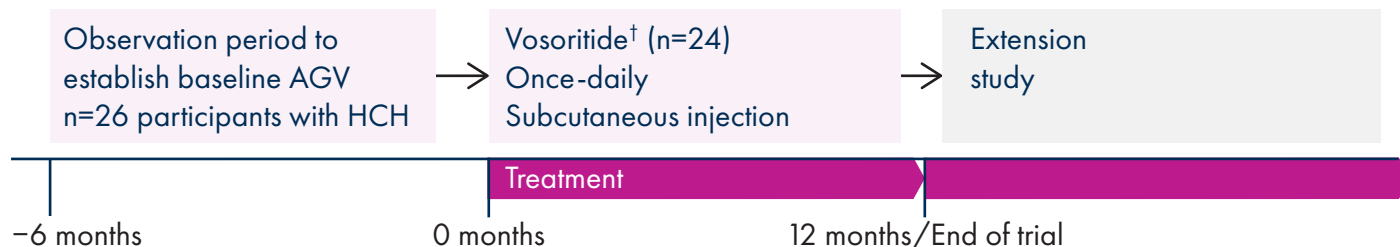


Vosoritide for Selected Genetic Causes of Short Stature: Spotlight on hypochondroplasia

Vosoritide is under investigation in children with HCH; it has not been approved for use or determined to be safe or effective

Study design, results and clinical interpretation

A **Phase 2, single-arm, open-label, investigator sponsored** trial (NCT04219007) assessing **vosoritide** as a therapeutic option for the **treatment of children with six genetic categories of short stature, including HCH***¹

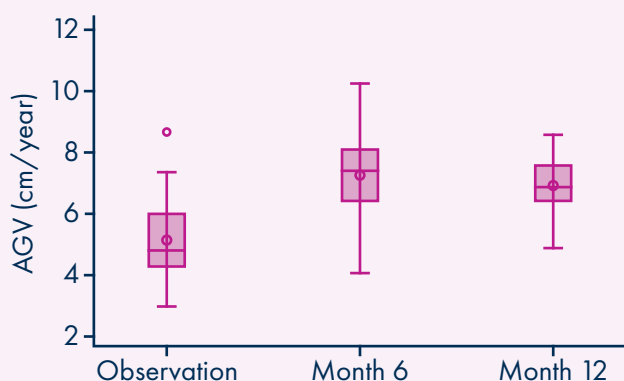


Primary outcomes¹

After 12 months of vosoritide treatment in children with HCH (n=24)



Absolute AGV increased by 1.81 (95% CI 1.16, 2.46) cm/year vs the observation period



AGV SDS increased by 2.26 (95% CI: 1.48, 3.05) and height SDS[‡] increased by 0.36 (95% CI: 0.26, 0.47) vs the observation period



There were **no treatment-related SAEs** and **no AE-related treatment discontinuations** with vosoritide

Most common AEs included: fever (54%), cough (50%), vomiting (46%), headache (25%), rhinorrhea (25%) and abdominal pain (21%)

76.9% of participants had **ISRs**



Secondary outcomes¹

Mean change from baseline over 12 months (95% CI):

- **Sitting height ratio:**[§] -0.16 (-0.44, 0.12)
- **Arm span minus height:**[§] -0.34 (-0.63, -0.06)
- **Bone age/chronological age ratio:** 0.01 (-0.03, 0.05)
- **CXM, ng/ml:** 17.92 (12.14, 23.69)



Extension study outcomes²

After 3 years of vosoritide treatment (n=13)^{||}



AGV SDS increased by 2.54 (95% CI: 1.52, 3.56)

