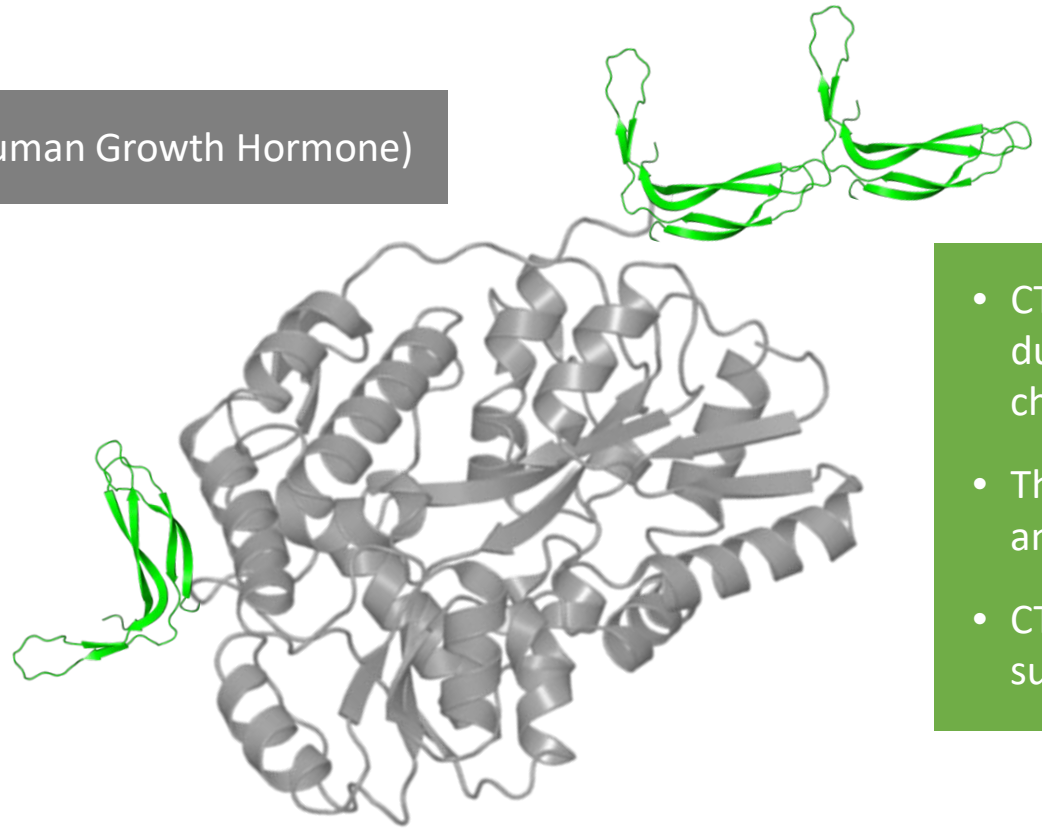
Update on Somatrogon Development for the Treatment of Growth Hormone Deficiency in Pediatric and Adult Subjects

Somatrogon – a Long-Acting CTP-hGH Protein

hGH (Human Growth Hormone)



- CTP (C-Terminal Peptide) – a natural peptide created during evolution to enhance the half-life of human chorionic gonadotropin (hCG)
- The glycosylated CTP extends the half-life of somatrogon and supports once-weekly administration
- CTP-FSH, which has been on the market over 10 years, is supportive of the safety and efficacy of CTP technology

Phase 3 Clinical Studies Evaluating Somatrogon for the Treatment of GHD in Adult and Pediatric Subjects

