Continued growth after puberty in participants with achondroplasia treated with vosoritide in a phase 3 long-term extension trial

Poster #
Sat-555

Julie E Hoover-Fong[1], Alice Huntsman Labed[2], Neil Lyon[2], Philippe F Backeljauw[3], Swati Mukherjee[2], Klaus Mohnike[4]

[1]Johns Hopkins University, Baltimore, MD, USA; [2]BioMarin (UK) Ltd, London, UK; [3]Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA; [4]Universitätskinderklinik Magdeburg, Otto-von-Guericke University, Magdeburg, Germany

Introduction

- Achondroplasia (ACH) is a rare genetic condition caused by a gain-of-function variant that constitutively activates the fibroblast growth factor receptor 3 (*FGFR3*) gene resulting in disproportionate short stature, health complications, and quality of life impairments[1]
- ACH is a multisystemic condition, with impaired bone growth affecting the skeletal, neurological and otolaryngological systems among others[2]
- Vosoritide is a recombinant C-type natriuretic peptide that downregulates FGFR3 signaling to induce endochondral bone growth[3]
- Vosoritide improves common complications associated with impaired endochondral bone growth,[4-6] increases linear growth,[2,7-10] and positively influences overall quality of life in children with ACH[11]
  - Vosoritide is an approved treatment for children with ACH until growth plate closure
- Untreated children with ACH experience less than half the linear growth of average-stature children during puberty[12,13]
- It is unknown how treatment with vosoritide affects residual linear growth after puberty, which is an important factor in final adult height

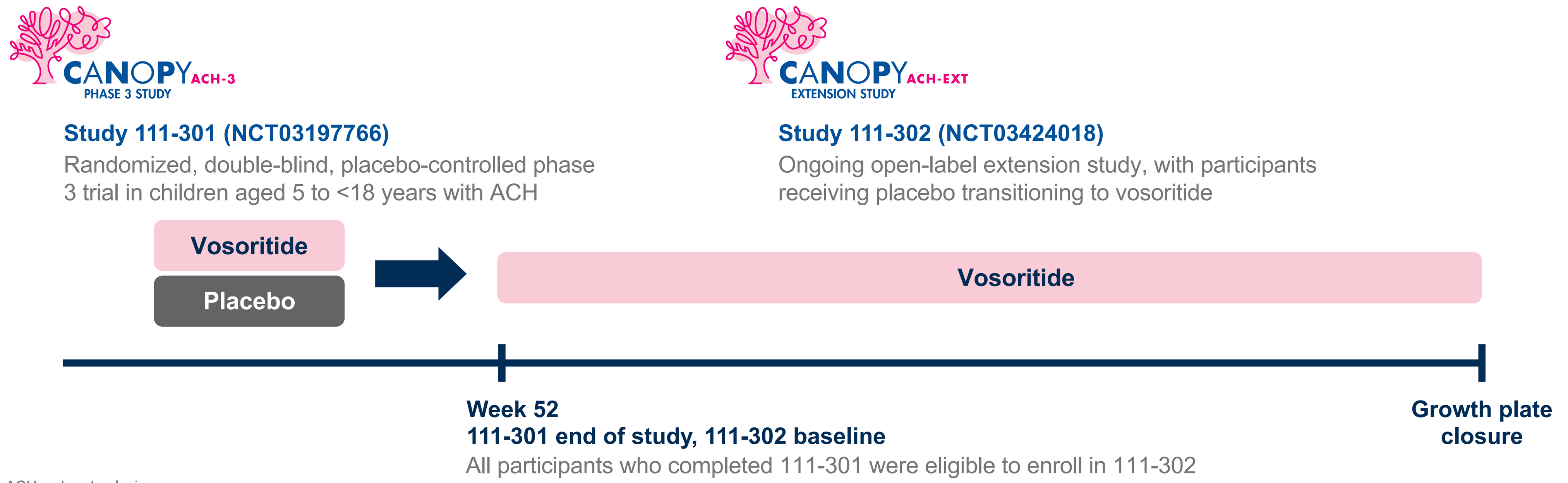
Objectives

- To determine the timing of puberty in children with ACH treated with vosoritide
- To evaluate the impact of vosoritide on linear growth after puberty onset in children with ACH compared with untreated children with ACH

Study design

- CANOPY ACH-EXT (111-302; NCT03424018) is an open-label, phase 3, long-term extension study of CANOPY ACH-3 (111-301; NCT03197766; **Figure 1**)
  - After enrolling in CANOPY ACH-EXT, all participants received 15 μg/kg vosoritide

Figure 1. Study design



ACH, achondroplasia.

