Free Communications 8 - Late Breaking

Vosoritide Increases Growth Velocity in Children With Hypochondroplasia: Phase 3 Trial Results

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DISCLOSURE STATEMENT

Andrew Dauber

☒ I have the following potential conflicts of interest to report:

- ☒ Research contracts
- ☒ Consulting
- ☐ Employment in the industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

☐ I declare that I have no potential conflict of interest.



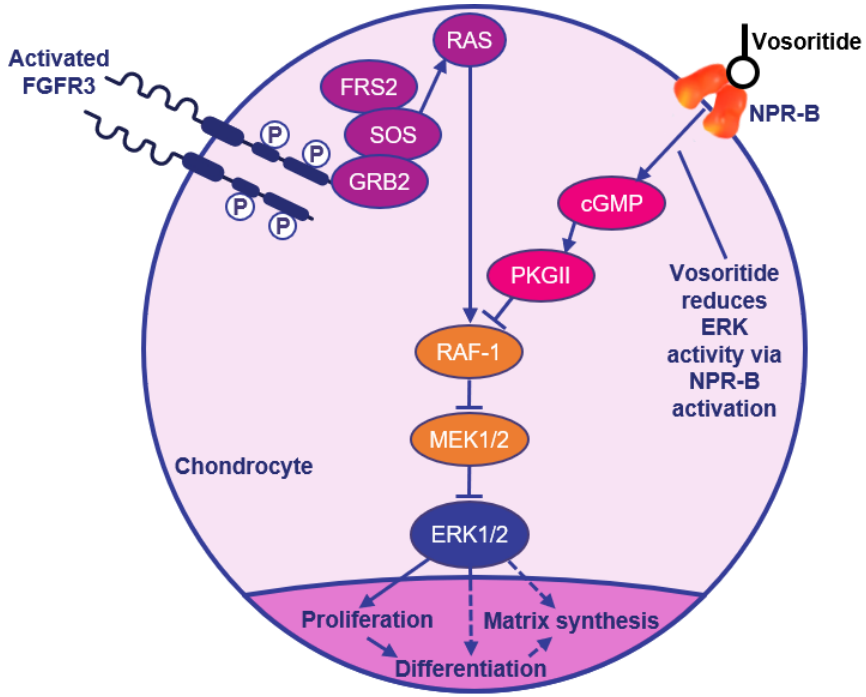
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Hypochondroplasia is an *FGFR3*-related skeletal dysplasia with no approved targeted treatment options

- Hypochondroplasia is a genetic skeletal condition caused by gain-of-function pathogenic variants in the fibroblast growth factor receptor 3 gene (*FGFR3*) that impairs endochondral bone growth and manifests as disproportionate short stature[1–5]
- No targeted therapies are currently approved for hypochondroplasia
- Vosoritide, a C-type natriuretic peptide analogue, binds to the CNP receptor and inhibits FGFR3-driven MAPK/ERK1/2 signaling in chondrocytes to improve bone growth[3,6]
- Vosoritide is approved in multiple countries, including the US and EU countries, for the treatment of achondroplasia, another *FGFR3*-related skeletal dysplasia, and is being investigated for hypochondroplasia[3,7–14]

Here, we report the results from the phase 3 trial, CANOPY HCH-3, evaluating the efficacy and safety of 52 weeks of daily vosoritide in children with hypochondroplasia

Vosoritide counteracts the effects of overactive FGFR3 signaling in hypochondroplasia[3,6]



CNP, C-type natriuretic peptide; ERK, extracellular signal-regulated kinase; FGFR3, fibroblast growth factor receptor 3; HCH, hypochondroplasia; MAPK, mitogen-activated protein kinase.