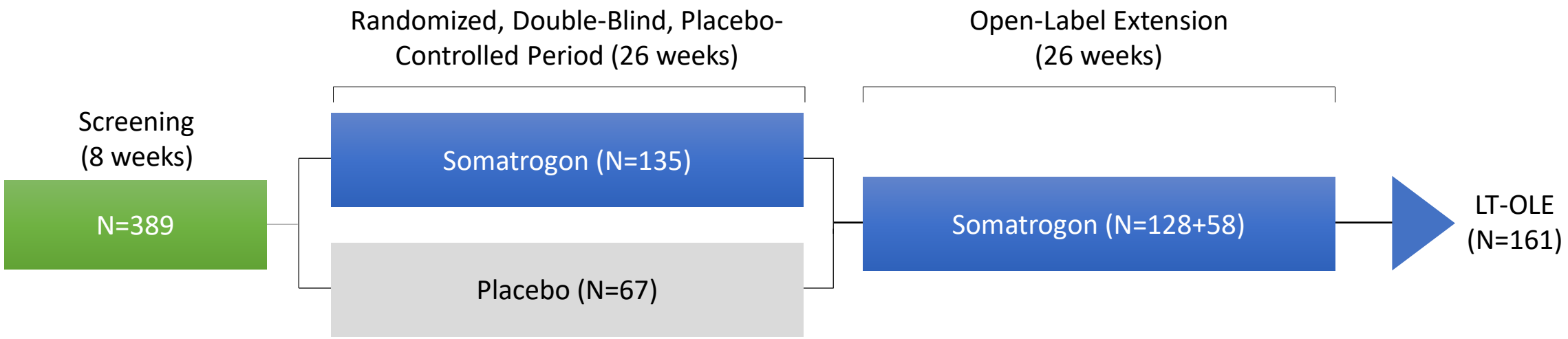
Adult Study

- CP-4-005 Adult Global Study
  - 198 subjects (133 somatrogon vs. 65 placebo)
  - Completed 52-week Main study + Open Label Extension

Pediatric Studies

- CP-4-006 Pediatric Global Study
  - 224 subjects (109 somatrogon vs. 115 daily Genotropin®)
  - Completed 52-week Main study + Long-term Open Label Extension Ongoing
- CP-4-009 Japanese Pediatric Study
  - 44 subjects (22 somatrogon vs. 22 daily Genotropin®)
  - Completed 52-week Main study + Long-term Open Label Extension Ongoing

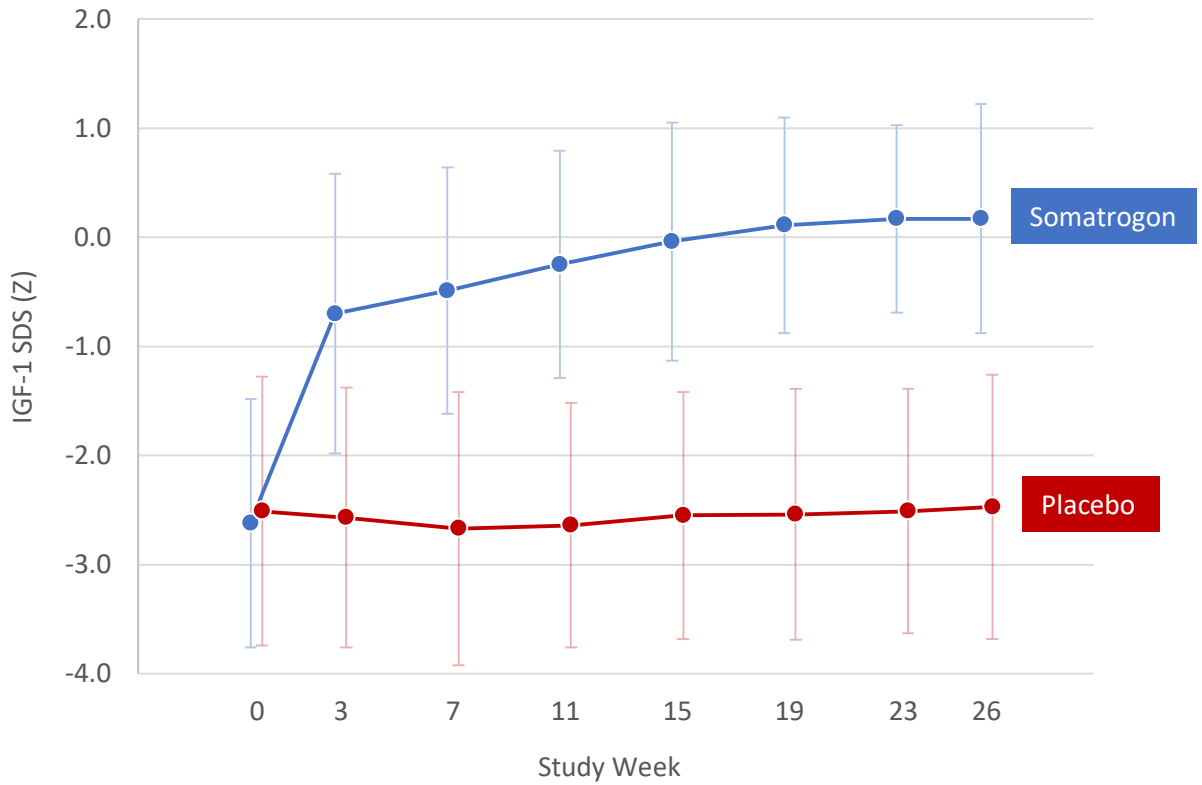
CP-4-005: Somatrogon Phase 3 Study in Adult Patients with GHD – Study Design