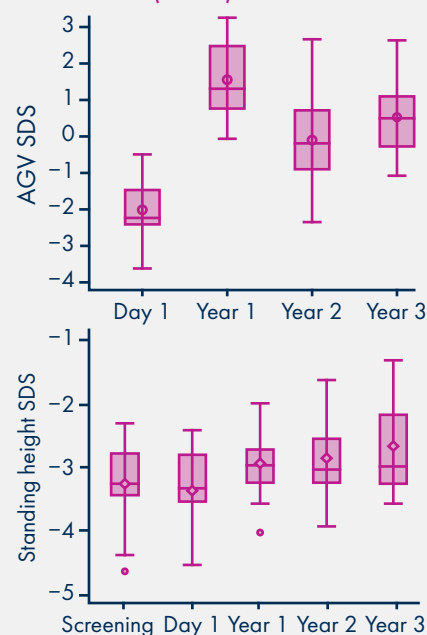


Height SDS[‡] increased by 0.72 (95% CI: 0.45, 0.99) in children with HCH



There were **no new safety concerns**

23.1% of participants had ISRs during Years 2 and 3^{||}



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Additional information



Key inclusion criteria^{1,3}

- Aged ≥ 3 to <11 years for males and ≥ 3 to <10 years for females
- Pre-pubertal
- Standing height of ≤ -2.25 SDS[†]
- Presence of confirmed mutation in the *FGFR3* gene
- Absence of growth hormone deficiency



Exclusion criteria³

- Growth plate fusion
- Malnutrition (defined as BMI <5 th percentile)

Medical History:

- Any clinically significant abnormality on screening tests
- Hypersensitivity to vosoritide or its excipients
- Additional medical conditions that affect growth
- Prior history of malignancy

Prior treatments related to or impacting growth:

- Concomitant treatment with growth hormone or recombinant insulin-like growth factor 1
- Prior treatment with a GnRH analog, aromatase inhibitor or oxandrolone
- Received any investigational drug within 90 days prior to the trial



Other outcomes³

Bone measures

- Change from baseline in BMD at 12 months

Safety profile

- Evaluation of immunogenicity and assessment of impact on safety and efficacy profiles over 12 months

HRQoL

- Percentage change from baseline in QoLISSY score at 12 months

Vosoritide PK and PD measures (at Day 1, Month 6 and Month 12)

- $AUC_{0-\infty}$ and AUC_{0-t}
- C_{max}
- Elimination half-life
- Apparent clearance
- Apparent volume of distribution during the terminal phase



Clinical trial location³

USA:

- Children's National Hospital – Washington, D.C.



For more information:
[Medical.BioMarin.Com](https://www.Medical.BioMarin.Com)

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*Other conditions were RASopathies, ACAN mutation carriers, carriers of heterozygous mutations in the *NPR2* gene, *SHOX* deficiency and carriers of the *NPPC* gene¹; [†]At a dose of 15 $\mu\text{g/kg/day}$ ¹; [‡]Referenced to CDC growth charts^{1,2}; [§]Age/sex adjusted SDS¹; ^{||}After 12 months of vosoritide treatment, children with AGV increases ≥ 1.6 cm/year compared with the observational period were eligible for the long-term extension trial⁴; [¶]Other AEs during the extension study: traumatic fractures (n=2), mild scoliosis (n=2), mild genu valgum (n=2)

1. Dauber A et al. *EClinicalMedicine*. 2024;71:102591; 2. Del Medico G et al. Presentation at Endocrine Society Annual Meeting, Chicago, IL, USA, June 13–16, 2026, oral presentation ORF47-08; 3. ClinicalTrials.gov. NCT04219007. Available at: <https://clinicaltrials.gov/study/NCT04219007>. Accessed July 2026; 4. Dauber A et al. *EClinicalMedicine*. 2024;71:102591 (supplement)

ACAN, aggrecan; AE, adverse event; AGV, annualized growth velocity; AUC, area under curve; BMD, bone mineral density; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CI, confidence interval; C_{max} , maximum concentration; CXM, collagen X biomarker; *FGFR3*, fibroblast growth factor receptor 3; GnRH, gonadotrophin-releasing hormone; HCH, hypochondroplasia; HRQoL, health-related quality of life; ISR, injection site reaction; NPPC, natriuretic peptide precursor C; *NPR2*, natriuretic peptide receptor 2; PD, pharmacodynamics; PK, pharmacokinetics; QoLISSY, Quality of Life of Short Stature Youth; SAE, serious adverse event; SDS, standard deviation score; *SHOX*, short stature homeobox gene