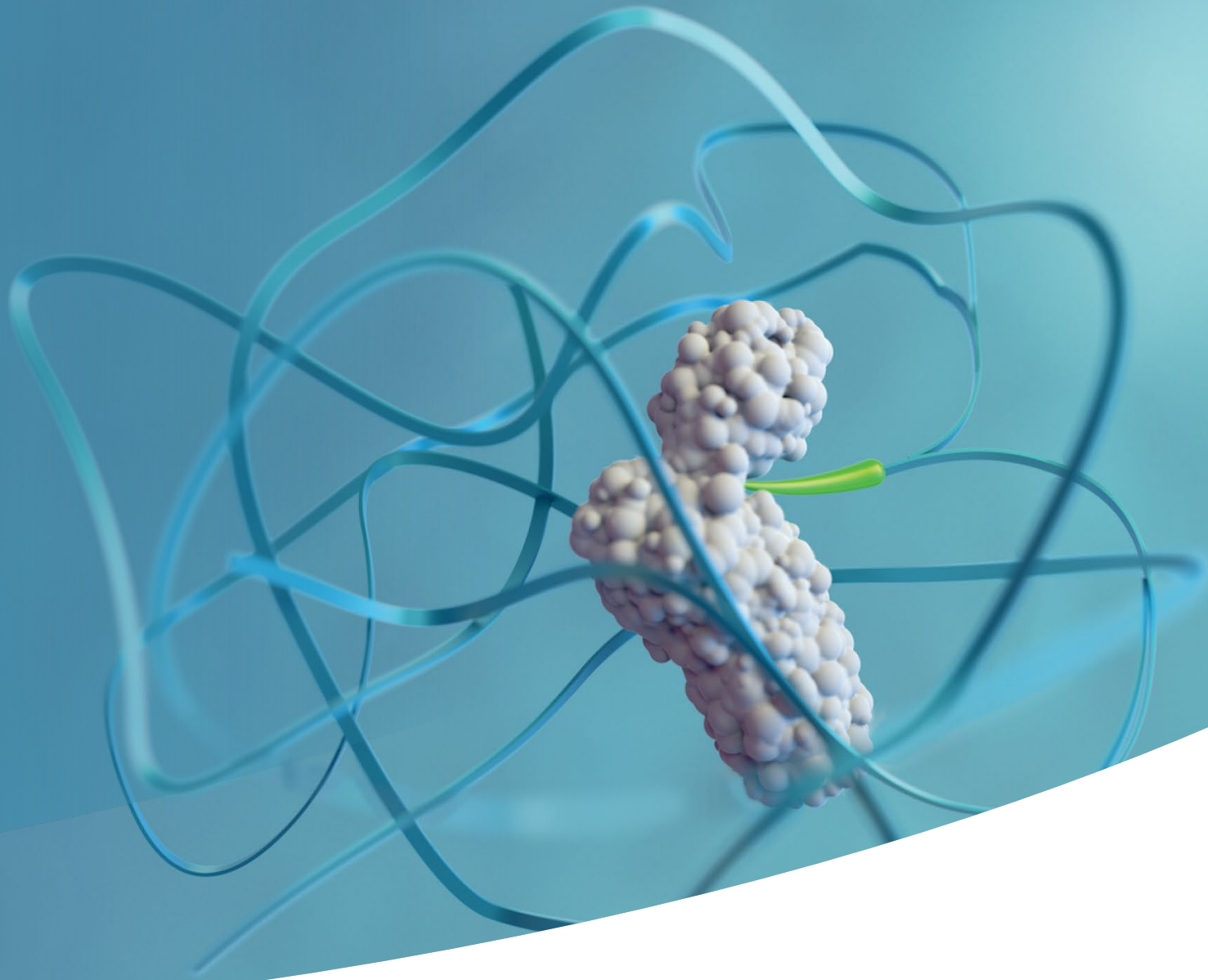
Ascendis Pharma A/S



52-Week Bone Morphometry Results ApproaCH Clinical Trial

Cautionary Note on Forward-Looking Statements

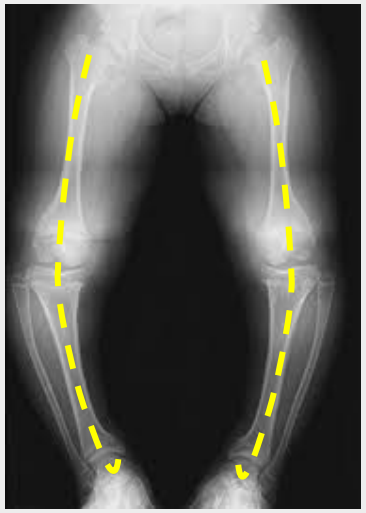
This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, such as statements regarding our products and prospective product candidates; clinical trial results; and future results of current and/or anticipated products and product candidates are forward-looking statements. These forward-looking statements are based on our current expectations and beliefs, as well as assumptions concerning future events. These statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the results discussed in the forward-looking statements. These risks, uncertainties and other factors are more fully described in our current and future reports filed with or submitted to the Securities and Exchange Commission ("SEC"), including, without limitation, our most recent Annual Report on Form 20-F filed with the SEC on February 12, 2025, particularly in the sections titled "Risk Factors" and "Operating and Financial Review and Prospects." In light of the significant uncertainties in our forward-looking statements, you should not place undue reliance on these statements or regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all. Any