Initial doses ranged from 2.0 – 4.0 mg/wk depending on age, gender and oral estrogen status and were adjusted to maintain IGF-1 between -0.5 and +1.5 SDS

Endpoint	Measures
Primary	• Change in trunk fat mass in kilograms from baseline to week 26 • Safety (adverse events, abnormal labs, immunogenicity, ECG) (52 weeks)
Secondary	• Changes in lean body mass, % trunk fat mass, total fat mass in kilograms from baseline to 26 and 52 weeks • Change in trunk fat mass in kilograms from baseline to 52 weeks

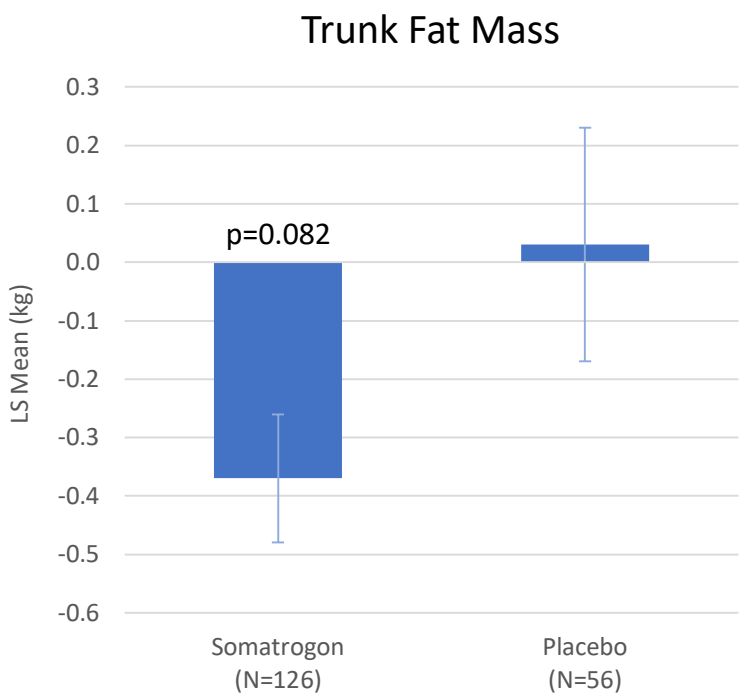
Change in IGF-1 SDS – Efficacy and Safety Biomarker