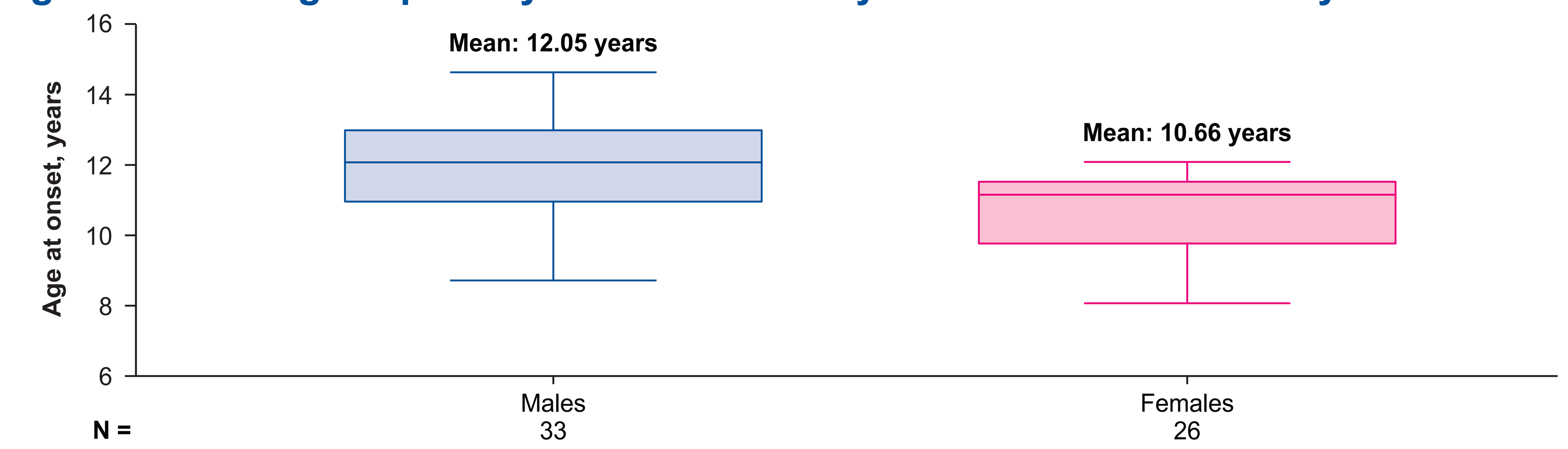
Methods

- A retrospective cohort of 1,374 untreated children with ACH with >37,000 anthropometric values from the CLARITY study were used as comparators[14]
- Puberty onset was defined as the increase of any Tanner stage from 1 to 2. For females, this was the earliest increase in either pubic hair or breast budding; for males, this was the earliest increase in either pubic hair or testicular volume
- Linear growth until adult height (age 18 years for males and 16 years for females) was based on summed annualized growth velocity across each integer age in CANOPY-ACH-EXT and CLARITY participants after the mean age of puberty onset in males and females

