Vosoritide Treatment In Children With Hypochondroplasia: Three-year Results From A Phase II Extension Trial

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DISCLOSURES

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BioMarin played no role in the design or conduct of the study, analysis of data, or preparation of the abstract or presentation.

Giulia Del Medico: Nothing to disclose

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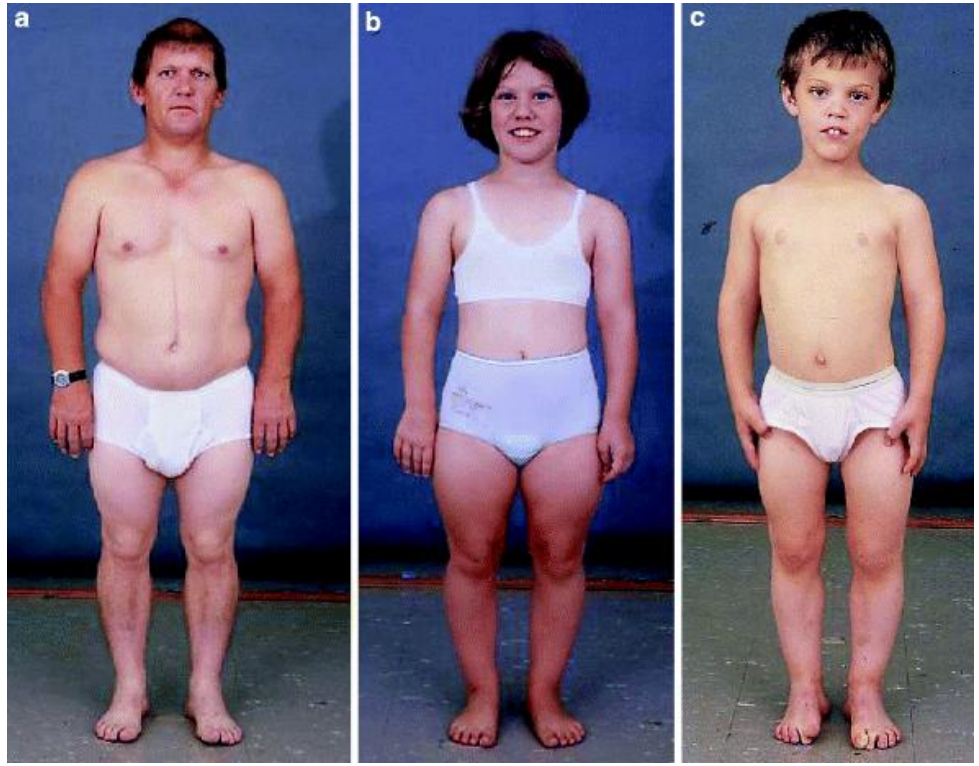
BACKGROUND: HYPOCHONDROPLASIA (HCH)

- Autosomal dominant skeletal dysplasia caused by activating *FGFR3* variants
- Clinical features:
  - Disproportionate short stature
  - Relative macrocephaly
  - Limb shortening
  - Limited elbow extension
  - Lower limb bowing



Hypochondroplasia. In: Chen, H. (eds) Atlas of Genetic Diagnosis and Counseling, 2012.

