Final analysis of the phase 1/2 trial of valoctocogene roxaparvovec for severe hemophilia A

PW-07-22

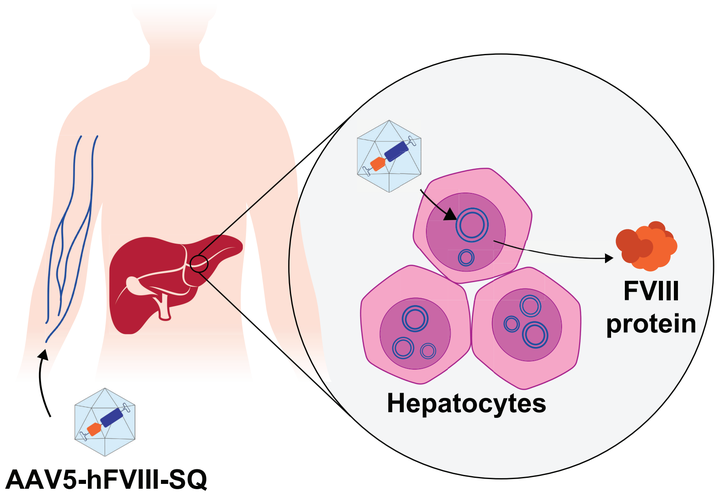
Priyanka Raheja[1], Emily Symington[2], Savita Rangarajan[3], Will Lester[4], Bella Madan[5], Glenn F. Pierce[6], Carolyn Millar[7], Dane Osmond[8], Mingjin Li[8], Catarina Kordsachia[8], Konstantia-Maria Chavele[8]

[1]Haemophilia Centre Royal London Hospital, Barts Health NHS Trust, London, UK; [2]Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [3]Faculty of Medicine, University of Southampton, Southampton, UK; [4]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [5]Guy's and St Thomas' NHS Foundation Trust, London, UK; [6]Independent Consultant, La Jolla, CA, USA; [7]Imperial College Healthcare NHS Trust and Centre for Haematology, Department of Immunology and Inflammation, Imperial College London, London, UK; [8]BioMarin UK Ltd, London, UK

Background

- Valoctocogene roxaparvovec (AAV5-hFVIII-SQ) is a liver-directed gene therapy that transfers a factor VIII (FVIII) coding sequence to enable endogenous FVIII production in people with severe hemophilia A (FVIII ≤1 IU/dL)[1]

Valoctocogene roxaparvovec for severe hemophilia A



AAV5, adeno-associated virus serotype 5; hFVIII-SQ, human FVIII, SQ variant

- Previously published results from this phase 1/2 trial (NCT02576795) and a phase 3 trial (GENEr8-1, NCT03370913) demonstrated the efficacy and safety of valoctocogene roxaparvovec[1-9]
- We present final efficacy and safety results and insights from across the full 7 years of the phase 1/2 trial

Methods

Study Design

- The design of this phase 1/2 trial has been described previously[1-5]
- Participants did not have a history of FVIII inhibitors, anti-AAV5 antibodies, significant liver dysfunction, significant liver fibrosis, or liver cirrhosis[1-5]

Endpoints

- Safety was assessed by adverse events (AEs)
- FVIII activity was assessed via chromogenic substrate assay and one-stage assay and are reported excluding data from participants who resumed prophylaxis
- Annualized treated bleeding rates (ABRs) and annualized FVIII infusion rates were calculated as described previously[1-5]
- Baseline ABRs were derived from the 12 months prior to enrollment

Statistics

- Data are presented with descriptive statistics
- Missing data were not imputed
- The yearly rate of change in FVIII activity was calculated using a linear regression model

Results

Participants

- Males aged ≥18 years of age with severe hemophilia A (FVIII ≤1 IU/dL) who were previously receiving exogenous FVIII received an infusion of $6x10^{13}$ (n = 7) or $4x10^{13}$ (n = 6) vg/kg valoctocogene roxaparvovec. All participants completed the study except 1 participant in the $4x10^{13}$ vg/kg cohort who was lost to follow-up by week 312

