Expanding possibilities with VOXZOGO

For children with achondroplasia[1,2]

Elijah

20 MONTHS OLD

on VOXZOGO since 12 months old as part of a clinical trial

VOXZOGO®
(vosoritide) for injection

[The only FDA-approved targeted therapy]

[Indicated to increase linear growth for children with achondroplasia from as early as birth until growth plates close.[1]]

INDICATION AND IMPORTANT SAFETY INFORMATION

VOXZOGO® (vosoritide) is indicated to increase linear growth in pediatric patients with achondroplasia and open growth plates.

- This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Warnings and Precautions for Risk of Low Blood Pressure

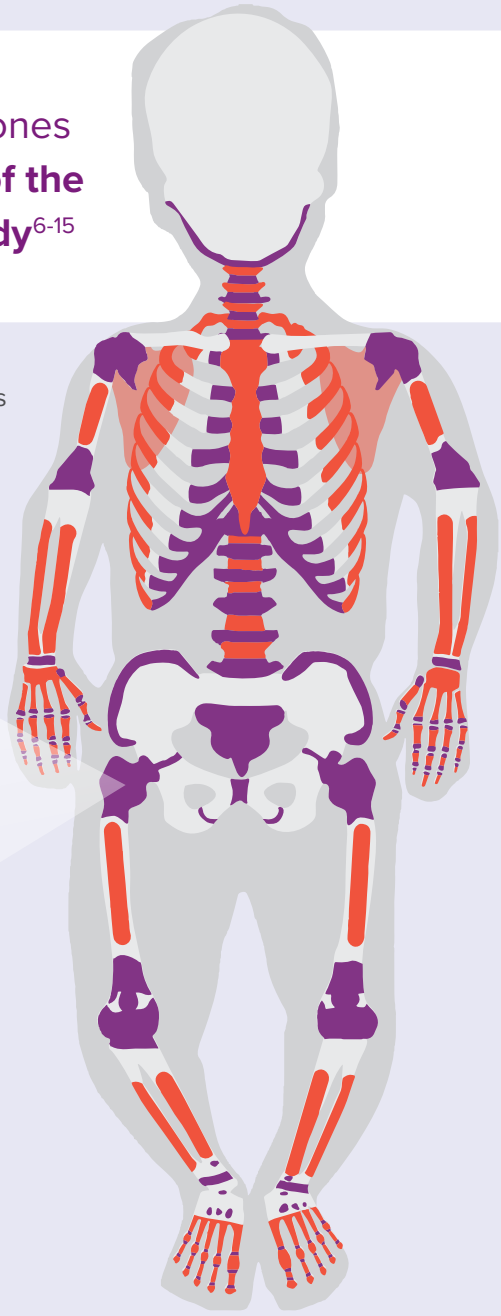
Transient decreases in blood pressure were observed in clinical studies. Patients with significant cardiac or vascular disease and patients on anti-hypertensive medicinal products were excluded from participation in VOXZOGO clinical trials. To reduce the risk of a decrease in blood pressure and associated symptoms (dizziness, fatigue, and/or nausea), patients should be well hydrated, have adequate food intake, and drink approximately 8-10 ounces of fluid in the hour prior to VOXZOGO administration.

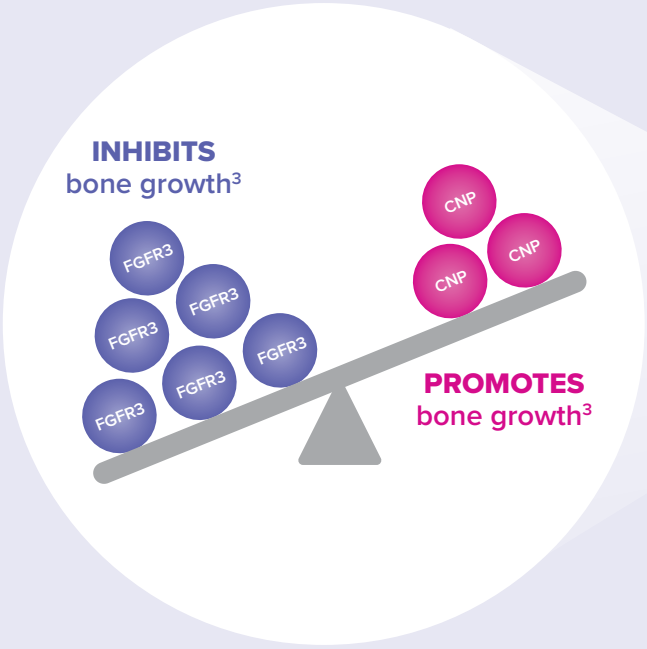
Please see additional Important Safety Information presented throughout, and full Prescribing Information.

Endochondral bone growth is inhibited in achondroplasia[3,4]

Endochondral bone growth is the predominant process of bone development in which cartilage is replaced by bone at open growth plates.[5,6]

Endochondral bones make up **>90% of the bones in the body**[6-15]





Overactive FGFR3 signaling relative to CNP signaling in growth plate cells is the underlying cause of inhibited bone growth in achondroplasia[3]

Endogenous CNP levels cannot adequately regulate overactive FGFR3 signaling.[3]

This simplified image is for illustrative purposes only.

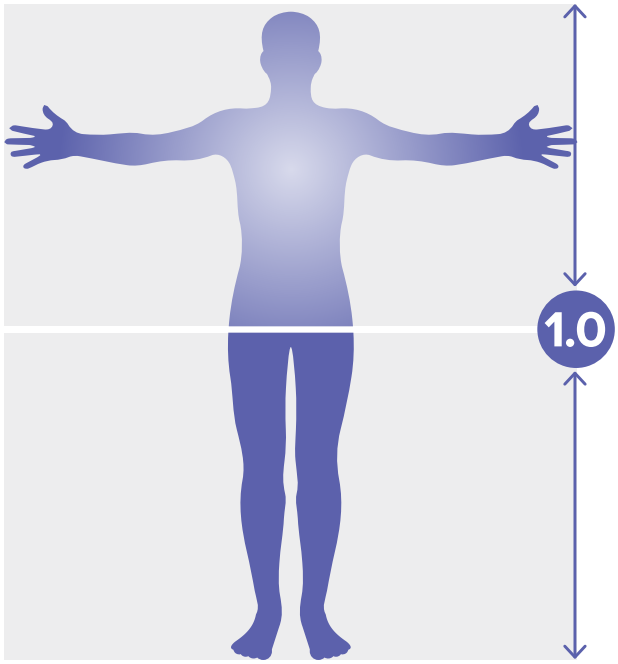
CNP, C-type natriuretic peptide; **FGFR3,** fibroblast growth factor receptor 3.