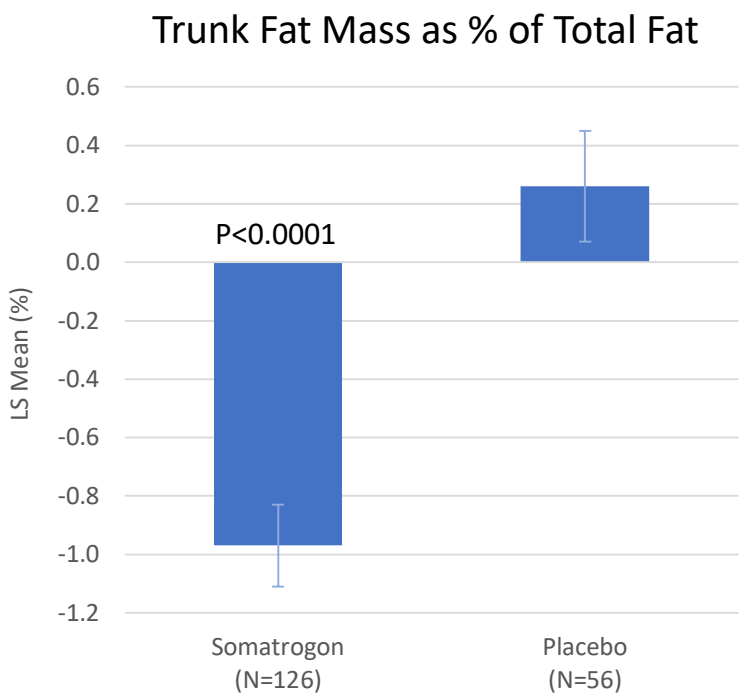


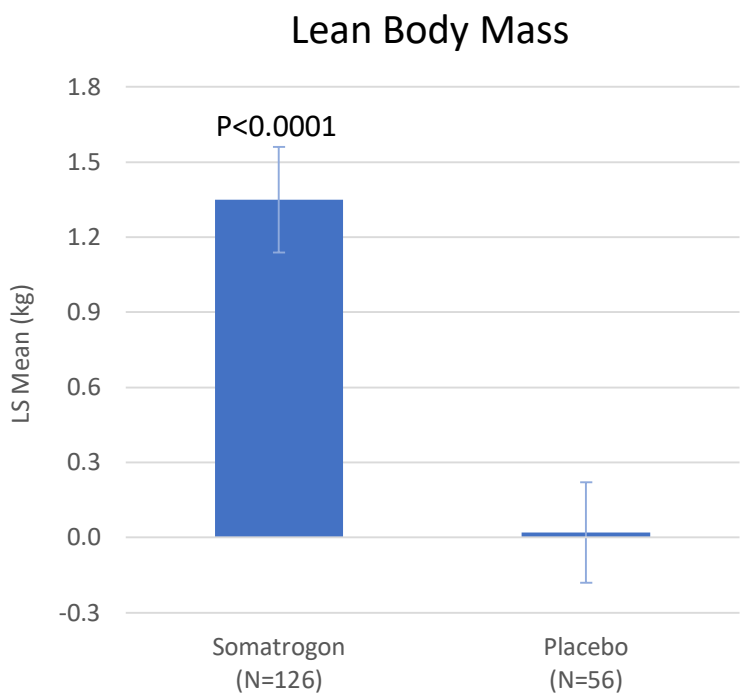
Number of Subjects Achieving IGF-1 SDS between -0.5 to 1.5 over the first 26 weeks

IGF-1 Normalization -0.5 ≤ SDS ≤ 1.5	Somatrogon n (%)	Placebo n (%)
Yes	130 (97.7)	4 (6.2)
No	3 (2.3)	61 (93.8)

Efficacy in Primary and Secondary Endpoints: Changes in Trunk Fat Mass, Trunk Fat Mass as % of Total Fat and Lean Body Mass from Baseline to 26 Weeks







A post-hoc sensitivity analysis that removes outliers was performed; the primary endpoint was then statistically significant

Conclusions and Developmental Status of Somatrogon in Adult Indication

Efficacy

- Although change in trunk fat mass was not statistically significant (p-value of 0.082), *post hoc* tipping point analysis with the removal of outliers demonstrated statistical significance
- Treatment with somatrogon demonstrated efficacy and statistical significance in key secondary endpoints: Trunk Fat Mass as % of Total Fat and Lean Body Mass
- Over 97% of the subjects achieved normalization of IGF-1 SDS levels between -0.5 and 1.5 SDS