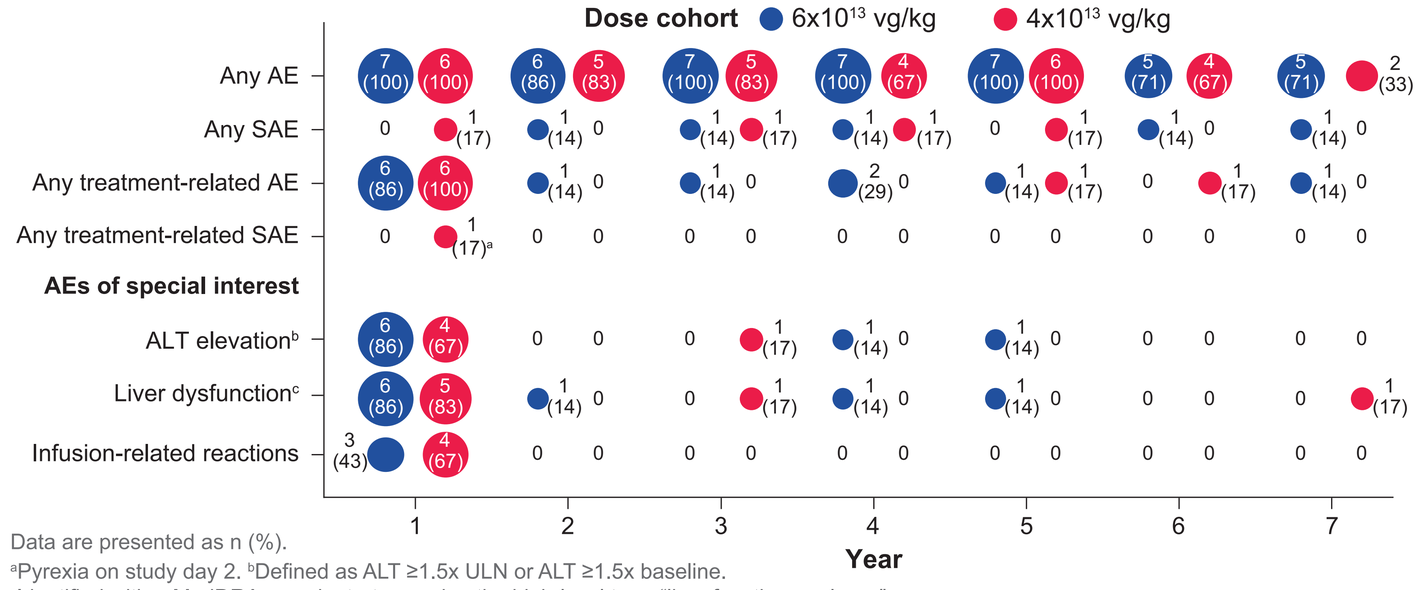
Baseline characteristic	$6x10^{13}$ vg/kg cohort (n = 7)	$4x10^{13}$ vg/kg cohort (n = 6)
Age, y		
Median (min, max)	30.0 (23.0, 42.0)	30.5 (22.0, 45.0)
ABR, bleeds/y		
Mean (SD)	17.6 (14.7)	12.2 (15.4)
Median (min, max)	24.0 (0.0, 40.0)	8.0 (0.0, 41.0)
AFR, infusions/y		
Mean (SD)	120.1 (45.9)	142.8 (48.8)
Median (min, max)	121.4 (27.4, 158.5)	155.8 (53.8, 184.3)

ABR, annualized bleeding rate; AFR, annualized factor VIII infusion rate; max, maximum; min, minimum; SD, standard deviation

Safety

- In year 1, the most common treatment-related AE was alanine aminotransferase (ALT) elevation
- No treatment-related serious AEs (SAEs) occurred after year 1
- No ALT elevations were reported after year 5
- In the last year, no new safety signals were reported
- Across the trial, no participants experienced thromboembolic events or developed FVIII inhibitors