Inhibited bone growth throughout the body can affect different aspects of development[3-6,25,26]

Inhibited endochondral bone growth leads to distinct characteristic features such as **reduced and disproportionate growth**[3,4,25]

Upper-to-lower body segment ratio is a common measure of body proportionality and is calculated by the length of the upper body divided by the length of the lower body.[27-29]

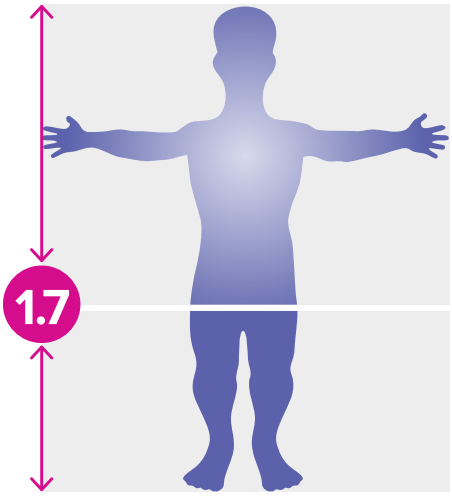
Adult with average stature



Upper-to-lower body segment ratio becomes proportional at 10 years old (ratio=1).[27,28]

Upper-to-lower body segment ratio

Adult with achondroplasia

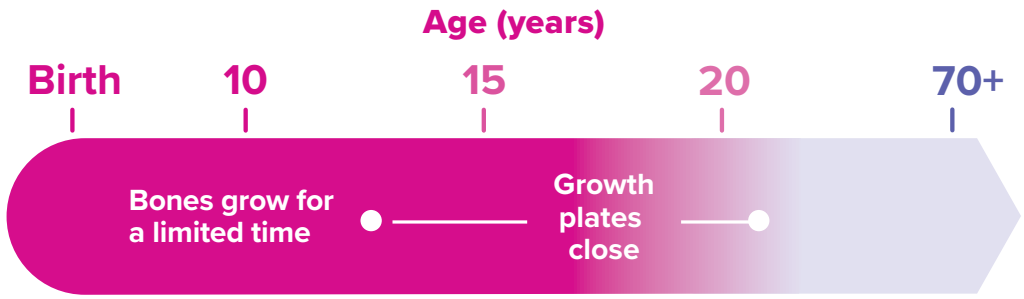


Upper-to-lower body disproportionality continues into adulthood (ratio>1).[27,28]

VOXZOGO promotes endochondral bone growth as early as birth[1]

VOXZOGO targets overactive FGFR3 signaling and works by mimicking the body's natural CNP to promote endochondral bone growth, but only while growth plates remain open.[1]

Maximize time on treatment by starting early and continuing until growth plates close[1,2,5,30]



International consensus guidelines support early initiation of VOXZOGO[2]

BioMarin provided funding for the *International consensus guidelines on the implementation and monitoring of vosoritide therapy in individuals with achondroplasia*, including honoraria to participants. BioMarin was not involved in the selection of the guidelines development group, defining the guidelines scope, the voting process, analysis of the results, or preparation of the submitted manuscript. Please see Acknowledgements section of publication for additional detail.[2]

CLICK OR SCAN THE QR CODE TO LEARN MORE

IMPORTANT SAFETY INFORMATION

Warnings and Precautions for Risk of Low Blood Pressure (cont'd)

In a 52-week, randomized, double-blind, placebo-controlled trial in 121 subjects with achondroplasia, subjects aged from 5.1 to 14.9 years, (Study 1) eight (13%) of 60 patients treated with VOXZOGO had a total of 11 events of transient decrease in blood pressure, compared to 3 (5%) of 61 patients on placebo, over a 52-week treatment period. The median time to onset from injection was 31 (18 to 120) minutes, with resolution within 31 (5 to 90) minutes in VOXZOGO-treated subjects. Two out of 60 (3%) VOXZOGO-treated patients each had one symptomatic episode of decreased blood pressure with vomiting and/or dizziness compared to 0 of 61 (0%) patients on placebo.

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

VOXZOGO has been studied in children aged 4 months to <18 years[1,31-33]

CANOPY-ACH-OS (Study 901)
Ongoing Observational Study[32,34]

- Age: 0 months to <18 years
- Establish baseline growth*

CANOPY ACH-2I (Study 206)†
Phase 2 Infant and Toddler Study[33,34]

- Age: 4 months to <5 years
- 52-week, double-blind, randomized, placebo-controlled

CANOPY ACH-EXT (Study 208)
Ongoing Open-label Extension Study[34,35]

- Duration: Near final adult height

CANOPY ACH-3 (Study 301)
Phase 3 Pivotal Study[31,34]

- Age: 5 to <18 years
- 52-week, double-blind, randomized, placebo-controlled

CANOPY ACH-EXT (Study 302)
Ongoing Open-label Extension Study[31,34,36]

- Duration: Final adult height

Data continue to be collected in ongoing clinical trials[37]

*Duration of ≥6 months if aged ≥3 months at study entry; duration of ≥3 months if aged <3 months at study entry.[32]
†Participants completed at least 3 or 6 months of an observational run-in growth study (either in CANOPY ACH-OS [Study 901] or CANOPY ACH-2I [Study 206]) to establish their baseline annualized growth velocity.[33,34]

IMPORTANT SAFETY INFORMATION

Adverse Reactions:

Adverse reactions that occurred in ≥5% of patients treated with VOXZOGO and at a rate greater than that of placebo in the phase 3 study are injection site reactions (including erythema, swelling, urticaria, pain, bruising, pruritus, hemorrhage, discoloration, and induration), vomiting, arthralgia, decrease in blood pressure, gastroenteritis, diarrhea, dizziness, ear pain, influenza, fatigue, seasonal allergy, and dry skin. VOXZOGO-treated patients had an increase in alkaline phosphatase levels (17%), and was noted as a laboratory abnormality.