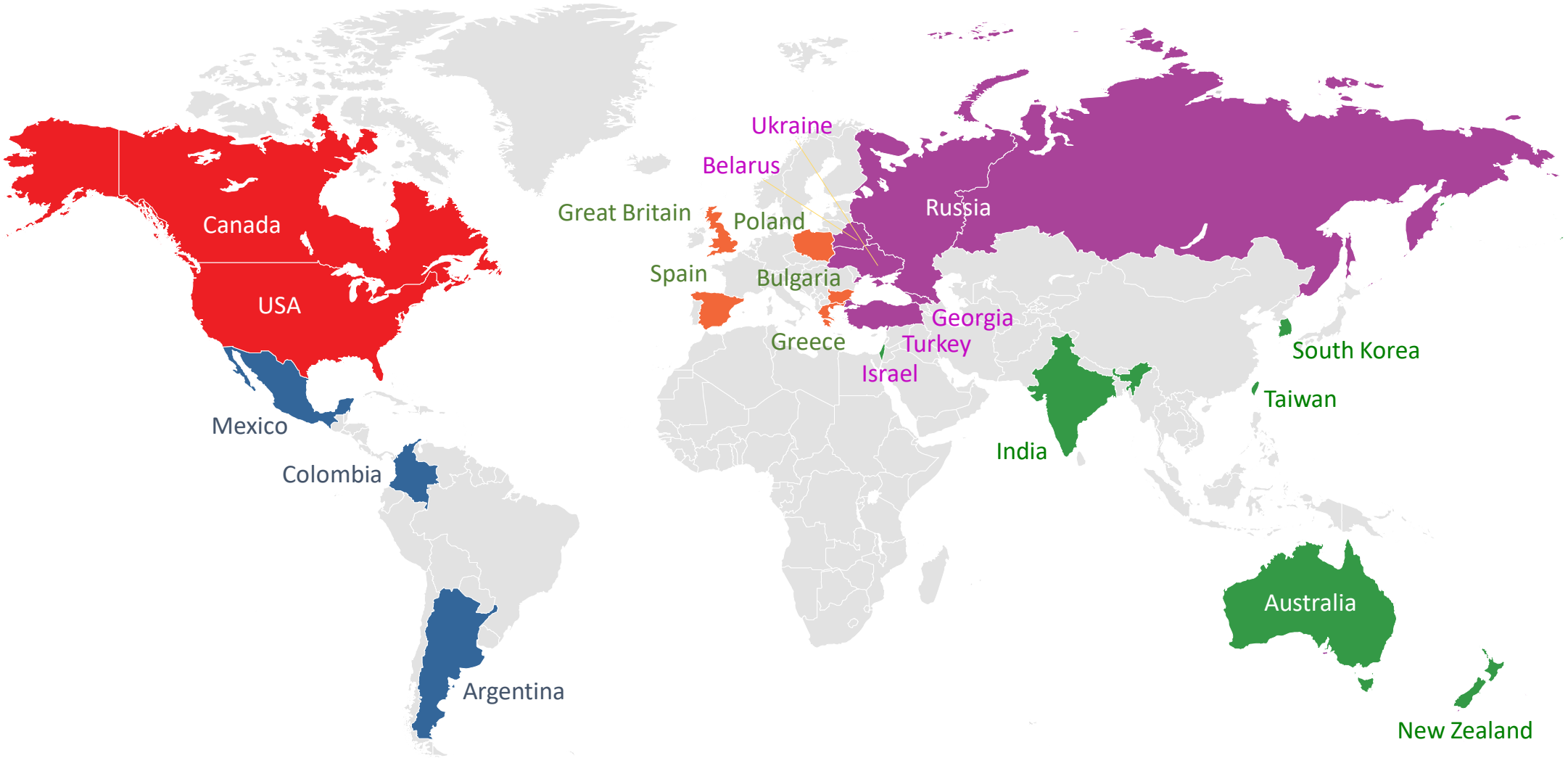
Safety and Tolerability

- Treatment with somatrogon had an acceptable safety and tolerability profile
- PT events occurring in ≥5% of the subjects in either treatment group were:
  - Injection site pain (somatrogon: 9.0%; placebo: 13.8%)
  - Headache (somatrogon: 8.3%; placebo: 7.7%)
  - Upper respiratory tract infection (somatrogon: 4.5%; placebo: 6.2%)
  - Nasopharyngitis (somatrogon: 3.8%; placebo: 7.7%)
  - Pain in extremity (somatrogon: 1.5%; placebo: 6.2%)