1. Hall BD, Spranger J. *Radiology*. 1979;133:95–100. 2. Lorget F, et al. *Am J Hum Genet*. 2012;91:1108–1114. 3. Allen DB, et al. *Horm Res Paediatr*. 2021;94:319–332. 4. Bellus GA, et al. *Nat Genet*. 1995;10:357–359. 5. Cheung MS, et al. *Am J Med Genet A*. 2024;194A:243–252. 6. Thrailkill KM, et al. *Front Pediatr*. 2022;10:1012816. 7. Dauber A, et al. *EClinicalMedicine*. 2024;71:102591. 8. Savarirayan R, et al. *Nat Rev Endocrinol*. 2025;21:314–324. 9. US Food and Drug Administration. 2021. Accessed February 12, 2026. https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-improve-growth-children-most-common-form-dwarfism. 10. European Medicines Agency. 2025. Accessed February 12, 2026. https://www.ema.europa.eu/en/medicines/human/EPAR/voxzogo. 11. Pharmaceuticals and Medical Devices Agency (Japan). 2025. Accessed February 12, 2026. https://www.pmda.go.jp/files/000278243.pdf. 12. Therapeutic Goods Administration (Australia). 2022. Accessed February 12, 2026. https://www.tga.gov.au/resources/auspmd/voxzogo. 13. National Health Surveillance Agency (Brazil). 2021. Accessed February 12, 2026. https://www.gov.br/anvisa/pt-br/assuntos/medicamentos/novos-medicamentos-e-indicacoes/voxzogo-vosoritida-novo-registro. 14. Health Canada Drug Product Database (Canada). 2026. Accessed February 12, 2026. https://pdf.hres.ca/dpd_pm/00083231.PDF.

Study design

CANOPY HCH-OS
observational study
(111-902;
NCT06212947)[1]

≥6 months' pretreatment standing height assessments to establish baseline AGV

1:1

Vosoritide (n = 41)

Once daily by subcutaneous injection for 52 weeks following a weight-band dosing regimen

Placebo (n = 40)

52-week treatment period

Two-week safety follow-up
OR
CANOPY HCH-EXT
open-label, long-term extension trial
(111-308;
NCT07073014)[2]

Key eligibility criteria

- Genetically diagnosed hypochondroplasia
- Age: ≥3 to <18 years old
- Height Z-score: ≤−2.0 SDS
- Approximately 20% participants with Tanner stage >I
- Approximately 20% participants with height Z-score >−3.0 and ≤−2.0 SDS compared with average stature

Primary endpoint

Change from baseline in AGV at week 52 for vosoritide versus placebo

Safety endpoint

Adverse events (AEs), serious AEs, and AEs of special interest

Key secondary endpoints

Change from baseline to week 52 in

1. **Standing height**
2. **Height Z-score referenced to CDC-based average stature**
3. **Arm span**
4. **U/L in participants aged <11 years at baseline**
5. **Caregiver-reported QoLISSY total score***
6. **Caregiver-reported QoLISSY physical score***

*Valid for participants aged ≥4 years.

AE, adverse event; AGV, annualized growth velocity; CDC, Centers for Disease Control and Prevention; HCH, hypochondroplasia; OS, observational study; QoLISSY, Quality of Life in Short Stature Youth; SDS, standard deviation score; U/L, upper to lower body segment ratio.

1. ClinicalTrials.gov identifier: NCT06212947. Updated April 3, 2025. Accessed April 8, 2026. https://clinicaltrials.gov/study/NCT06212947. 2. ClinicalTrials.gov identifier: NCT07073014. Updated July 18, 2025. Accessed November 12, 2025. https://clinicaltrials.gov/study/NCT07073014.

Participant characteristics at baseline were generally balanced between the treatment groups