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

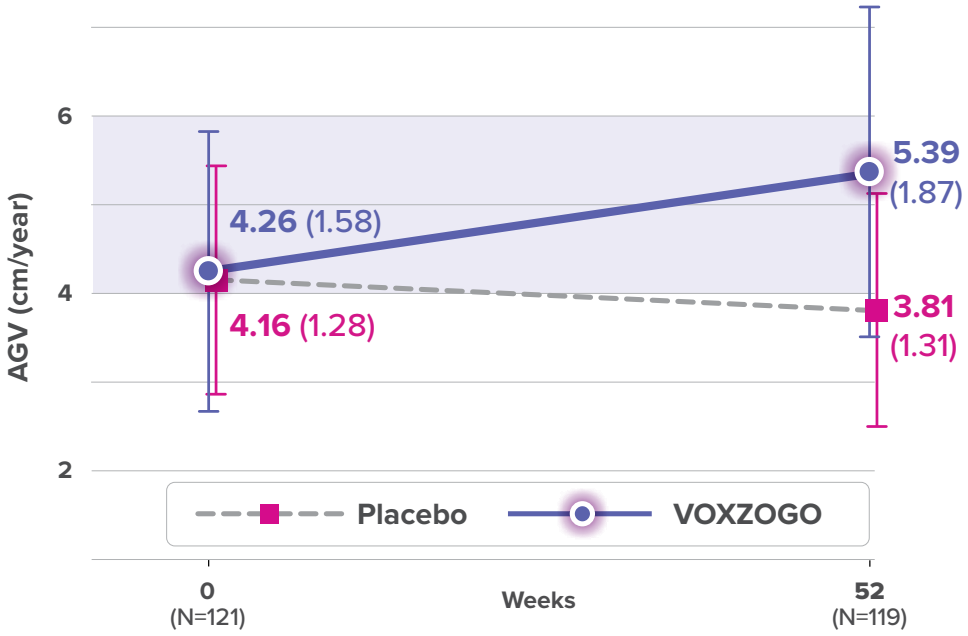
VOXZOGO® (vosoritide) for injection

Children with achondroplasia on VOXZOGO can grow faster than without treatment[1,38]

CANOPY ACH-3 (Study 301)

Phase 3 pivotal trial in children aged 5 to 15 years (N=121)[31,34]

Mean (±SD) AGV over time[38]



AGV difference from placebo at 1 year in the primary analysis:

+1.57 cm/yr[1*†‡]

P<0.0001 (95% CI: 1.22, 1.93)

AGV increase maintained over baseline at

4 years

in VOXZOGO-treated children from the open-label extension study (N=105)[38]

Mean (±SD) AGV at 4 years:
VOXZOGO (n=49): 4.77 (2.17)
Placebo to VOXZOGO (n=56): 4.43 (2.35)

Study design[1,34,38]

4 years of data were collected from VOXZOGO-treated patients aged 5 to 15 years across the CANOPY ACH-3 (Study 301) pivotal trial and CANOPY ACH-EXT (Study 302), the open-label extension study evaluating the long-term efficacy and safety profile of VOXZOGO.

Primary endpoint[1]

Change from baseline in AGV at Week 52 compared to placebo.

AGV is a measure of linear growth expressed as the change in height or length units over 1 year.

AGV, annualized growth velocity; **CI,** confidence interval; **LS,** least squares; **SD,** standard deviation.

*Improvement in AGV was consistent across all predefined subgroups, including sex, age, and Tanner stage.[1]

†All randomized subjects. Two patients in the VOXZOGO group discontinued from the study before Week 52; the values for these 2 patients were imputed assuming baseline growth rate for the period with missing data.[1]

‡LS means were estimated from the ANCOVA (analysis of covariance) model, which included treatment, stratum defined by sex and Tanner stage, baseline age, baseline AGV, and baseline height Z-score.[1]

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

97% (58/60) of the patients in the phase 3 pivotal trial remained on treatment during the 1-year study[1]

IMPORTANT SAFETY INFORMATION

Adverse Reactions: (cont'd)

Injection site reactions: In Study 1, injection site reactions occurred in 51 (85%) subjects receiving VOXZOGO and 50 (82%) subjects receiving placebo over a 52-week period of treatment. Patients receiving VOXZOGO experienced a total of 6983 events of injection site reactions, while patients receiving placebo experienced a total of 1776 events of injection site reactions, over a 52-week period, representing 120.4 events per patient/year exposure and 29.2 events per patient/year exposure, respectively. Two patients in the VOXZOGO arm discontinued treatment due to adverse events of pain and anxiety with injections.

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

VOXZOGO®
(vosoritide) for injection

10+ years of clinical trial experience in achondroplasia[37]

Evelyn

20 MONTHS OLD

on VOXZOGO since 11 months old as part of a clinical trial

Additional preliminary data continue to be collected

VOXZOGO is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).[1]

The following information is being provided to inform healthcare providers on the ongoing assessment and experience of patients in the clinical trial program.

These data are not included in the US Prescribing Information and do not establish a clinical benefit or conclusions on efficacy. The analyses are preliminary and exploratory and should be interpreted cautiously.