Results

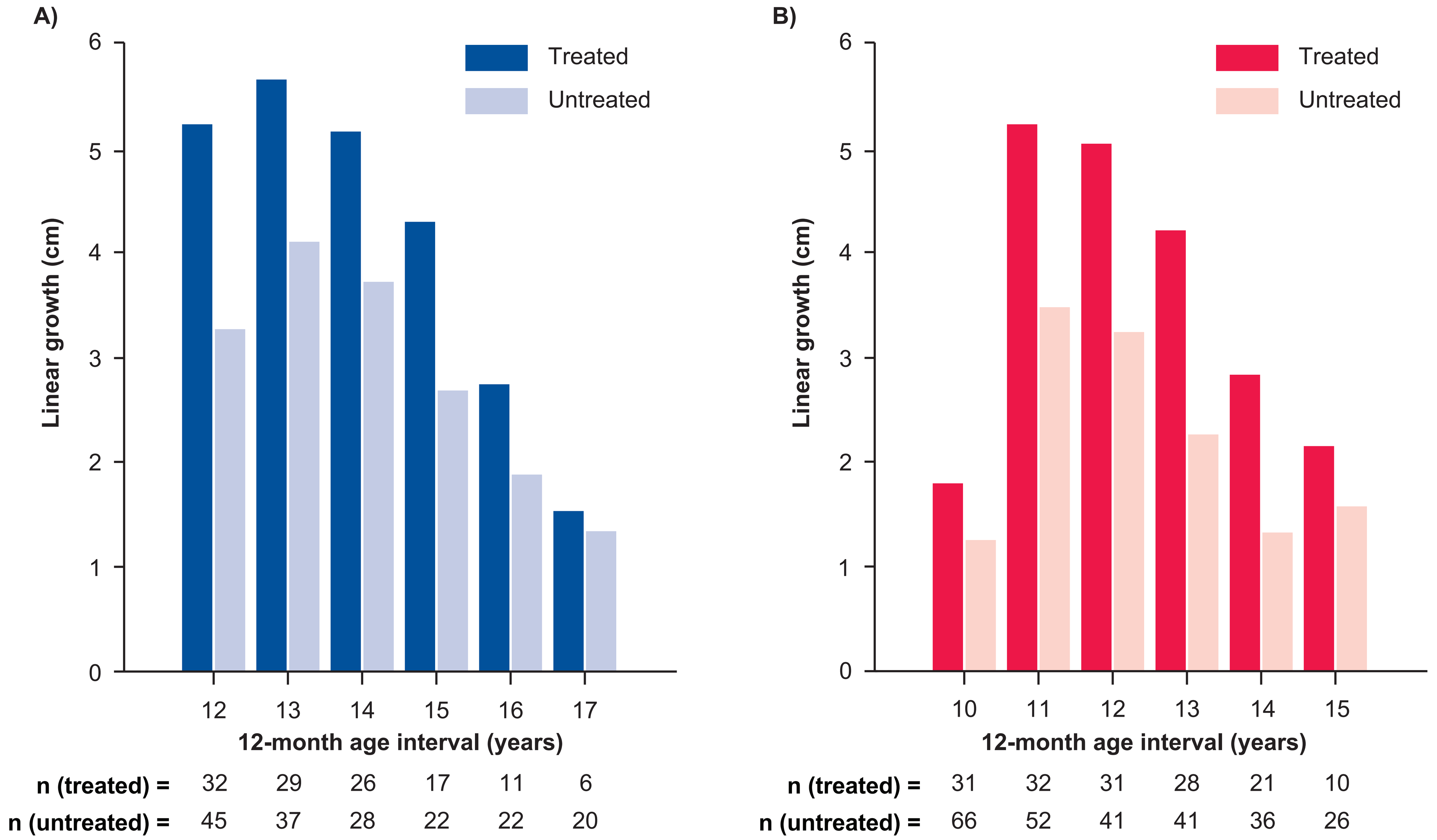
- A total of 33 males and 26 females could be assessed for puberty onset in CANOPY ACH-EXT (**Figure 2**); the mean ages of puberty onset from these participants were used for linear growth analyses
- While both treated and untreated children with ACH experienced linear growth after puberty, treated male and female children experienced more (**Figures 3 and 4**)

Figure 2. Mean age of puberty onset was 12.05 years in males and 10.66 years in females



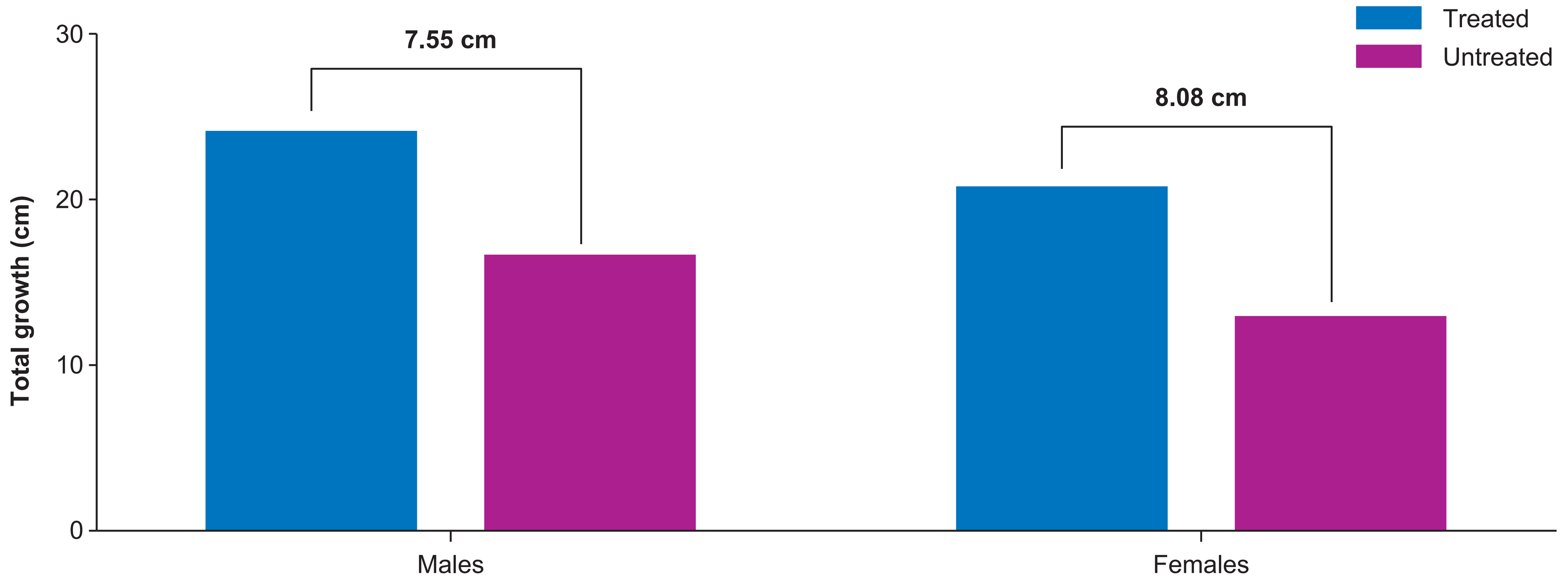
Age of puberty onset in male and female children with ACH treated with vosoritide. Horizontal lines represent medians, boxes represent interquartile ranges, and whiskers represent ranges. ACH, achondroplasia.