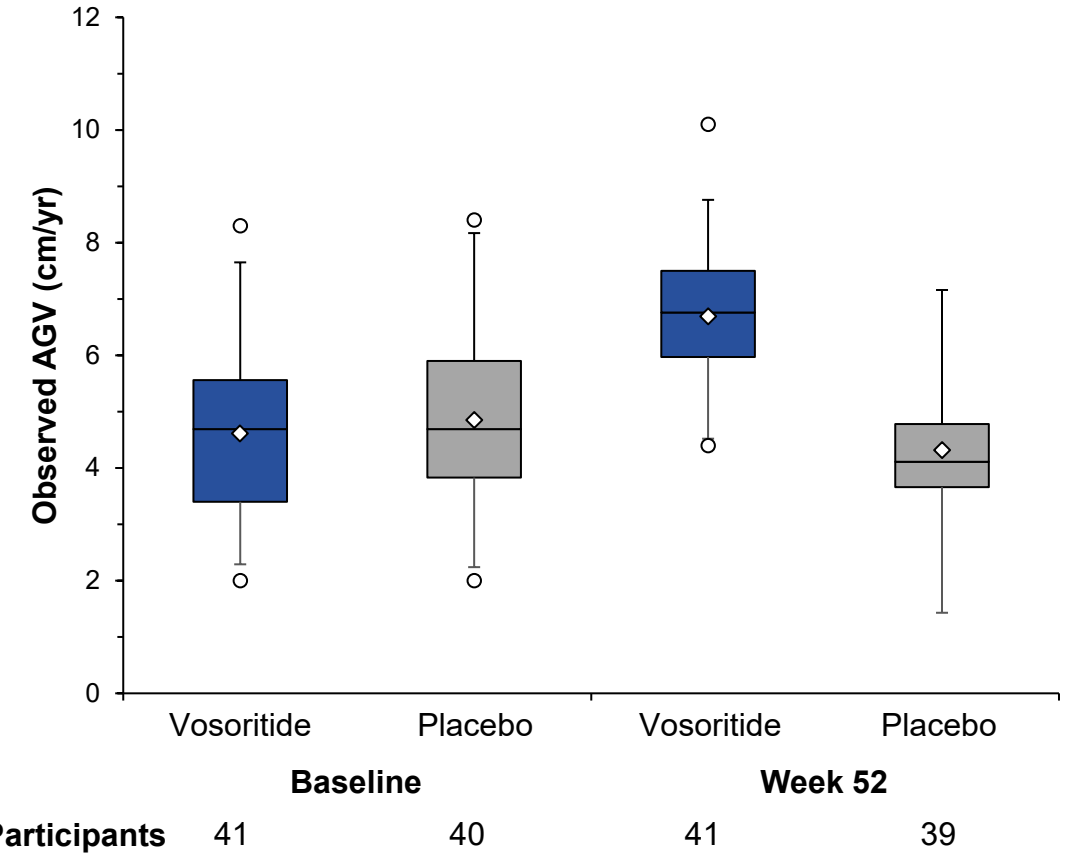
	Vosoritide (n = 41)	Placebo (n = 40)
Age at day 1, median, years	8.05	7.69
Mean ± SD	7.84 ± 2.93	8.15 ± 3.08
Age group at screening, n (%)		
≥3 to <6 years	15 (36.6)	10 (25.0)
≥6 to <12 years	23 (56.1)	23 (57.5)
≥12 to <18 years	3 (7.3)	7 (17.5)
Sex, n (%)		
Male	24 (58.5)	20 (50.0)
Female	17 (41.5)	20 (50.0)
Race, n (%)		
White	23 (56.1)	31 (77.5)
Asian	8 (19.5)	4 (10.0)
Black or African American	1 (2.4)	1 (2.5)
Multiple	2 (4.9)	0
Not reported	7 (17.1)	4 (10.0)

	Vosoritide (n = 41)	Placebo (n = 40)
FGFR3 variant, n (%)		
c.1620C>A (p.Asn540Lys)	18 (43.9)	21 (52.5)
c.1620C>G (p.Asn540Lys)	16 (39.0)	16 (40.0)
Other*	7 (17.1)	3 (7.5)
Tanner stage, n (%)		
I or not evaluated due to age <5 years	37 (90.2)	34 (85.0)
>I	4 (9.8)	6 (15.0)
AGV, mean ± SD, cm/year	4.61 ± 1.59	4.85 ± 1.56
Height Z-score (referenced to CDC-based average stature), mean ± SD, SDS†	−3.54 ± 0.72	−3.76 ± 0.67

One participant in the placebo group discontinued trial treatment on day 7 and withdrew from the trial on day 56

*Other *FGFR3* variants were as follows: c.1052C>G, c.970C>G, c.1950G>C, c.1619A>G, c.1626C>A, c.1663G>C, and c.551C>T. †≤−3 SDS (~80%); >−3 SDS to ≤−2 SDS (~20%).
AGV, annualized growth velocity; CDC, Centers for Disease Control and Prevention; *FGFR3*, fibroblast growth factor receptor 3 gene; SD, standard deviation; SDS, standard deviation score.

Vosoritide resulted in significant improvement in annualized growth velocity after 52 weeks of treatment



AGV LSM difference from placebo at 52 weeks in the primary analysis*,†

2.33 cm/yr

(95% CI, 1.85 to 2.82)

2-sided *P* <0.0001

	Vosoritide (n = 41)	Placebo (n = 40)
LSM change from baseline (95% CI), cm/year	1.95 (1.61 to 2.28)	−0.39 (−0.73 to −0.04)