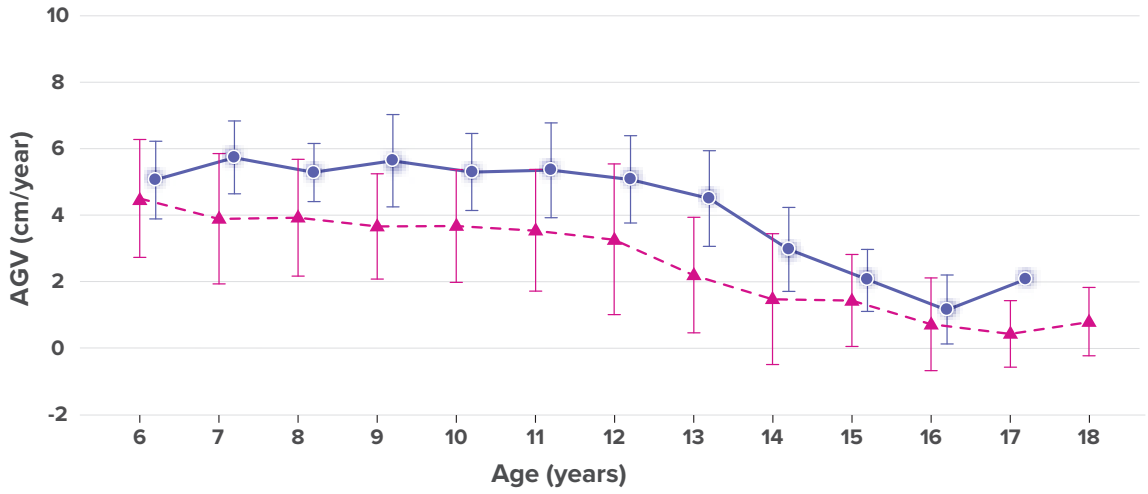
Impact on final adult height has not been established and continues to be evaluated as studies are ongoing

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

VOXZOGO®
(vosoritide) for injection

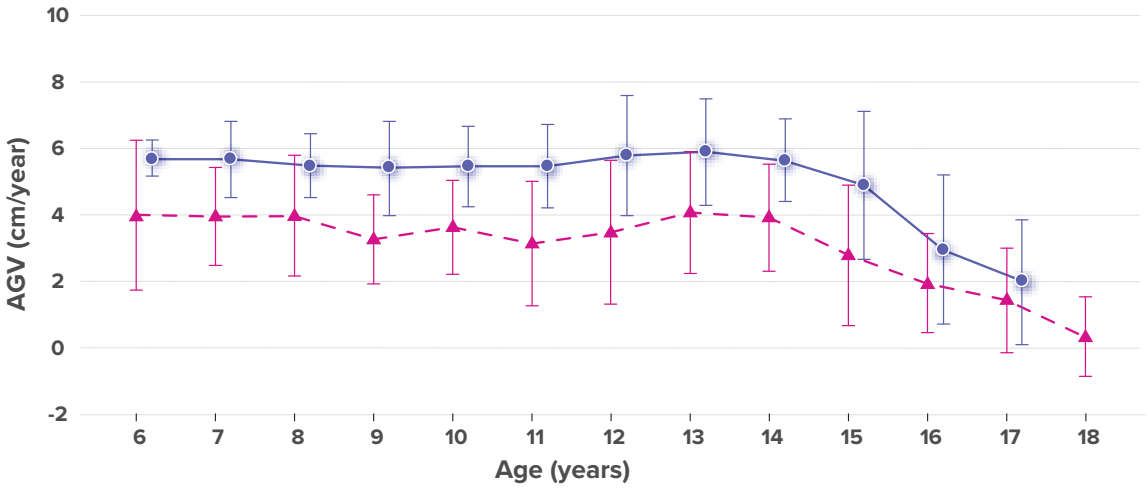
AGV by age in VOXZOGO-treated children was compared to a separate untreated control group[39]

Mean female AGV (±SD) by age[39]*



	6	7	8	9	10	11	12	13	14	15	16	17	18
ACH Treated	10	18	23	26	22	20	26	23	16	6	2	1	0
ACH Untreated	102	82	77	72	61	48	37	39	33	26	17	13	6

Mean male AGV (±SD) by age[39]*



	6	7	8	9	10	11	12	13	14	15	16	17	18
ACH Treated	9	21	26	28	28	27	22	22	15	11	7	4	0
ACH Untreated	117	88	79	62	62	52	45	35	24	20	21	19	8

ACH, achondroplasia; **AGV,** annualized growth velocity; **EXT,** extension; **SD,** standard deviation.

*Adapted from Savarirayan R, et al. *Med.* 2024:100566.[39]

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

Data Limitations

- The VOXZOGO-treated and untreated groups are from different studies. Comparison of inter-study results should be interpreted with caution due to potential differences in study design and methods.[39]
- The effect of VOXZOGO on final adult height has not been established and continues to be assessed. These preliminary results are not in the US label, reflect a cross-sectional mix of treatment durations, are descriptive, and may result from chance.[39]

Study Design

As a primary endpoint of CANOPY ACH-EXT (Study 302), AGV was calculated by age and sex in VOXZOGO-treated children (full analysis set; age 5 to <18 years; N=119) and plotted against the AGV of age- and sex-matched untreated children with ACH from an external ACH natural history study (CLARITY Study). For the VOXZOGO-treated children, AGV was derived for height assessments 12 ± 3 months apart and linked to a specific age integer considering the age at the midpoint of the 12-month interval.[34,39]

The mean (SD) VOXZOGO treatment duration at data cutoff was 4.0 (0.8) years (min: 1.7 years, max: 6.2 years).[39]

IMPORTANT SAFETY INFORMATION

Pediatric Patients 0 to <5 Years:

The safety of VOXZOGO in pediatric patients 0 to <5 years with achondroplasia was evaluated in a 52-week randomized, double-blind, placebo-controlled study (Study 2). In this study, 64 patients from birth to <5 years of age were randomized to receive either a daily vosoritide dose with similar exposure to that characterized to be safe and effective in children with ACH aged ≥5 years old, or placebo. An additional 11 patients received open-label treatment as part of this study. The most common adverse reactions (>10%) reported in pediatric patients 0 to <5 years were injection site reactions (86%) and rash (28%). The overall safety profile of VOXZOGO in pediatric patients 0 to <5 years was similar to that seen in older pediatric patients.