No approved growth-promoting therapy currently exists for HCH

BACKGROUND: VOSORITIDE

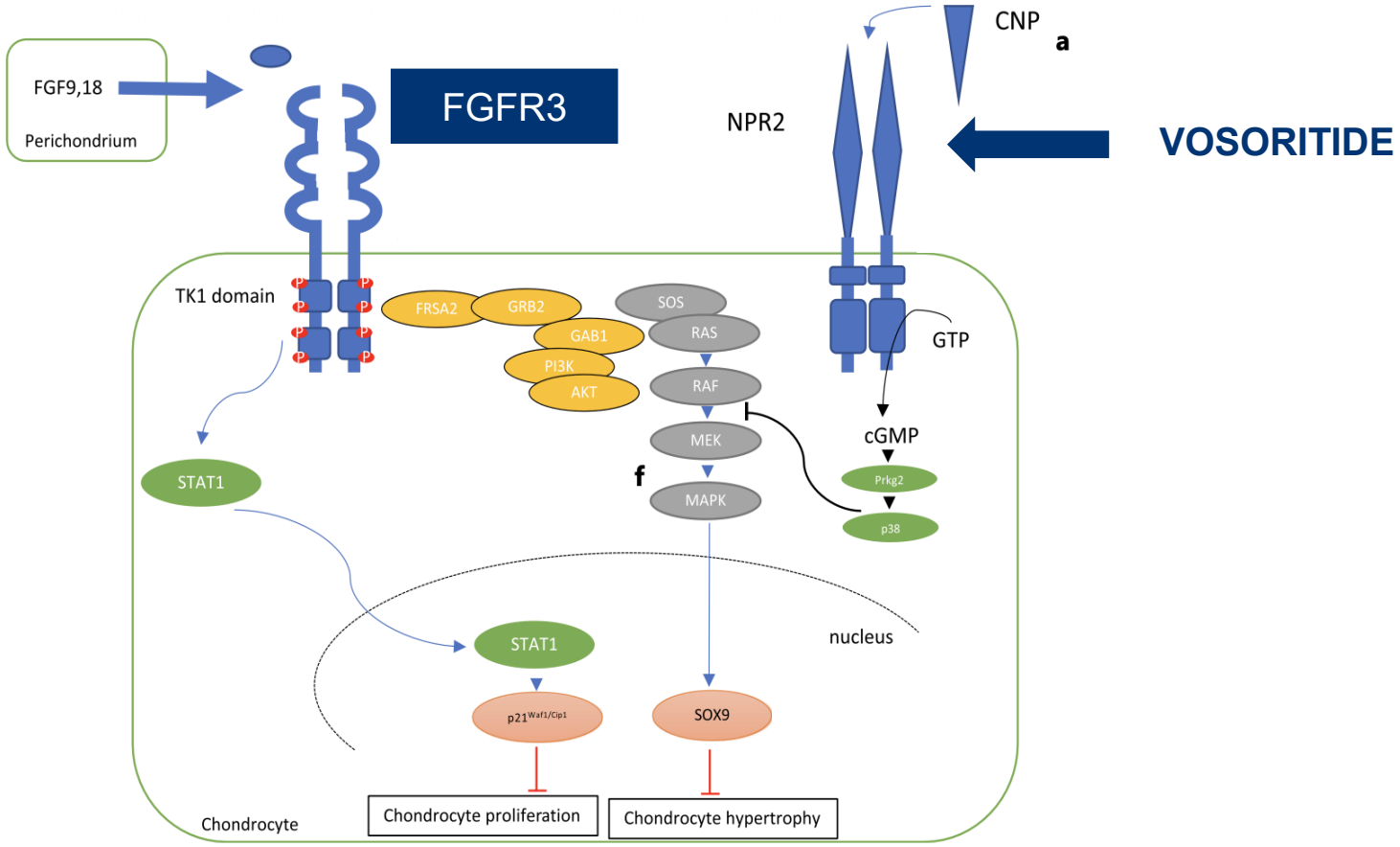
CNP analog that inhibits the FGFR3/MAPK signaling promoting endochondral growth

↓

Approved for treatment of short stature in achondroplasia (ACH)

↓

Potential therapeutic target in HCH due to shared FGFR3 pathophysiology



Galetaki DM, Dauber A. Hormone Research in Paediatrics, 2025.