Primary endpoint met

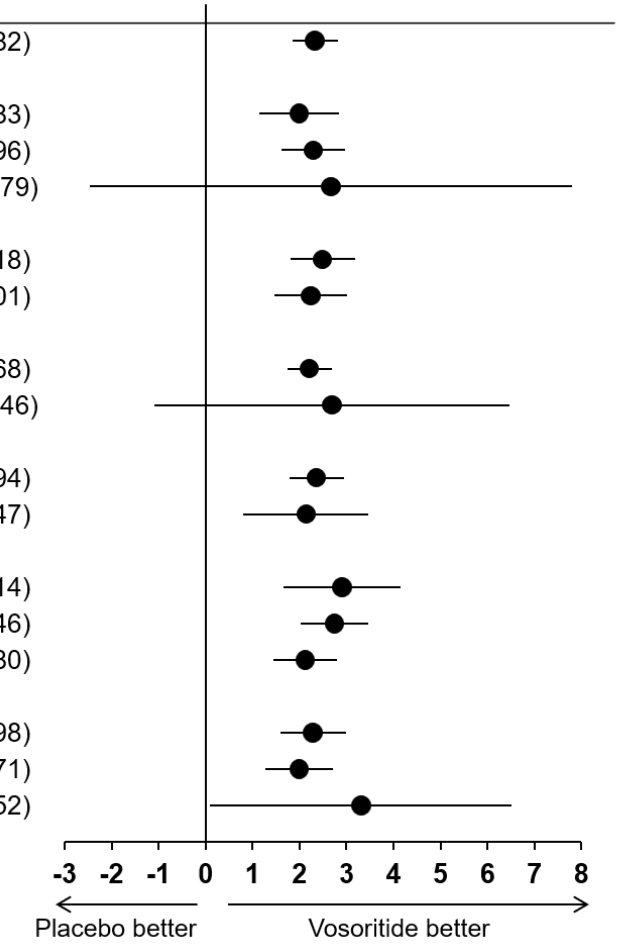
Box and whisker plot was based on observed data at baseline and 52 weeks after the first dose of trial drug by treatment arm. Box plots display the 25th and 75th percentiles (box edges), the median (midline), the mean (diamond symbol), the 2.5th and 97.5th percentiles (whiskers), and the outliers (circles).

*Covariates for ANCOVA model included treatment, baseline age, sex, baseline Tanner stage, baseline AGV, and baseline height Z-score (referenced to average stature). †A multiple imputation approach was applied for the 1 participant in the placebo group who discontinued treatment, for whom missing data were imputed based solely on placebo group data.

AGV, annualized growth velocity; ANCOVA, analysis of covariance; CI, confidence interval; LSM, least squares mean.

Subgroup analyses of annualized growth velocity favored vosoritide across all categories

	Number of participants, n (%)		Difference (vosoritide−placebo) in LSM change from baseline (95% CI), cm/yr
	Vosoritide	Placebo	
Overall	41 (100.0)	40 (100.0)	2.33 (1.85 to 2.82)
Age			
≥3 to <6 years	15 (36.6)	10 (25.0)	1.99 (1.15 to 2.83)
≥6 to <12 years	23 (56.1)	22 (55.0)	2.29 (1.62 to 2.96)
≥12 to <18 years	3 (7.3)	7 (17.5)	2.67 (−2.46 to 7.79)
Sex			
Male	24 (58.5)	20 (50.0)	2.49 (1.81 to 3.18)
Female	17 (41.5)	19 (47.5)	2.24 (1.47 to 3.01)
Tanner stage			
I or not evaluated due to age <5 years	37 (90.2)	33 (82.5)	2.21 (1.74 to 2.68)
>I	4 (9.8)	6 (15.0)	2.69 (−1.08 to 6.46)
Baseline height Z-score			
≤−3.0 SDS	32 (78.0)	33 (82.5)	2.36 (1.79 to 2.94)
>−3.0 and ≤−2.0 SDS	9 (22.0)	6 (15.0)	2.14 (0.80 to 3.47)
Baseline annualized growth velocity			
≤3.5 cm/year	11 (26.8)	8 (20.0)	2.90 (1.65 to 4.14)
>3.5 to ≤4.5 cm/year	7 (17.1)	9 (22.5)	2.74 (2.02 to 3.46)
>4.5 cm/year	23 (56.1)	22 (55.0)	2.12 (1.44 to 2.80)
FGFR3 variant			
c.1620C>G	16 (39.0)	15 (37.5)	2.28 (1.59 to 2.98)
c.1620C>A	18 (43.9)	21 (52.5)	1.99 (1.27 to 2.71)
Other	7 (17.1)	3 (7.5)	3.31 (0.10 to 6.52)



Forest plot of difference in LSM change from baseline in annualized growth velocity at week 52 by subgroup. ANCOVA models were applied to determine LSM and difference in LSM.
ANCOVA, analysis of covariance; CI, confidence interval; *FGFR3*, fibroblast growth factor receptor 3 gene; LSM, least squares mean; SDS, standard deviation score.