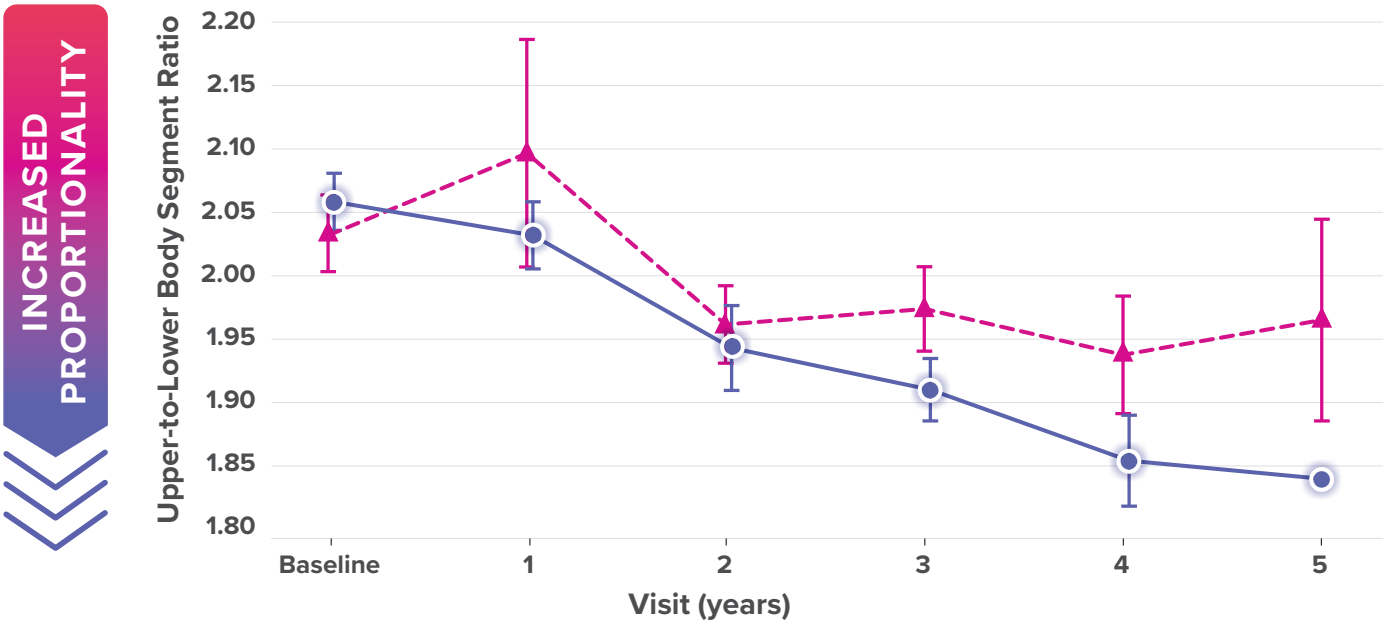
Please see additional Important Safety Information presented throughout, and full Prescribing Information.

VOXZOGO®
(vosoritide) for injection

Body proportionality was measured over 5 years in a subset of children treated with VOXZOGO[39]

CANOPY ACH-3 (Study 301): After 1 year in the pivotal trial, the secondary endpoint of LS mean change from baseline in upper-to-lower body segment ratio was -0.02 in the placebo group (n=61) and -0.03 in the VOXZOGO group (n=58). The difference in LS mean change from baseline was -0.01 (95% CI: -0.05, 0.02; *P*=0.5).[1,34,40]

Mean (±SE) upper-to-lower body segment ratio[39]*



	Baseline	1	2	3	4	5
ACH Treated	48	42	41	48	20	1
ACH Untreated	29	25	26	29	18	6

ACH, achondroplasia; **CI,** confidence interval; **LS,** least squares; **SE,** standard error.

*Adapted from Savarirayan R, et al. *Med*. 2024:100566.[39]

†In average-stature children, average upper-to-lower body segment ratio is 1.7 at birth and decreases to 1.0 at 10 years old. In ACH, the ratio never reaches 1.0 but still declines from birth up to ~age 10 years in girls and 11 years in boys.[39]

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

Vihaan

7 YEARS OLD

on VOXZOGO since 5½ years old as part of a clinical trial

5-Year Data Limitations

- Due to potential differences in study design, care should be taken when interpreting the inter-trial comparison of the VOXZOGO-treated and untreated groups.[39]
- The effect of VOXZOGO on final adult height and proportionality has not been established and continues to be assessed. These preliminary results are not in the US label, are not statistically powered, should be cautiously interpreted, and may result from chance.[1,39]

Study Design

As an exploratory endpoint of CANOPY ACH-EXT (Study 302), body proportionality was measured by upper-to-lower body segment ratio in a subset of VOXZOGO-treated children with assessments at age <11 (girls) or <12 years (boys); all children were age 5 to <18 years. Assessments beyond these ages are excluded from analysis.[34,39,41†]

Upper-to-lower body segment ratio of age-matched untreated children with ACH were also measured in a separate untreated control group; the untreated children were from CANOPY ACH-OS (Study 901) and the placebo arm of CANOPY ACH-3 (Study 301).[34,39,41]

IMPORTANT SAFETY INFORMATION

Administration and Monitoring:

VOXZOGO is administered as a daily subcutaneous injection. Prior to use, instruct caregivers on proper preparation and administration of VOXZOGO, and ensure caregivers have demonstrated the ability to perform a subcutaneous injection.

Monitor and assess patient body weight, growth, and physical development regularly every 3-6 months. Adjust dosage according to the patient's actual body weight. Permanently discontinue treatment with VOXZOGO upon confirmation of no further growth potential, indicated by closure of epiphyses.