OBJECTIVES

To evaluate the long-term safety and efficacy of vosoritide in children with HCH

Endpoints:

- Incidence of adverse events (AE)
- Change from baseline in absolute and age-sex standardized annualized growth velocity (AGV)
- Change from baseline in height standardized deviation score (SDS)

METHODS

CORE STUDY

- **Design**: Single-arm, open-label, phase 2 trial (NCT04219007)
- **Population**:
  - Genetically confirmed HCH
  - Prepubertal
  - Age 3-11 years for males and 3-10 years for females
  - Standing height ≤ -2.25 SD (CDC growth charts)
- **Timeline**: Screening → 6-month observation period → 12 months of daily subcutaneous vosoritide (15 µg/kg/day)

EXTENSION

- **Eligibility:** Participants with **AGV increase >1.6 cm/year** during core study
- **Follow up**:
  - In-person visits every 6 months
  - Interim phone monitoring
  - Treatment continuation until growth cessation
- **Endpoints**: Unchanged compared to core study

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PREVIOUS 12-MONTH RESULTS

- **24 children** with HCH were treated in the core study
- After 12 months of vosoritide:
  - Standing height increase: **+0.36 SD**
  - AGV increase: **+1.81 cm/year** (+2.26 SD)
  - No new safety concerns were reported

Vosoritide treatment for children with hypochondroplasia: a phase 2 trial

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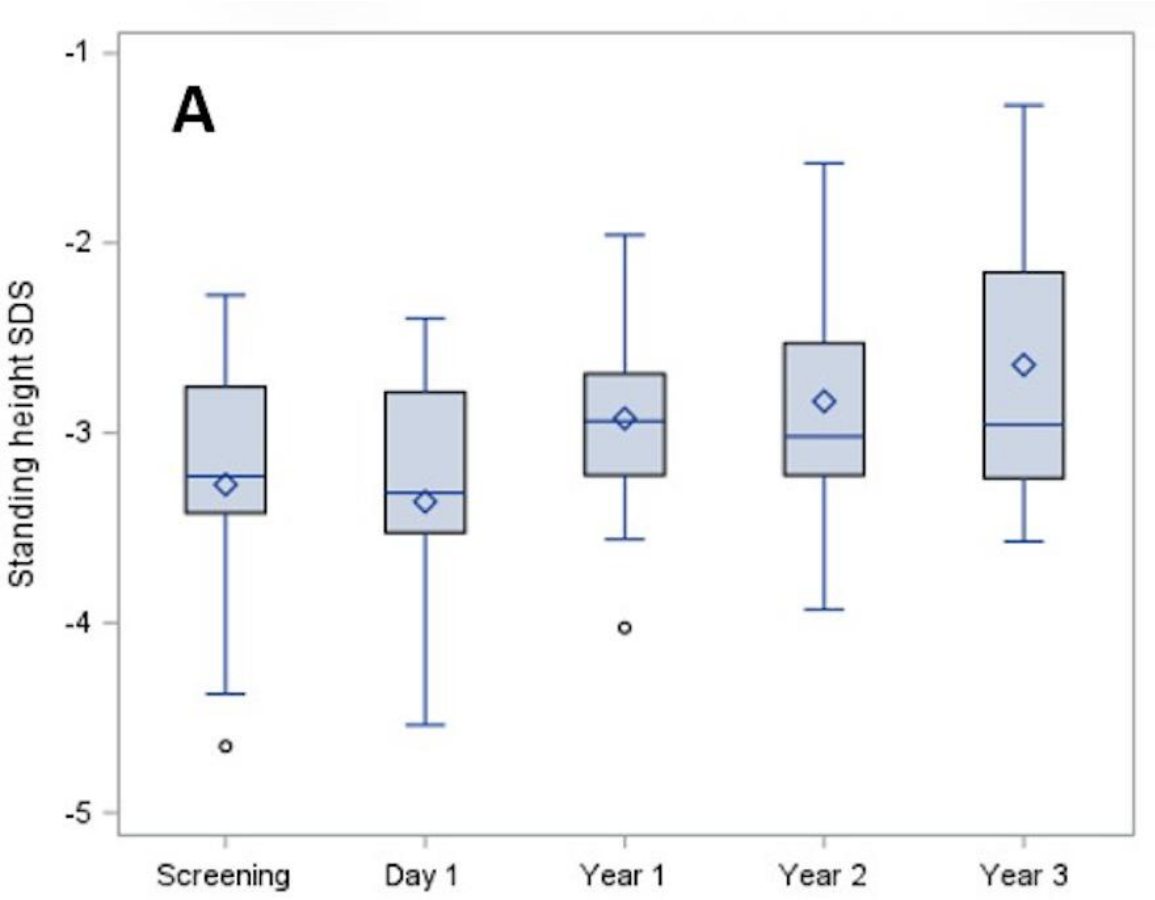
RESULTS FROM 3 YEARS IN THE EXTENSION STUDY