forward-looking statement made by us in this presentation speaks only as of the date of this presentation and represents our estimates and assumptions only as of the date of this presentation. Except as required by law, we assume no obligation to update these statements publicly, whether as a result of new information, future events, changed circumstances or otherwise after the date of this presentation.

This presentation concerns Ascendis Pharma approved products as well as Ascendis Pharma investigational product candidates that are or have been under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration, European Medicines Agency or other foreign regulatory authorities. These investigational product candidates are currently limited by law to investigational use, and no representations are made as to their safety or effectiveness for the purposes for which they are being investigated. This presentation is for investor and insurance carrier communications only. Not for use in product promotion.

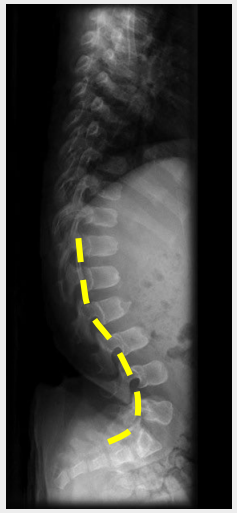
Achondroplasia: A Skeletal Dysplasia with Orthopaedic Complications

The pathogenic *FGFR3* variants of achondroplasia result in skeletal abnormalities beyond short stature, which are associated with pain, impaired physical functioning, orthopaedic surgeries and reduced HRQoL[1-5]