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

VOXZOGO® (vosoritide) for injection

The safety profile of VOXZOGO has been rigorously evaluated[1]

Children 5 to 15 years old

Adverse reactions that occurred in ≥5% of patients aged 5 to 15 years treated with VOXZOGO and at a percentage greater than placebo over 1 year.[1*]

ADVERSE REACTIONS	PLACEBO (n=61)	VOXZOGO (n=60)
Injection site erythema[†]	42 (69%)	45 (75%)
Injection site swelling[†]	22 (36%)	37 (62%)
Vomiting	12 (20%)	16 (27%)
Injection site urticaria[†]	6 (10%)	15 (25%)
Arthralgia	4 (7%)	9 (15%)
Decreased blood pressure	3 (5%)	8 (13%)
Gastroenteritis[‡]	5 (8%)	8 (13%)
Diarrhea	2 (3%)	6 (10%)
Dizziness[§]	2 (3%)	6 (10%)
Ear pain	3 (5%)	6 (10%)
Influenza	3 (5%)	6 (10%)
Fatigue[‖]	2 (3%)	5 (8%)
Seasonal allergy	1 (2%)	4 (7%)
Dry skin	0 (0%)	3 (5%)

- Adverse reactions reported in the 1-year phase 3 study are consistent with those seen in the long-term safety study[36]

VOXZOGO may cause serious side effects including a temporary decrease in blood pressure in some patients; to reduce the risk of a decrease in blood pressure and associated symptoms (dizziness, feeling tired, or nausea), patients should be well fed and hydrated in the hour before receiving VOXZOGO.[1]

Children under 5 years old

The overall safety profile of VOXZOGO in pediatric patients <5 years was similar to that seen in older pediatric patients.[1]

- The most common adverse reactions (>10%) reported in pediatric patients <5 years were injection site reactions (86%) and rash (28%)[1]

*Includes adverse reactions occurring more frequently in the VOXZOGO arm and with a risk difference of ≥5% (ie, difference of >2 subjects) between treatment arms.[1]
[†]Injection site reactions occurring more frequently in VOXZOGO-treated patients than placebo.[1]
[‡]Includes the preferred terms: gastroenteritis and gastroenteritis, viral.[1]
[§]Includes the preferred terms: dizziness, presyncope, procedural dizziness, and vertigo.[1]
[‖]Includes the preferred terms: fatigue, lethargy, and malaise.[1]

Eve

3 YEARS OLD

on VOXZOGO since 16 months old as part of a clinical trial

Administering VOXZOGO

VOXZOGO is a once-daily subcutaneous injection, administered at home by a trained caregiver.[1]

Make sure to:

Monitor and assess patient body weight, growth, and physical development every 3-6 months and adjust the dosage according to the patient's actual body weight[1]

Discontinue VOXZOGO upon confirmation of no further growth potential, indicated by closure of growth plates[1]

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

VOXZOGO® (vosoritide) for injection

3,800+ infants and children with achondroplasia around the world are being prescribed VOXZOGO[42]

Vihaan

7 YEARS OLD

on VOXZOGO since 5½ years old as part of a clinical trial

Widespread coverage for your patients and their families[1,43,44]

97% of insured patients have secured coverage for VOXZOGO[43*†]

96% of eligible families with commercial insurance paid $0 out of pocket for VOXZOGO[44*‡§]

BioMarin provides personalized support services every step of the way

BioMarin RareConnections™

Case managers assist with financial barriers, specialty pharmacy coordination, and coverage education

BioMarin Clinical Coordinators

One-on-one injection training, product education, and support

*BioMarin RareConnections™ Data on File. VOXZOGO patients included are eligible VOXZOGO patients who have enrolled in BioMarin RareConnections and are on commercial therapy.

†BioMarin RareConnections data from April through December 2023.

‡BioMarin RareConnections data from January through December 2023.

§Terms and Conditions apply. Valid only for patients with commercial prescription insurance coverage who have a valid prescription for an FDA-approved indication and who meet additional eligibility criteria. Not valid for prescriptions reimbursed, in whole or in part, by any federal, state, or government-funded insurance programs (for example, Medicare, Medicare Advantage, Medigap, Medicaid, VA, DoD, or TRICARE) or where prohibited by law or by the patient's health insurance provider. If at any time a patient begins receiving prescription drug coverage under any federal, state, or government-funded healthcare program, the patient will no longer be able to use the program and patient must notify BioMarin RareConnections at 1-866-906-6100 to stop participation. Patients residing in or receiving treatment in certain states may not be eligible for some or all of the program elements. Patients may not seek reimbursement for value received from the program from any third-party payers. Additional restrictions may apply. Offer subject to change or discontinuance without notice. This assistance offer is not health insurance. See BioMarin-copay-terms.com for full Terms and Conditions.

Please see additional Important Safety Information presented throughout, and accompanying full Prescribing Information.

VOXZOGO® (vosoritide) for injection

Indication and Important Safety Information

VOXZOGO® (vosoritide) is indicated to increase linear growth in pediatric patients with achondroplasia and open growth plates.

- This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Warnings and Precautions for Risk of Low Blood Pressure

Transient decreases in blood pressure were observed in clinical studies. Patients with significant cardiac or vascular disease and patients on anti-hypertensive medicinal products were excluded from participation in VOXZOGO clinical trials. To reduce the risk of a decrease in blood pressure and associated symptoms (dizziness, fatigue, and/or nausea), patients should be well hydrated, have adequate food intake, and drink approximately 8-10 ounces of fluid in the hour prior to VOXZOGO administration.

In a 52-week, randomized, double-blind, placebo-controlled trial in 121 subjects with achondroplasia, subjects aged from 5.1 to 14.9 years, (Study 1) eight (13%) of 60 patients treated with VOXZOGO had a total of 11 events of transient decrease in blood pressure, compared to 3 (5%) of 61 patients on placebo, over a 52-week treatment period. The median time to onset from injection was 31 (18 to 120) minutes, with resolution within 31 (5 to 90) minutes in VOXZOGO-treated subjects. Two out of 60 (3%) VOXZOGO-treated patients each had one symptomatic episode of decreased blood pressure with vomiting and/or dizziness compared to 0 of 61 (0%) patients on placebo.