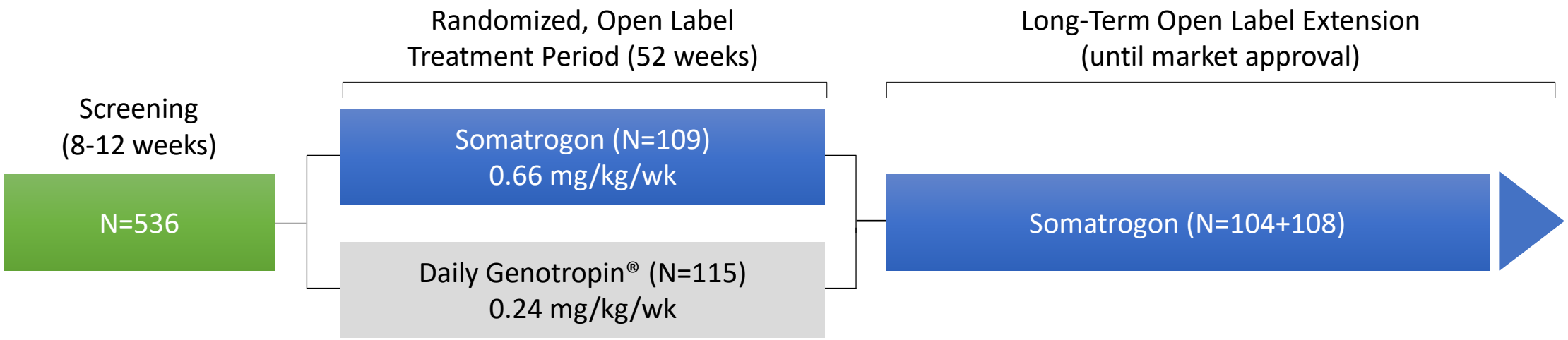
Developmental Status

- Pfizer and OPKO are evaluating the potential submission of an Adult BLA following the Pediatric BLA submission

Somatrogon Pediatric Global Phase 3 Study – 84 Clinical Sites in 21 Countries



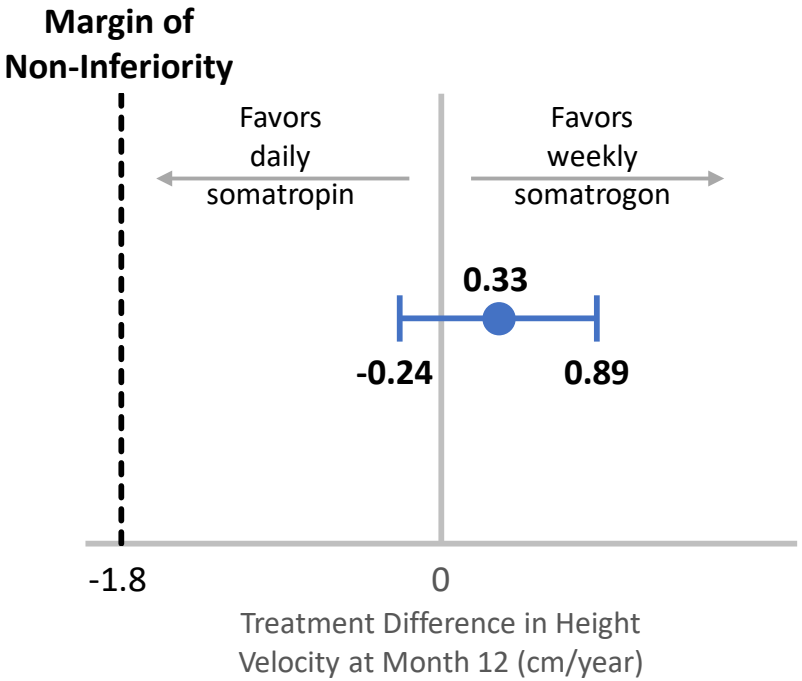
CP-4-006: Somatrogon Global Phase 3 in Pediatric GHD – Study Design