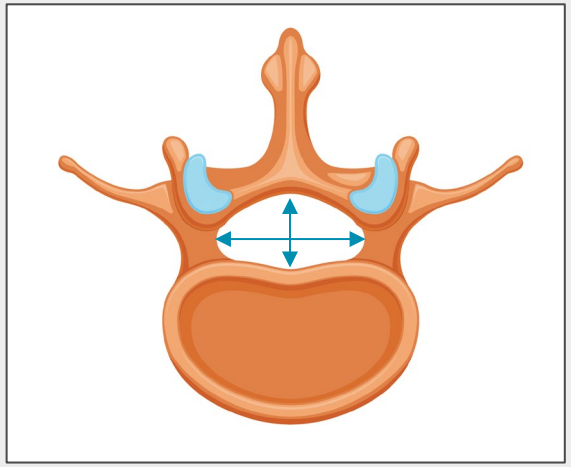
Genu Varum



Kyphosis/Lordosis



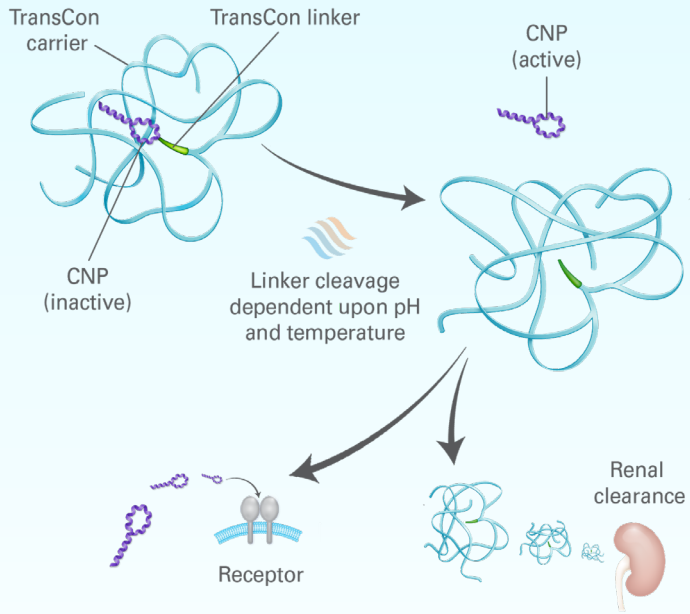
Spinal Stenosis



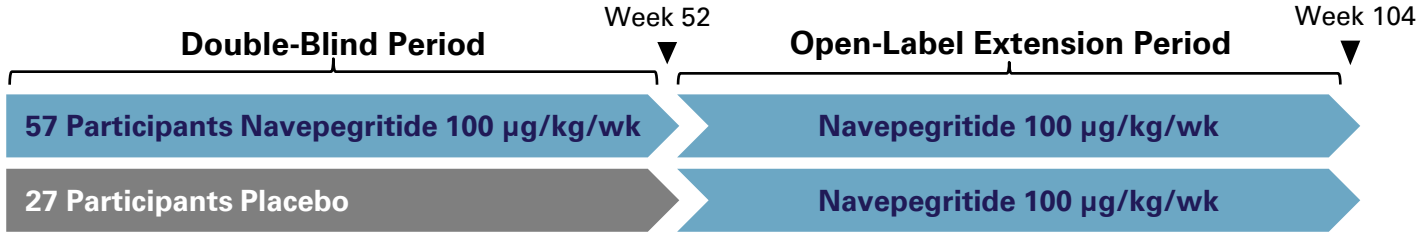
The goal of this study was to determine whether navepegritide improved not only linear growth, but also orthopaedic parameters associated with the underlying skeletal dysplasia

1. Hunter AG, et al. *J Med Genet.* 1998;35(9):705-712. 2. Matsushita M, et al. *Calcif. Tissue Int.* 2019;104(4):364-372. 3. Savarirayan R, et al. *Nat Rev Endocrinol.* 2022;18(3):173-89. 4. Murton MC, et al. *Adv Ther.* 2023;40(9):3639-80. 5. Nahm NJ, et al. *Orphanet J Rare Dis.* 2023;18(1):139.

Navepegritide and ApproaCH Pivotal Trial Design



Navepegritide is an investigational prodrug of C-type natriuretic peptide (CNP), administered once-weekly and designed to provide continuous exposure to active CNP[1]



84 participants with achondroplasia (age 2-11y), randomized 2:1

Primary Endpoint

- Annualized growth velocity (AGV) at Week 52

Safety Endpoints

- Incidence of treatment emergent adverse events (TEAEs)

Exploratory Endpoints

- **Change from baseline in bone morphometric parameters of the spine and lower extremity as assessed by X-ray**

Countries

- US, Canada, Denmark, Ireland, Spain, Australia, New Zealand

ApproaCH Baseline Characteristics

Full Analysis Set	Navepegritide (n=57)	Placebo (n=27)	Overall (N=84)
Age (years), mean (SD)	5.6 (2.6)	6.0 (2.7)	5.7 (2.6)
Sex, n (%) Female Male	 26 (45.6) 31 (54.4)	 13 (48.1) 14 (51.9)	 39 (46.4) 45 (53.6)
Height (cm), mean (SD)	88.9 (12.9)	89.1 (11.5)	89.0 (12.4)
ACH-specific height Z-score, mean (SD)	0.18 (0.92)	-0.11 (0.73)	0.09 (0.87)
CDC height Z-score, mean (SD)	-4.90 (0.98)	-5.21 (0.93)	-5.00 (0.97)
AGV (cm/year), mean (SD)	4.0 (1.9)	3.8 (2.0)	3.9 (1.9)