Adverse Reactions:

Adverse reactions that occurred in ≥5% of patients treated with VOXZOGO and at a rate greater than that of placebo in the phase 3 study are injection site reactions (including erythema, swelling, urticaria, pain, bruising, pruritus, hemorrhage, discoloration, and induration), vomiting, arthralgia, decrease in blood pressure, gastroenteritis, diarrhea, dizziness, ear pain, influenza, fatigue, seasonal allergy, and dry skin. VOXZOGO-treated patients had an increase in alkaline phosphatase levels (17%), and was noted as a laboratory abnormality.

Injection site reactions: In Study 1, injection site reactions occurred in 51 (85%) subjects receiving VOXZOGO and 50 (82%) subjects receiving placebo over a 52-week period of treatment. Patients receiving VOXZOGO experienced a total of 6983 events of injection site reactions, while patients receiving placebo experienced a total of 1776 events of injection site reactions, over a 52-week period, representing 120.4 events per patient/year exposure and 29.2 events per patient/year exposure, respectively. Two patients in the VOXZOGO arm discontinued treatment due to adverse events of pain and anxiety with injections.

Pediatric Patients 0 to <5 Years:

The safety of VOXZOGO in pediatric patients 0 to <5 years with achondroplasia was evaluated in a 52-week randomized, double-blind, placebo-controlled study (Study 2). In this study, 64 patients from birth to <5 years of age were randomized to receive either a daily vosoritide dose with similar exposure to that characterized to be safe and effective in children with ACH aged ≥5 years old, or placebo. An additional 11 patients received open-label treatment as part of this study. The most common adverse reactions (>10%) reported in pediatric patients 0 to <5 years were injection site reactions (86%) and rash (28%). The overall safety profile of VOXZOGO in pediatric patients 0 to <5 years was similar to that seen in older pediatric patients.

Administration and Monitoring:

VOXZOGO is administered as a daily subcutaneous injection. Prior to use, instruct caregivers on proper preparation and administration of VOXZOGO, and ensure caregivers have demonstrated the ability to perform a subcutaneous injection.

Monitor and assess patient body weight, growth, and physical development regularly every 3-6 months. Adjust dosage according to the patient's actual body weight. Permanently discontinue treatment with VOXZOGO upon confirmation of no further growth potential, indicated by closure of epiphyses.

Special Populations:

- There are no available data on the use of VOXZOGO in pregnant women, or data on the presence of VOXZOGO in human milk, the effects on the breastfed infant, or the effects on milk production.
- The influence of renal impairment on the pharmacokinetics of VOXZOGO has not been evaluated. No dosage adjustment is needed for patients with eGFR ≥60 mL/min/1.73 m^2. VOXZOGO is not recommended for patients with eGFR <60 mL/min/1.73 m^2.

You may report side effects to the FDA at **1-800-FDA-1088** or **www.fda.gov/medwatch**. You may also report side effects to BioMarin at **1-866-906-6100**.

Please see additional safety information in the full Prescribing Information.