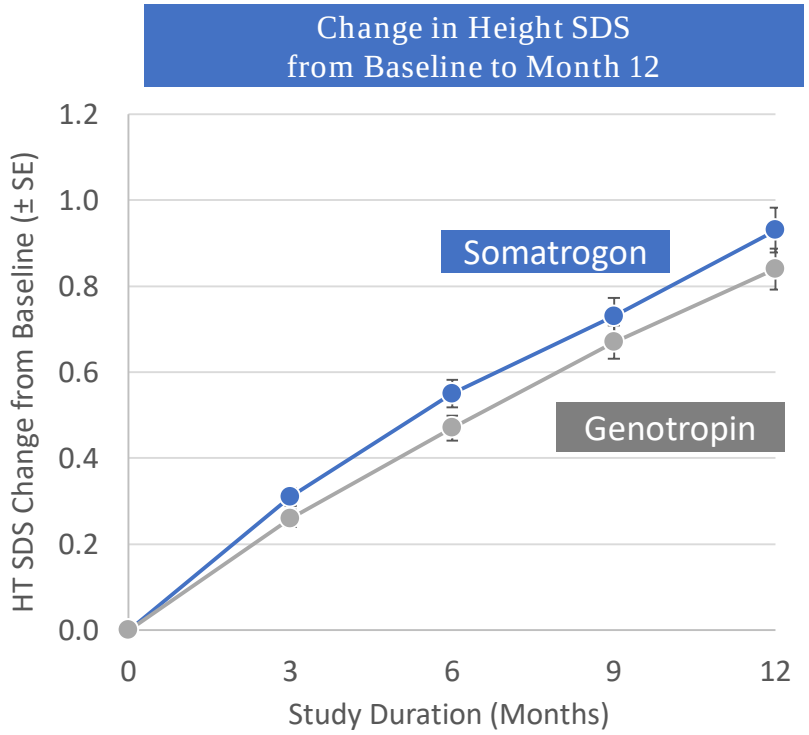


Endpoint	Measures
Primary	• Annualized height velocity (cm/year) at month 12
Secondary	• Annualized height velocity at month 6 • Change in height standard deviation score (HT SDS) at months 6 and 12 • Change in bone maturation at month 12

Primary Efficacy Endpoint – Annual Height Velocity (cm/year) at Month 12

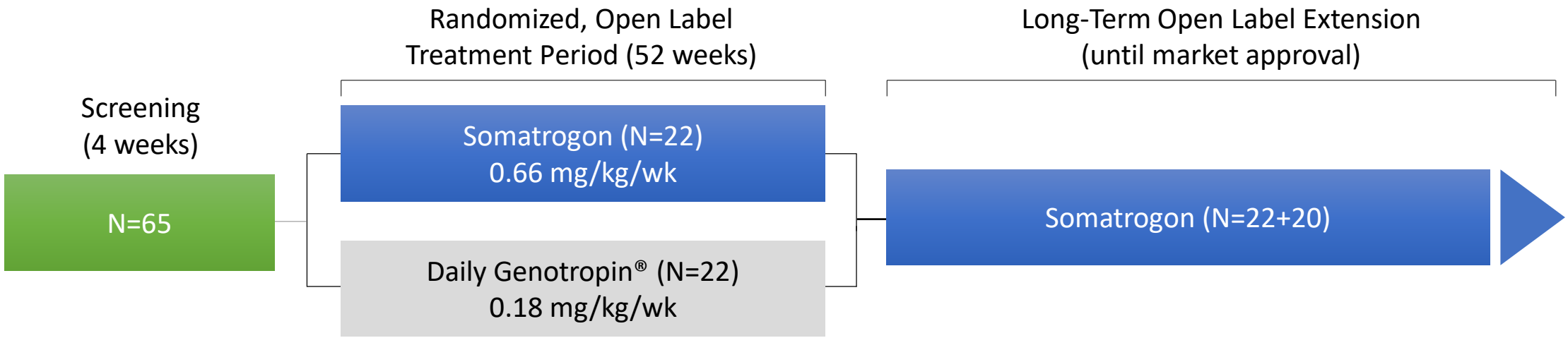
	Somatrogon (N=109)	Genotropin® (N=115)	Treatment Difference
LS Means Estimate	10.10	9.78	0.33
95% Confidence Interval			[-0.24, 0.89]