Trial population was balanced between treatment arms, and representative of children with achondroplasia

ACH, achondroplasia; AGV, annualized growth velocity; CDC, Centers for Disease Control and Prevention

Orthopaedic Measurement on Standing Lower Limb X-Rays

TFA:

Tibia-Femoral Angle

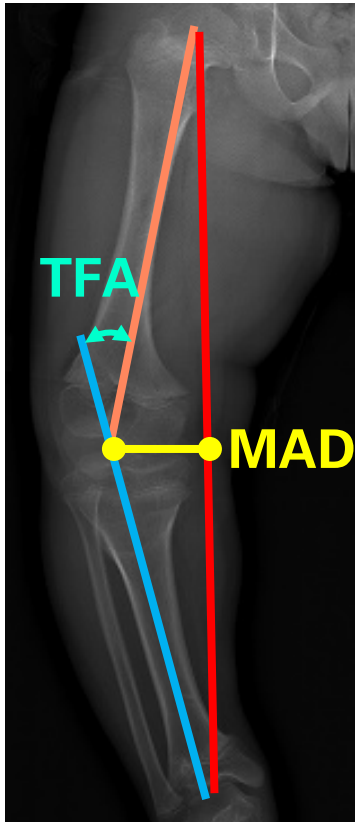
Angle between the mechanical axes of the femur and the tibia

MAD:

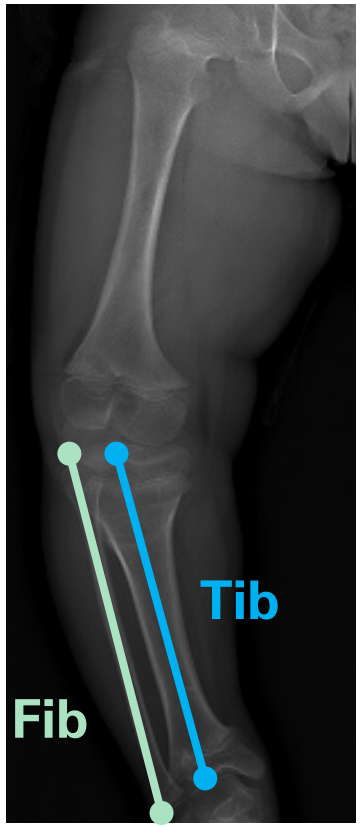
Mechanical axis deviation

Distance from the center of the knee to a line drawn from the center of the femoral head to the ankle *(mechanical axis of the leg)*