Vosoritide resulted in significant improvements in linear growth and arm span at week 52

Key secondary endpoint	Vosoritide (n = 41)	Placebo (n = 40)
Standing height*		
LSM change from baseline (95% CI), cm	6.68 (6.34 to 7.01)	4.32 (3.98 to 4.67)
Height Z-score (referenced to CDC-based average stature)†		
LSM change from baseline (95% CI), SDS	0.34 (0.27 to 0.42)	−0.05 (−0.12 to 0.03)
Arm span‡		
LSM change from baseline (95% CI), cm	6.07 (5.55 to 6.60)	5.05 (4.50 to 5.59)

LSM difference§

2.35 cm
(95% CI, 1.86 to 2.85)
2-sided *P* <0.0001

0.39 SDS
(95% CI, 0.28 to 0.50)
2-sided *P* <0.0001

1.03 cm
(95% CI, 0.27 to 1.79)
2-sided *P* = 0.0082

A multiple imputation approach was applied for the 1 participant in the placebo group who discontinued treatment, for whom missing data were imputed based solely on placebo group data.
*Covariates for ANCOVA model included treatment, baseline age, sex, baseline Tanner stage, baseline AGV, baseline height Z-score (referenced to average stature), and baseline standing height. †Covariates for ANCOVA model included treatment, baseline age, sex, baseline Tanner stage, baseline AGV, and baseline height Z-score (referenced to average stature). ‡Covariates for ANCOVA model included treatment, baseline age, sex, baseline Tanner stage, baseline arm span AGV, baseline height Z-score (referenced to average stature), and baseline arm span. §Difference is vosoritide minus placebo.
AGV, annualized growth velocity; ANCOVA, analysis of covariance; CDC, Centers for Disease Control and Prevention; CI, confidence interval; LSM, least squares mean; SDS, standard deviation score.

Body proportion remained stable with vosoritide and numerical increases were observed in QoLISSY scores

Key secondary endpoint	Vosoritide (n = 35)	Placebo (n = 31)
U/L for participants aged <11 years at baseline*		
LSM change from baseline (95% CI)	−0.045 (−0.062 to −0.028)	−0.042 (−0.061 to −0.023)
Key secondary endpoint	**Vosoritide (n = 32)**	**Placebo (n = 31)**
Caregiver-reported QoLISSY total score (valid for participants aged ≥4 years)†		
LSM change from baseline (95% CI)	3.99 (−0.23 to 8.21)	0.07 (−4.31 to 4.46)
Caregiver-reported QoLISSY physical score (valid for participants aged ≥4 years)‡		
LSM change from baseline (95% CI)	7.14 (1.79 to 12.50)	2.38 (−3.16 to 7.93)

LSM difference§

−0.003
(95% CI, −0.029 to 0.023)
2-sided *P* = 0.8159 (NS)

3.91¶
(95% CI, −2.25 to 10.08)

4.76¶
(95% CI, −3.06 to 12.58)

A multiple imputation approach was applied for the 1 participant in the placebo group who discontinued treatment, for whom missing data were imputed based solely on placebo group data.
*Covariates for ANCOVA model included sex, Tanner stage (actual), treatment, baseline age, baseline annualized growth velocity, baseline height Z-score (average stature), and baseline upper to lower body segment ratio. †Covariates for ANCOVA model included sex, Tanner stage (actual), treatment, baseline age, and baseline total score. ‡Covariates for ANCOVA model included sex, Tanner stage (actual), treatment, baseline age, and baseline physical score. §Difference is vosoritide minus placebo. ¶Because the stepwise hierarchical testing procedure did not advance beyond U/L in participants aged <11 years at baseline (2-sided *P* value was not statistically significant), all CIs for the analyses of the caregiver-reported QoLISSY total and physical scores should be interpreted descriptively.
ANCOVA, analysis of covariance; CI, confidence interval; LSM, least squares mean; NS, not significant; QoLISSY, Quality of Life in Short Stature Youth; U/L, upper to lower body segment ratio.