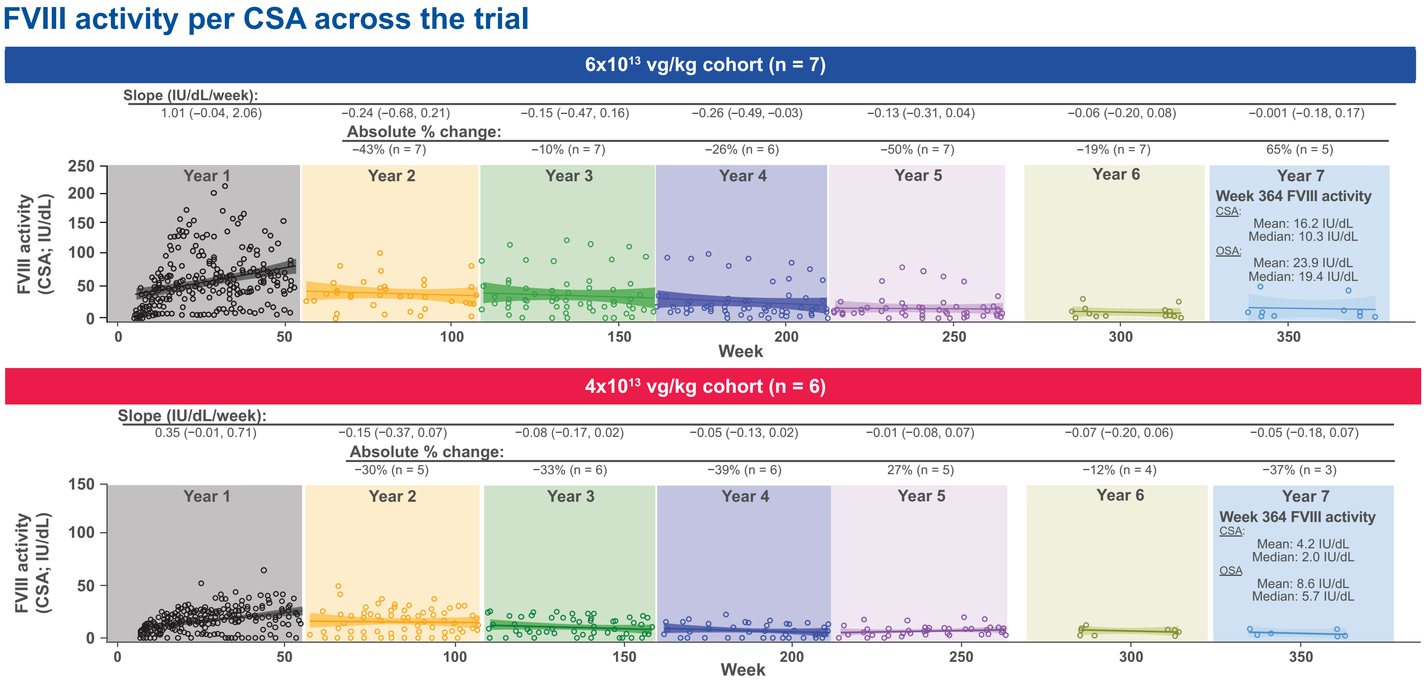
Summary of incidence of AEs in each year by cohort



Data are presented as n (%).
[a]Pyrexia on study day 2. [b]Defined as ALT ≥1.5x ULN or ALT ≥1.5x baseline.
[c]Identified with a MedDRA search strategy using the high-level term "liver function analyses".
AE, adverse event; ALT, alanine aminotransferase; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious AE; ULN, upper limit of normal.

FVIII activity

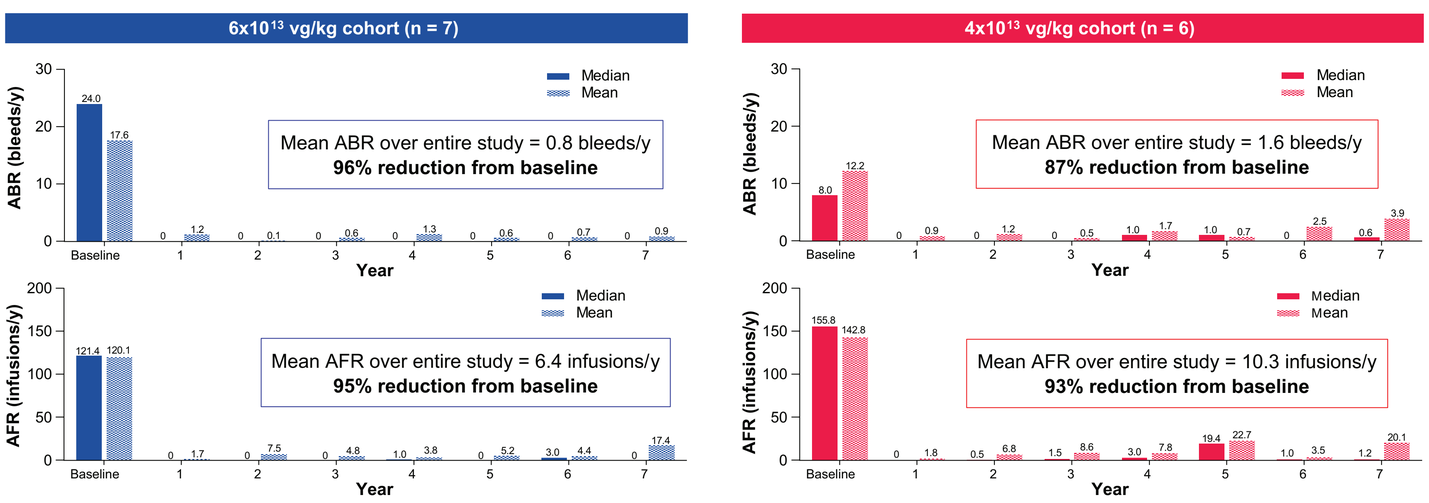
FVIII activity per CSA across the trial



CSA, chromogenic substrate assay; FVIII, factor FVIII; OSA, one-stage assay.