Alignment



Proportionality



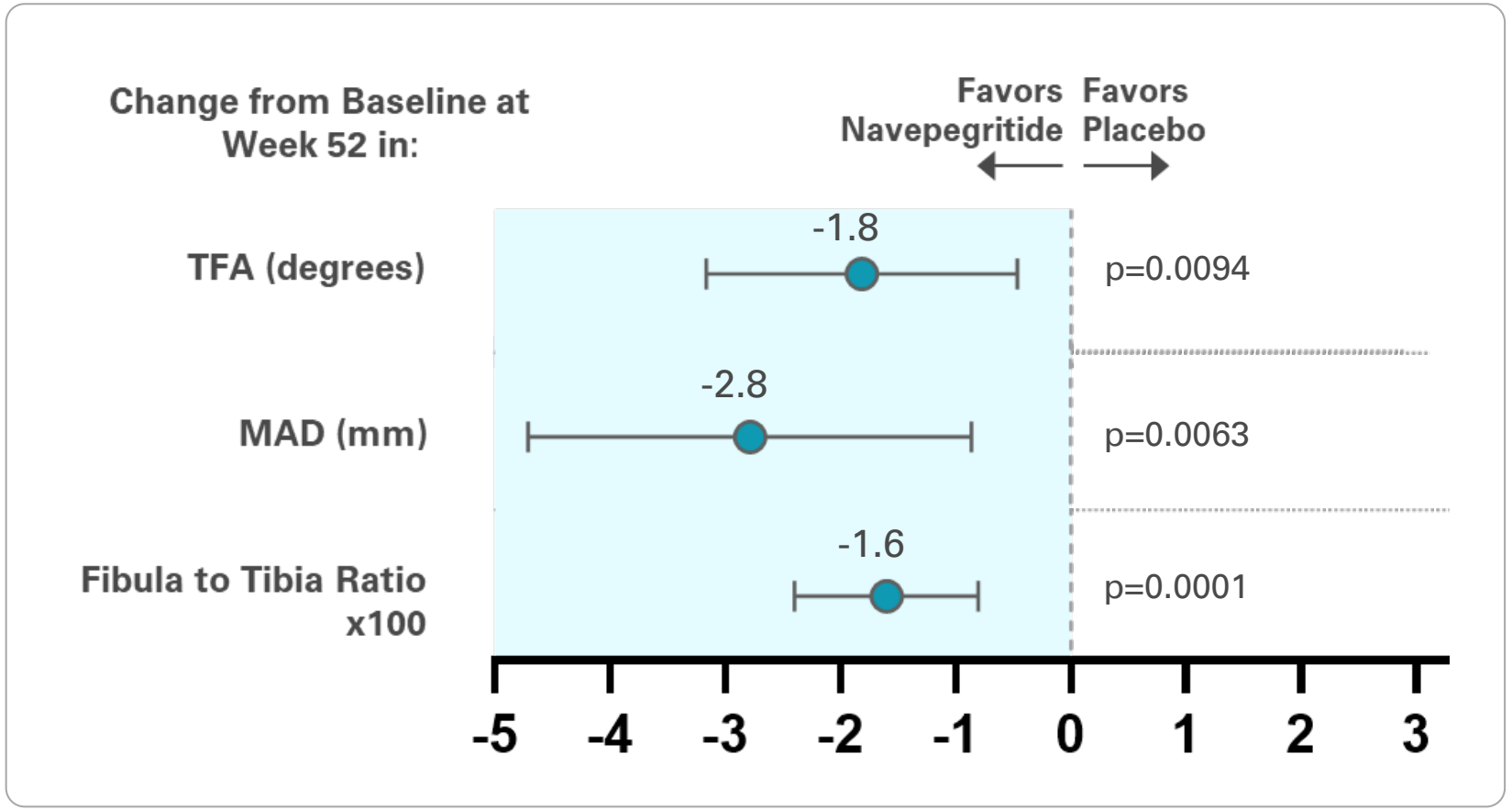
Fibular “overgrowth” is a key contributor to the progression of leg curvature

Fib/Tib:

Fibula to Tibia Ratio

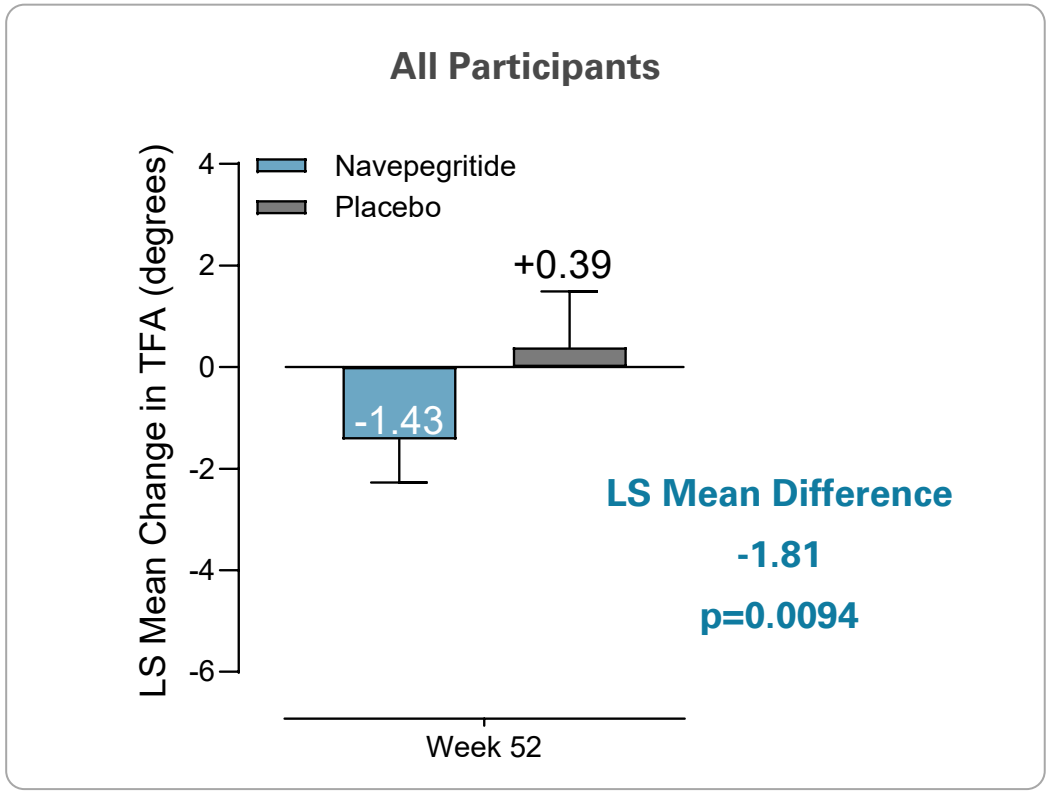
Ratio of fibula length to tibia length

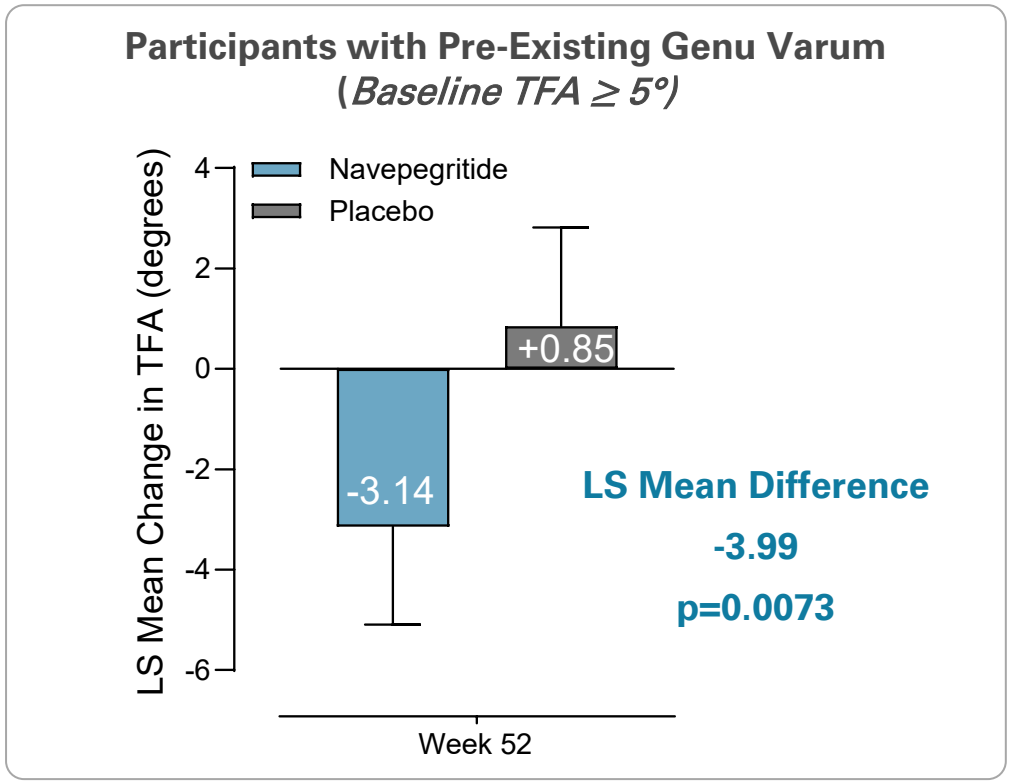
Navepegritide Improved Lower Extremity Alignment and Proportional Growth