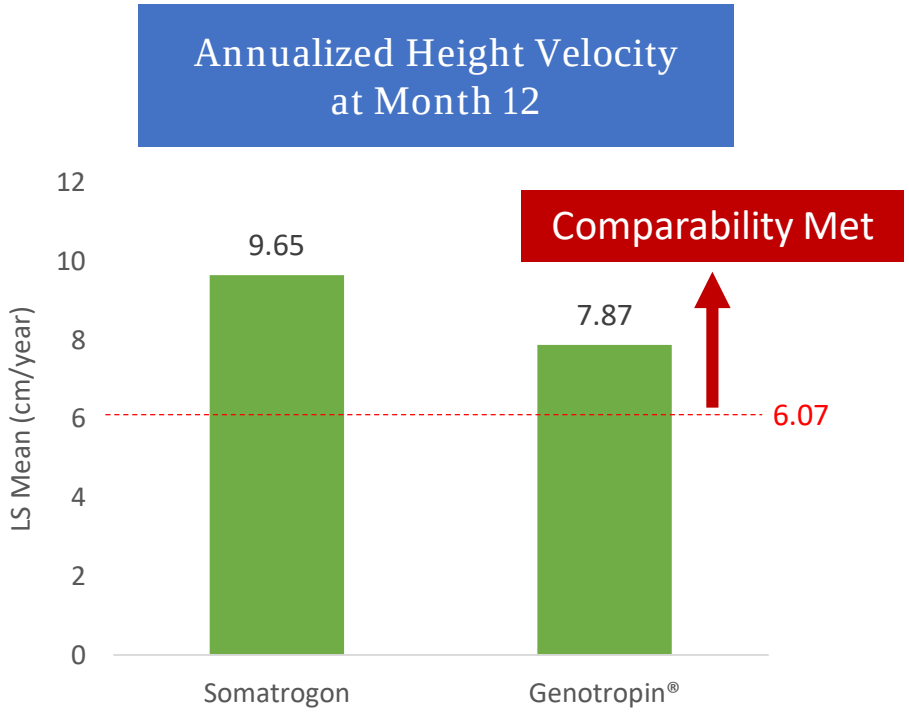
Once weekly somatrogon was non-inferior to daily GH with respect to annualized HV after 12 months of treatment in subjects with pediatric GHD

CP-4-009: Somatrogon Japanese Phase 3 in Pediatric GHD – Study Design



Endpoint	Measures
Primary	• Annualized height velocity (cm/year) at month 12
Secondary	• Annualized height velocity at month 6 • Change in height standard deviation score (HT SDS) at months 6 and 12 • Change in bone maturation at month 12 • Evaluate the PK and PD profiles

CP-4-009 Japanese Study Efficacy at Month 12



Endpoint	Statistics	Somatrogon (N=22)	Genotropin (N=22)	Treatment Difference
Height Velocity (cm/year)	LS mean [95% CI]	9.65	7.87	1.79 [0.97, 2.60]
Change in Height SDS	LS mean [95% CI]	0.94	0.52	0.42 [0.23, 0.61]

Subjects on Somatrogon achieved a height velocity treatment difference of 1.79 cm/year compared to Genotropin® at Month 12

Conclusions and Developmental Status of Somatrogon in Pediatric Indication

Efficacy

- The Phase 3 Global Pediatric Study demonstrated non-inferiority compared to Genotropin® in the primary endpoint of height velocity at 12 months
    - Secondary endpoints (height velocity at month 6, change in Ht SDS at months 6 and 12) were also met
- The estimated mean IGF-1 SDS levels were below 2 in over 95% of the subjects following somatrogon treatment for 12 months

Safety and Tolerability

- The safety and tolerability profile of somatrogon was comparable to Genotropin®

Developmental Status

- All pivotal phase 3 studies have been completed and the pediatric open label extension studies are ongoing
- BLA submission expected in the second half of 2020 in the US; Japanese, European and Canadian submissions are expected to follow

Thank You