Hemostatic efficacy

- Overall, 5 of 7 participants in the $6x10^{13}$ cohort and 3 of 5 participants in the $4x10^{13}$ cohort remained off prophylaxis (1 participant in the $4x10^{13}$ cohort was lost to follow-up)[5]
- Reductions in treated bleeds and FVIII infusion rates were maintained across the trial



ABR, annualized bleeding rate; AFR, annualized FVIII infusion rate; FVIII, factor VIII.

Conclusions

- Safety outcomes following doses of $6x10^{13}$ and $4x10^{13}$ vg/kg valoctocogene roxaparvovec remained consistent with previous reports[1-5]
- The most common treatment-related AE in year 1 was ALT elevation; no treatment-related SAEs occurred after year 1
- No participants experienced thromboembolic events or developed FVIII inhibitors
- Despite the slow decline in FVIII levels, valoctocogene roxaparvovec continues to support hemostasis for the majority of participants
- Rates of treated bleeds declined 96% and 87% from baseline for the $6x10^{13}$ and $4x10^{13}$ vg/kg cohorts, respectively; FVIII infusion rates declined 95% and 93% from baseline

References

1. Rangarajan S, et al. *N Eng J Med.* 2017;3877(26):2519-30. **2.** Pasi KJ, et al. *N Eng J Med.* 2020;382:29-40. **3.** Pasi KJ, et al. *Haemophilia.* 2021;27(6):947-56. **4.** Symington E, et al. *Haemophilia.* 2024;30:320-30. **5.** Symington E, et al. *Haemophilia.* 2024;30(5):1138-47. **6.** Ozelo MC, et al. *N Eng J Med.* 2022;386:1013-25. **7.** Mahlangu J, et al. *N Eng J Med.* 2023;388(8):694-705. **8.** Madan B, et al. *J Thromb Haemost.* 2024;22(7):1880-93. **9.** Leavitt AD, et al. *RPTH.* 2024;8:e102615.

Acknowledgments

Funding for this study was provided by BioMarin Pharmaceutical Inc. Project management support was provided by Gillian Clague, CMPP, of BioMarin Pharmaceutical Inc. Medical writing support was provided by Rachel Corrigan, PhD, of AlphaBioCom, a Red Nucleus company, and funded by BioMarin Pharmaceutical Inc.

Disclosures

PR has received grant/travel support from CSL Behring, Sobi and Takeda, and advisory honoraria from BioMarin, CSL Behring, LFB, Pfizer and Sobi. **ES** received grants from BioMarin and travel support from CSL Behring and Novo Nordisk. **SR** received grants from Roche and Sangamo; travel support from Reliance Life Sciences and Shire/Takeda; and consulting payments from Pfizer, Reliance Life Sciences, Sanofi, and Shire/Takeda. **WL** received grants from BioMarin; personal fees from Bayer, LFB Biopharmaceuticals, Novo Nordisk, Sobi, and Takeda; and travel support from Takeda and CSL. **BM** has received speaker fees from BioMarin. GFP received consulting payments from BioMarin, Decibel Therapeutics, Frontera, Generation Bio, Regeneron Pharmaceuticals, Spark Therapeutics, and Third Rock Ventures; and is a board member of Be Bio, the Medical and Scientific Advisory Council of the US National Hemophilia Foundation, Metagenomi, Pfizer, Spark Therapeutics, Voyager Therapeutics, and the World Federation of Hemophilia. **CM** has received research support from Baxter/Takeda, CSL Behring, and Grifols; honoraria or consultation fees from CSL Behring, LFB Biopharmaceuticals, Octapharma, and Takeda; and has participated in advisory boards for CSL Behring and Takeda. **DO, ML,** and **K-MC** are employees and shareholders of BioMarin.

To view a copy of this poster, scan this QR code. Copies of this poster obtained through the QR code are for personal use only and may not be reproduced without permission from the authors.

Presented at the GTH 70th Annual Meeting: February 17–20, 2026, Bonn, Germany

©2026 BioMarin Pharmaceutical Inc. All rights reserved.