Notes: Figure shows TFA, calibrated data of MAD and uncalibrated data of fibula to tibia ratio.
Blue dot indicates LS mean difference between navepegritide 100 µg/kg/week and placebo; error bar indicates 95% CI. ANCOVA model included treatment, stratification factor, baseline age and baseline value as covariates.
ANCOVA, Analysis of covariance; CI, confidence interval; LS, least squares; MAD, mechanical axis deviation; TFA, Tibia-femoral angle

Greater Improvements in Lower Extremity Alignment with Navepegritide in Participants with Genu Varum at Baseline

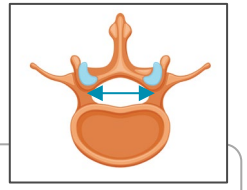




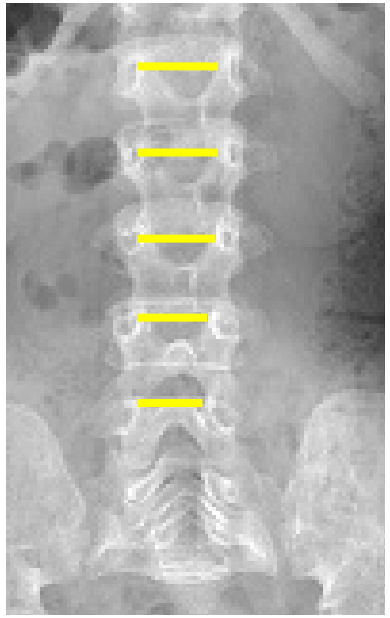
Greater benefits observed in participants with genu varum ≥ 5° at baseline

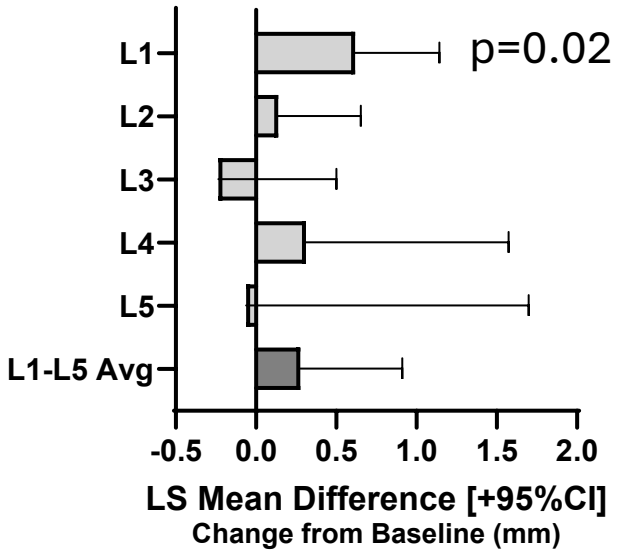
Error bars indicate 95% CI. CI, confidence interval; LS, least squares; TFA, Tibia-femoral angle

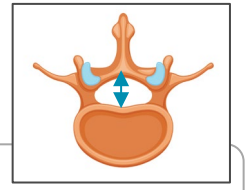
Navepegritide Improved Spinal Canal Dimensions vs Placebo at Week 52



