow or interrupt administration. Re-start administration at a slower infusion once resolved.

Hepatotoxicity/Hepatocellular Carcinoma

Post-dose, monitor for elevated transaminase levels. Consider corticosteroid treatment should elevations occur. The integration of liver-targeting AAV vector DNA into the genome may carry the theoretical risk of hepatocellular carcinoma development. For patients with preexisting risk factors for hepatocellular carcinogenicity, perform regular (eg, annual) abdominal ultrasound and alpha-fetoprotein testing following administration.

Immune-mediated neutralization of the AAV5 vector capsid

Preexisting neutralizing anti-AAV antibodies may impede transgene expression at desired levels.

Monitoring Laboratory Tests

In addition to monitoring liver function, monitor for Factor IX activity and Factor IX inhibitors after administration.

Adverse Reactions

The most common adverse reactions (incidence ≥5%) were elevated ALT, headache, blood creatine kinase elevations, flu-like symptoms, infusion-related reactions, fatigue, nausea, malaise, and elevated AST.

Indication

HEMGENIX®, etranacogene dezaparvovec-drlb, is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with Hemophilia B (congenital Factor IX deficiency) who:

- Currently use Factor IX prophylaxis therapy, or
- Have current or historical life-threatening hemorrhage, or
- Have repeated, serious spontaneous bleeding episodes.

HEMGENIX is for single use intravenous infusion only.

Contraindications: None.

Please see full prescribing information for HEMGENIX.

To report SUSPECTED ADVERSE REACTIONS, contact the CSL Behring Pharmacovigilance Department at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

HEMGENIX is manufactured by uniQure Inc. and distributed by CSL Behring LLC.

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