Figure 3. Linear growth continued from puberty onset until A) age 18 for males and B) age 16 for females



Bars represent the linear growth in each interval age after puberty onset in males and females. Growth during the sex-specific year of puberty onset is reduced to account for the partial year of growth remaining after onset.
ACH, achondroplasia.

Figure 4. Both male and female children with ACH experienced additional linear growth after puberty onset compared with untreated children with ACH



Total linear growth after onset of puberty in male and female children with ACH treated with vosoritide compared with natural history. Bars represent the sum of growth in each interval age after puberty onset until age 18 for males and 16 for females. The value of each bar is based on varying sample sizes during each year of growth.
ACH, achondroplasia.

Conclusions

- Linear growth is one of several important parameters used to evaluate treatment benefit in ACH
- Vosoritide continues to improve linear growth after puberty onset in children with ACH compared with the natural history of untreated children with ACH
- Increasing linear growth during adolescence for children with ACH may extend the window for epiphysiodesis
- These results suggest that children with ACH benefit from vosoritide treatment during and after puberty and that treatment should continue beyond puberty onset in children with ACH

References

1. Savarirayan R, et al. *Nat Rev Endocrinol.* 2022;18(3):173–89. **2.** Savarirayan R, et al. *Lancet Child Adolesc Health*. 2024;8(1):40–50. **3.** Savarirayan R, et al. *Nat Rev Endocrinol.* 2025;21(5):314–24. **4.** Lourenco P, et al. *Genet Med Open.* 2025;3(suppl 2):102121. **5.** Reincke S, et al. *J Endocr Soc.* 2025;9(5):bvaf041. **6.** Sawamura K, et al. *J Pediatr Orthop.* 2025; 10.1097/BPO.0000000000002980. **7.** Savarirayan R, et al. *N Eng J Med.* 2019;381910:25–35. **8.** Savarirayan R, et al. *Lancet.* 2020;396(10252):684–92. **9.** Savarirayan R, et al. *Med.* 2024;100566. **10.** Savarirayan R, et al. *Genet Med.* 2021;23(12):2443–7. **11.** Savarirayan R, et al. *Genet Med.* 2024;26(12):101274. **12.** Cole TJ, et al. *Ann Human Bio.* 2021;48(1):8–14. **13.** Cole TJ. *Ann Human Bio.* 2020;47(2):181–98. **14.** Hoover-Fong JE, et al. *Genet Med.* 2020;23(8):1498–505.

Acknowledgments

Medical writing support was provided by Amin Ghane, PhD, of Red Nucleus, and funded by BioMarin Pharmaceutical Inc.
Project management support was provided by Justin Potuzak, PhD, of BioMarin Pharmaceutical Inc.

Disclosures

JEH-F has participated in advisory boards and served as a consultant for Ascendis, AstraZeneca, BioMarin Pharmaceutical Inc., Children's Mercy Research Institute, Medscape, Pfizer, QED, and Therachon and has received research support from AstraZeneca, BioMarin Pharmaceutical Inc., and QED. **AHL**, **NL**, and **SM** are employees and shareholders of BioMarin Pharmaceutical Inc. **PFB** has consulted for or received honoraria from Ascendis, BioMarin Pharmaceuticals Inc., Eton Pharmaceuticals, ICON, Novo Nordisk, Pfizer, Upsher-Smith Laboratories, and Wolters Kluwer and receives research support from the National Institutes of Health/National Heart, Lung, and Blood Institute (U01HL133883). **KM** has received honoraria from BioMarin Pharmaceutical Inc., Novo Nordisk, and QED/BridgeBio for speaking, for participating in advisory board meetings, and as a member of steering committees.

Presented at American Society for Bone and Mineral Research (ASBMR) annual meeting; September 5–8, 2025; Seattle, WA, USA