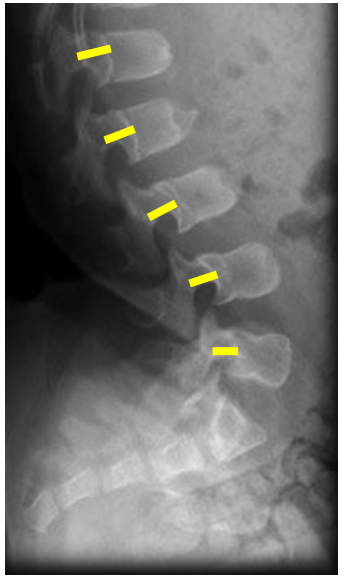
Interpedicular Distance (IPD)

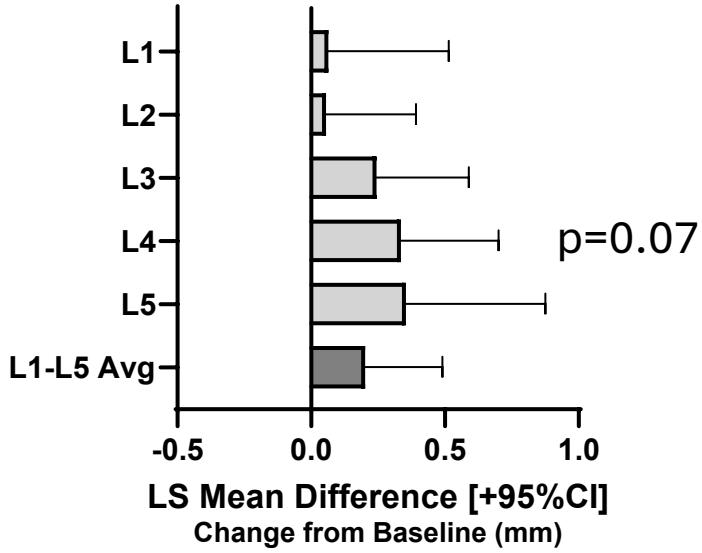






Pedicle Width (PW)





Greater expansion of the spinal canal was in line with the observed increase in linear growth

Error bars indicate 95% CI. CI, confidence interval; LS, Least squares

Navepegritide Showed a Safety and Tolerability Profile Comparable to Placebo

	Navepegritide (n=57)	Placebo (n=27)
Any Treatment-emergent Adverse Event, n (%)	52 (91.2)	26 (96.3)
Adverse Events ≥15% in either treatment group, n (%)		
Pyrexia	20 (35.1)	6 (22.2)
Nasopharyngitis	18 (31.6)	10 (37.0)
Otitis media	14 (24.6)	7 (25.9)
Upper respiratory tract infection	11 (19.3)	3 (11.1)
Vomiting	11 (19.3)	3 (11.1)
Headache	10 (17.5)	3 (11.1)
Serious Adverse Events (SAE), n (%)	3 (5.3)	3 (11.1)
Treatment-Related Adverse Events, n (%)	12 (21.1)	7 (25.9)
Treatment-Related Serious Adverse Events	0	0
Injection site reaction (ISR), n (%)	11 (19.3)	4 (14.8)
ISR events per Patient Year of Exposure	0.41	0.15
Mean change in bone/chronological age ratio	0.000	-0.013

Treatment with navepegritide showed:

- very few occurrences of ISRs
- no treatment-related SAEs
- no cases of symptomatic hypotension
- no accelerated bone age or fracture
- no cases of osteonecrosis or SCFE

Safety analysis set; summary is based on double-blind period
AE, adverse event; ISR, injection site reaction; SAE, serious AE; SCFE, Slipped capital femoral epiphysis

Summary and Conclusions: The ApproaCH Trial

- Navepegritide demonstrated superiority over placebo in **AGV** at week 52, with a **safety and tolerability profile comparable to placebo**
- Navepegritide improved aspects of bone morphometry at week 52, including **improvement in lower limb alignment** and **increasing spinal canal dimensions**

By changing the trajectory of skeletal dysplasia, navepegritide has the potential to reduce future complications due to lower limb malalignment and spinal stenosis, such as pain, impaired mobility, and need for surgery

AGV, Annualized Growth Velocity