PARTICIPANT BASELINE CHARACTERISTICS

Total enrolled subjects	**N = 13**
Age at screening (years)	
Mean (SD); median (IQR)	5.78 (1.13); 5.70 (1.70)
Sex	
Female	7 (53.8%)
Male	6 (46.2%)
Previously treated with growth hormone	
Yes	1 (7.7%)
No	12 (92.3%)
Genetic Variant	
Asn540Lys	11 (84.6%)
Gly342Cys	1 (7.7%)
Ser351Phe	1 (7.7%)
Standing height SDS at Screening	
SDS -2.25 to -3	4 (30.8%)
SDS -3 to -4	7 (53.8%)
SDS below -4	2 (15.4%)

RESULTS: STANDING HEIGHT

	Mean (SD) Height at Each Timepoint				
	Screening	Day 1	Year 1	Year 2	Year 3
Standing height SDS CDC	**-3.27** (0.71)	-3.36 (0.64)	-2.92 (0.57)	-2.83 (0.70)	**-2.64** (0.79)
Standing height SDS HCH-specific charts	**-0.32** (0.79)	-0.43 (0.73)	0.06 (0.77)	0.17 (0.94)	**0.40** (1.05)

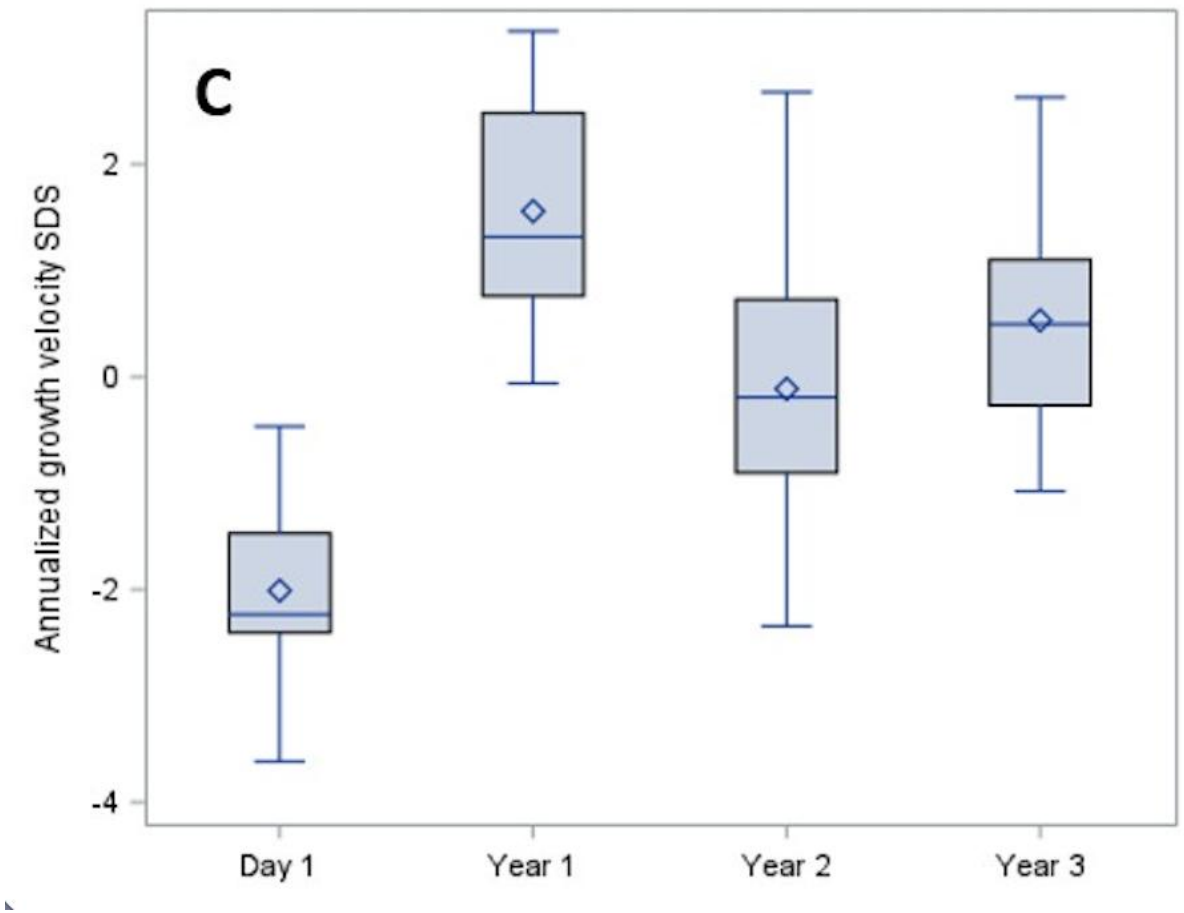


RESULTS: STANDING HEIGHT

	Mean difference (95% CI) [Two-sided p value]				
	Screening to Day 1	Day 1 to Year 1	Year 1 to Year 2	Year 2 to Year 3	Day 1 to Year 3
Standing height SDS CDC	-0.09 (-0.16,-0.02) [0.01]	0.44 (0.29,0.59) [<.0001]	0.09 (-0.02,0.20) [0.11]	0.20 (0.05,0.34) [0.01]	**0.72** (0.45,0.99) [<0.0001]
Standing height SDS HCH-specific charts	-0.11 (-0.19,-0.04) [0.006]	0.49 (0.35,0.63) [<.0001]	0.11 (-0.03,0.24) [0.10]	0.23 (0.05,0.41) [0.02]	**0.83** (0.51,1.15) [0.0001]