References: 1. VOXZOGO [package insert]. Novato, CA: BioMarin Pharmaceutical Inc; 2024. **2.** Savarirayan R, Hoover-Fong J, Ozono K, et al. International consensus guidelines on the implementation and monitoring of vosoritide therapy in individuals with achondroplasia. *Nat Rev Endocrinol*. 2025;21(5):314-324. **3.** Horton WA, Hall JG, Hecht JT. Achondroplasia. *Lancet*. 2007;370(9582):162-172. **4.** Savarirayan R, Ireland P, Irving M, et al. International Consensus Statement on the diagnosis, multidisciplinary management and lifelong care of individuals with achondroplasia. *Nat Rev Endocrinol*. 2022;18(3):173-189. **5.** Mackie EJ, Tatarczuch L, Mirams M. The skeleton: a multi-functional complex organ: the growth plate chondrocyte and endochondral ossification. *J Endocrinol*. 2011;211(2):109-121. **6.** Clarke B. Normal bone anatomy and physiology. *Clin J Am Soc Nephrol*. 2008;3(suppl 3):S131-S139. **7.** Breeland G, Sinkler MA, Menezes RG. Embryology, bone ossification. In: StatPearls. StatPearls Publishing; 2023. Accessed April 23, 2025. https://www.ncbi.nlm.nih.gov/books/NBK539718/ **8.** Berendsen AD, Olsen BR. Bone development. *Bone*. 2015;80:14-18. **9.** Cowan PT, Launico MV, Kahai P. Anatomy, bones. In: StatPearls. StatPearls Publishing; 2024. Accessed April 23, 2025. https://www.ncbi.nlm.nih.gov/books/NBK537199/ **10.** Johns Hopkins Medicine. Anatomy of the bone. Accessed April 23, 2025. https://www.hopkinsmedicine.org/health/wellness-and-prevention/anatomy-of-the-bone **11.** Jin SW, Sim KB, Kim SD. Development and growth of the normal cranial vault: an embryologic review. *J Korean Neurosurg Soc*. 2016;59(3):192-196. **12.** Anderson BW, Kortz MW, Black AC, et al. Anatomy, head and neck, skull. In: StatPearls. StatPearls Publishing; 2023. Accessed April 23, 2025. https://www.ncbi.nlm.nih.gov/books/NBK499834/ **13.** Encyclopaedia Britannica. Science & Tech. Skull. Accessed April 23, 2025. https://www.britannica.com/science/skull **14.** Hall R, Beals K, Neumann H, et al. *Introduction to Human Osteology*. Grand Valley State University; 2008. **15.** Encyclopaedia Britannica. Science & Tech. Clavicle. Accessed April 23, 2025. https://www.britannica.com/science/clavicle **16.** Baron J, Sävendahl L, De Luca F, et al. Short and tall stature: a new paradigm emerges. *Nat Rev Endocrinol*. 2015;11(12):735-746. **17.** Shahzad F. Pediatric mandible reconstruction: controversies and considerations. *Plast Reconstr Surg Glob Open*. 2020;8(12):e3285. **18.** Bartleby. Henry Gray (1825-1861). *Anatomy of the Human Body*. 1918. Fig. 237. Accessed May 7, 2025. https://www.bartleby.com/lit-hub/anatomy-of-the-human-body/fig-237/ **19.** Encyclopaedia Britannica. Science & Tech. Pelvis. Accessed May 7, 2025. https://www.britannica.com/science/pelvis **20.** Mayo Clinic. Growth plate fracture. Accessed May 7, 2025. https://www.mayoclinic.org/diseases-conditions/growth-plate-fractures/multimedia/growth-plate-fracture/img-20005879 **21.** International Center for Limb Lengthening. Growth arrest. Accessed June 10, 2025. https://www.limblength.org/conditions/growth-arrest/ **22.** Hsieh YL, Wei X, Wang Y, et al. Chondrocyte Tsc1 controls cranial base bone development by restraining the premature differentiation of synchondroses. *Bone*. 2021;153:116142. **23.** Musculoskeletal Key. Cranial and pelvic "vertebrae" are they real vertebrae? Accessed June 10, 2025. https://musculoskeletalkey.com/cranial-and-pelvic-vertebrae-are-they-real-vertebrae/ **24.** Young M, Selleri L, Capellini TD. Genetics of scapula and pelvis development: An evolutionary perspective. *Curr Top Dev Biol*. 2019;132:311-349. **25.** Witt S, Rohenkohl A, Bullinger M, et al. Understanding, assessing and improving health-related quality of life of young people with achondroplasia – a collaboration between a patient organization and academic medicine. *Pediatr Endocrinol Rev*. 2017;15(suppl 1):109-118. **26.** Hoover-Fong J, Cheung MS, Fano V, et al. Lifetime impact of achondroplasia: current evidence and perspectives on the natural history. *Bone*. 2021;146:115872. **27.** Hoover-Fong JE, Schulze KJ, McGready J, et al. Age-appropriate body mass index in children with achondroplasia: interpretation in relation to indexes of height. *Am J Clin Nutr*. 2008;88(2):364-371. **28.** Chilbule SK, Dutt V, Madhuri V. Limb lengthening in achondroplasia. *Indian J Orthop*. 2016;50(4):397-405. **29.** Nwosu BU, Lee MM. Evaluation of short and tall stature in children. *Am Fam Physician*. 2008;78(5):597-604. **30.** Kvist O, Dallora AL, Nilsson O, et al. A cross-sectional magnetic resonance imaging study of factors influencing growth plate closure in adolescents and young adults. *Acta Paediatr*. 2021;110(4):1249-1256. **31.** Savarirayan R, Tofts L, Irving M, et al. Once-daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomised, double-blind, phase 3, placebo-controlled, multicentre trial. *Lancet*. 2020;396(10252):684-692. **32.** Savarirayan R, Tofts L, Irving M, et al. Once-daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomised, double-blind, phase 3, placebo-controlled, multicentre trial. *Lancet*. 2020;396(10252):684-692. Supplementary Appendix. **33.** Savarirayan R, Wilcox WR, Harmatz P, et al. Vosoritide therapy in children with achondroplasia aged 3-59 months: a multinational, randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Child Adolesc Health*. 2024;8(1):40-50. **34.** Data on file [1]. BioMarin Pharmaceutical Inc; 2025. **35.** ClinicalTrials.gov. Identifier: NCT03989947. Accessed April 23, 2025. https://www.clinicaltrials.gov/study/NCT03989947 **36.** Savarirayan R, Tofts L, Irving M, et al. Safe and persistent growth-promoting effects of vosoritide in children with achondroplasia: 2-year results from an open-label, phase 3 extension study. *Genet Med*. 2021;23(12):2443-2447. **37.** ClinicalTrials.gov. Search: Achondroplasia, BioMarin Pharmaceutical. Accessed April 23, 2025. https://www.clinicaltrials.gov/search?cond=Achondroplasia&term=BioMarin%20Pharmaceutical&viewType=Table **38.** Data on file [2]. BioMarin Pharmaceutical Inc; 2025. **39.** Savarirayan R, Irving M, Wilcox WR, et al. Sustained growth-promoting effects of vosoritide in children with achondroplasia from an ongoing phase 3 extension study. *Med*. 2024;30:100566. **40.** ClinicalTrials.gov. Identifier: NCT03197766. Accessed April 23, 2025. https://www.clinicaltrials.gov/study/NCT03197766 **41.** Savarirayan R, Irving M, Wilcox WR, et al. Sustained growth-promoting effects of vosoritide in children with achondroplasia from an ongoing phase 3 extension study. *Med*. 2024;30:100566. Supplementary Appendix. **42.** Data on file [3]. BioMarin Pharmaceutical Inc; 2025. **43.** Data on file [4]. BioMarin Pharmaceutical Inc; 2023. **44.** Data on file [5]. BioMarin Pharmaceutical Inc; 2023.

Questions about VOXZOGO?

Contact your BioMarin representative to get the conversation started.

VOXZOGO®
(vosoritide) for injection

[VOXZOGO is the only FDA-approved targeted therapy for children with achondroplasia[1]]

[Indicated to increase linear growth in children with achondroplasia and open growth plates.[1]]

VOXZOGO targets the underlying cause of inhibited endochondral bone growth.[1,3,4]

VOXZOGO promotes statistically significant growth.[1]*
Growth increase was maintained over baseline at 4 years.[1,38]

*Compared to placebo.

Maximize time on treatment by starting early and continuing until growth plates close.[1,2,5]

BioMarin is a leader in skeletal conditions, with over 10 years of VOXZOGO clinical trial experience in achondroplasia[37]

VOXZOGO®
(vosoritide) for injection

Scan the QR code or go to VOXZOGO.com/HCP to enroll your patients

IMPORTANT SAFETY INFORMATION

Special Populations:

- There are no available data on the use of VOXZOGO in pregnant women, or data on the presence of VOXZOGO in human milk, the effects on the breastfed infant, or the effects on milk production.
- The influence of renal impairment on the pharmacokinetics of VOXZOGO has not been evaluated. No dosage adjustment is needed for patients with eGFR ≥60 mL/min/1.73 m^2. VOXZOGO is not recommended for patients with eGFR <60 mL/min/1.73 m^2.

Please see additional Important Safety Information presented throughout, and full Prescribing Information.

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