Vosoritide was overall well tolerated

	Vosoritide (n = 41)		Placebo (n = 40)	
	Incidence, n (%)*	Event rate, m (rate)†	Incidence, n (%)*	Event rate, m (rate)†
Participants with any AE	36 (87.8)	158 (3.85)	29 (72.5)	106 (2.71)
AEs leading to drug interruption	4 (9.8)	11 (0.27)	5 (12.5)	10 (0.26)
AEs leading to trial drug discontinuation	0	0	0	0
Any grade ≥3 AEs	0	0	0	0
Treatment-related AEs‡	10 (24.4)	18 (0.44)	2 (5.0)	4 (0.10)
Participants with any SAE	0	0	1 (2.5)	1 (0.03)
Seizure	0	0	1 (2.5)	1 (0.03)

- Treatment-related AEs were higher in the vosoritide group, consistent with the known adverse drug reaction profile of vosoritide

Participants with events of interest	Vosoritide (n = 41)		Placebo (n = 40)	
	Incidence, n (%)*	Event rate, m (rate)†	Incidence, n (%)*	Event rate, m (rate)†
Injection site reactions CTCAE grade ≥2	0	0	1 (2.5)	1 (0.03)
Injection site reactions (excluding bruising) lasting >24 h	2 (4.9)	7 (0.17)	1 (2.5)	1 (0.03)
Heart rate change	0	0	1 (2.5)	1 (0.03)
Hypersensitivity (SMQ narrow terms)	9 (22.0)	18 (0.44)	7 (17.5)	7 (0.18)
Avascular necrosis or osteonecrosis	0	0	0	0
Slipped capital femoral epiphysis	0	0	0	0
Otitis	3 (7.3)	3 (0.07)	3 (7.5)	5 (0.13)
Seizures	0	0	1 (2.5)	1 (0.03)
Any hypotension	2 (4.9)	2 (0.05)	0	0
Fractures	1 (2.4)	1 (0.02)	0	0

- Only 1 of the 2 events of hypotension was symptomatic, and it was related to treatment
- The single event of radial fracture was assessed as not related to treatment by the investigator

*Percentages were calculated using the total number of participants in the safety set (n for each treatment group) as the denominator. Participants with more than 1 AE of the same category were counted only once for that category. †Exposure-adjusted event rates were calculated by dividing the total number of events (m) by the total duration of follow-up to the date of trial completion or discontinuation in each treatment group. ‡Dizziness, headache, presyncope, syncope, hypertrichosis, hair growth abnormal, vomiting, abdominal discomfort, constipation, nausea, injection site urticaria, procedural dizziness, blood pressure decreased, hypotension, and pain in extremity.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; SAE, serious adverse event; SMQ, standardized Medical Dictionary for Regulatory Activities query.

Conclusions

One year of vosoritide treatment significantly increased linear and upper limb growth in children with hypochondroplasia aged ≥3 to <18 years

Subcutaneously administered vosoritide was well tolerated, with mild injection site reactions and no discontinuations

- A longer treatment period is likely needed to fully characterize the impact of vosoritide on body proportion and health-related quality of life in hypochondroplasia

- No new safety findings were identified compared with previously published reports on vosoritide-treated children with hypochondroplasia or achondroplasia[1–3]

Additional studies are required to evaluate the long-term effect of vosoritide on achieving final adult height and the effect in younger children with hypochondroplasia

CANOPY HCH-EXT EXTENSION STUDY

Study 111-308[4] (NCT07073014)

Ongoing phase 3, open-label extension trial that will help gain further insights into the long-term safety and efficacy of daily doses of vosoritide for the treatment of hypochondroplasia

CANOPY HCH-2I PHASE 2 INFANT STUDY

Study 111-212[5] (NCT07126262)

Ongoing phase 2, randomized, double-blind, placebo-controlled, multicenter trial that will evaluate the safety and efficacy of daily doses of vosoritide in infants and young children with hypochondroplasia 0 to <36 months of age

1. Dauber A, et al. *EClinicalMedicine*. 2024;71:102591. 2. Savarirayan R, et al. *Lancet*. 2020;396:684–692. 3. Savarirayan R, et al. *Med*. 2025;6:100566.4. ClinicalTrials.gov identifier: NCT07073014. Updated July 18, 2025. Accessed November 12, 2025. https://clinicaltrials.gov/study/NCT07073014. 5. ClinicalTrials.gov identifier: NCT07126262. Updated March 31, 2026. Accessed June 25, 2026. https://clinicaltrials.gov/study/NCT07126262.

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ORIGINAL ARTICLE

A Phase 3 Trial of Vosoritide in Children with Hypochondroplasia

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