RESULTS: AGV

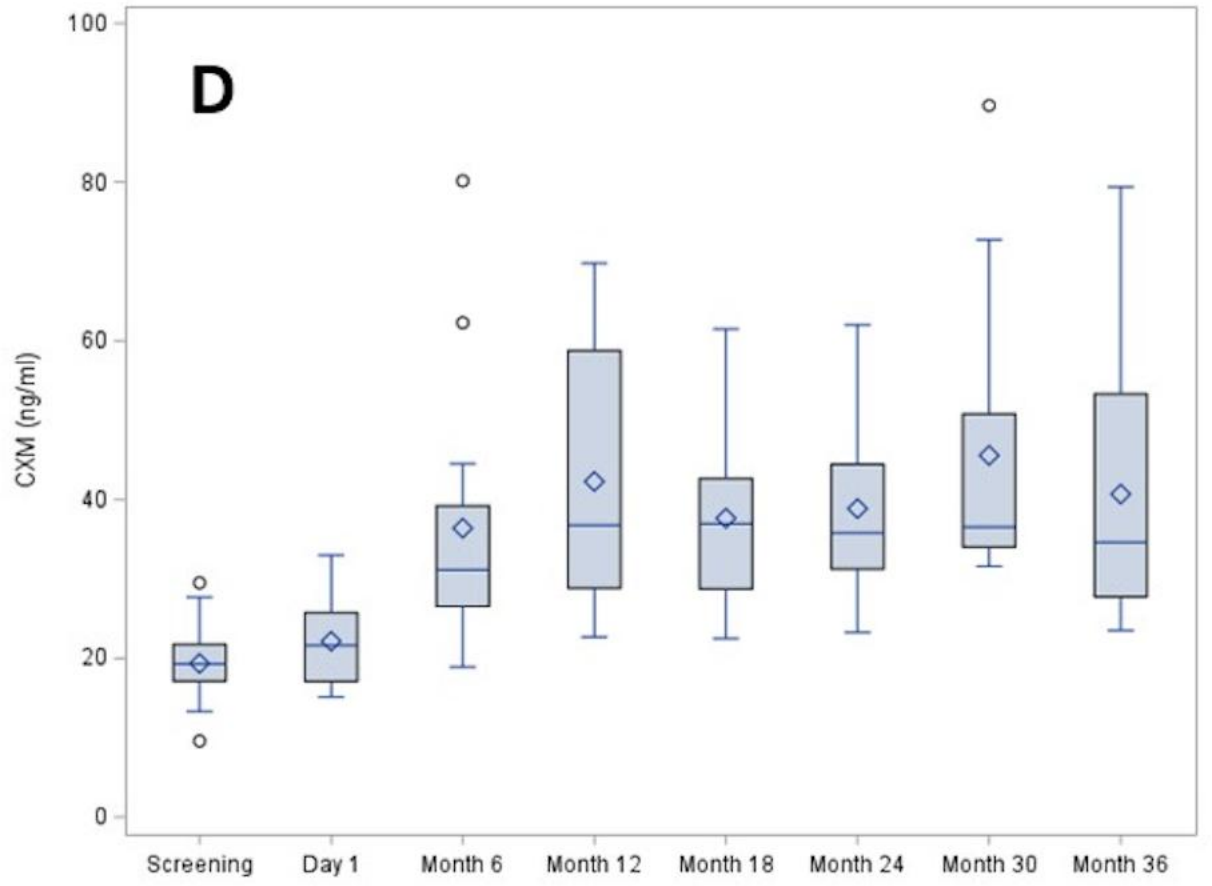
	Mean (SD) AGV at Each Timepoint				
	Screening	Day 1	Year 1	Year 2	Year 3
Annualized growth velocity (cm/yr)	N/A	**4.27** (0.70)	7.24 (0.80)	5.55 (1.02)	**6.13** (1.27)
Annualized growth velocity SDS	N/A	**-2.01** (0.78)	1.56 (1.03)	-0.11 (1.41)	**0.53** (1.20)



RESULTS: AGV

	Mean difference (95% CI) [Two-sided p value]				
	Screening to Day 1	Day 1 to Year 1	Year 1 to Year 2	Year 2 to Year 3	Day 1 to Year 3
Annualized growth velocity (cm/yr)	N/A	2.97 (2.40,3.54) [<.0001]	-1.69 (-2.38,-0.99) [0.0002]	0.58 (-0.25,1.42) [0.16]	**1.86** (0.82,2.90) [0.002]
Annualized growth velocity SDS	N/A	3.57 (2.81,4.33) [<.0001]	-1.67 (-2.61,-0.73) [0.002]	0.64 (-0.10,1.38) [0.08]	**2.54** (1.52,3.56) [0.0002]

RESULTS: COLLAGEN X BIOMARKER (CXM) LEVELS



RESULTS: SAFETY

Reported AE:

- Injection site reactions
  - Year 1: 76.9%
  - Years 2–3: 23.1%
- Other events
  - Traumatic fractures (n=2) → healed without complications
  - Mild scoliosis (n=2)
  - Mild genu valgum (n=2)

Overall:

- Vosoritide was well tolerated
- No treatment-related serious AE
- No treatment discontinuations

CONCLUSIONS

- Three years of vosoritide treatment increased height SDS by **+0.72 SD** in selected children with HCH.
- AGV improved most during Year 1 and remained above baseline through Year 3.
- Vosoritide was generally well tolerated with no new safety concerns.
- Findings suggest sustained growth-promoting effects in HCH, similar to those observed in ACH.
- Interpretation is limited by small sample size, lack of control group, and selection of initial good responders.
- Long-term follow up will further evaluate safety and final adult height.