Results of Global Phase 3 Study of Once-Weekly Somatrogon in Growth Hormone Deficient Children

Cheri L. Deal, PhD, MD, FRCPC
Chief, Pediatric Endocrinology and Diabetes, CHU Sainte-Justine
Tenured Professor of Pediatrics, Université de Montréal, Canada

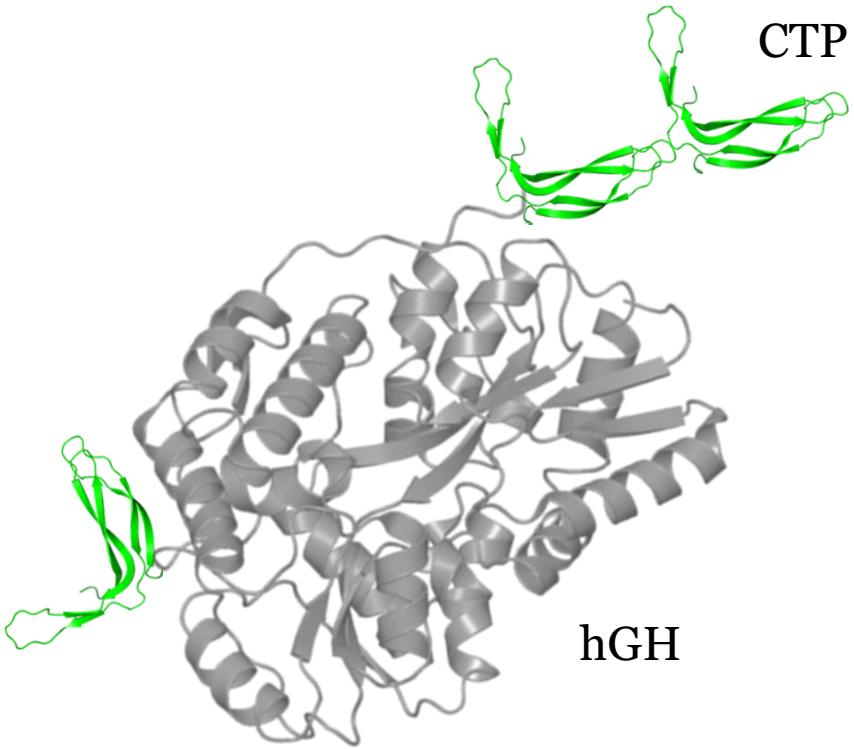
→ On behalf of the study investigators who contributed to the somatrogon trial (CP-4-006)

→ *With a particular thanks to all the participating patients and their families on behalf of their doctors and all the other patients hoping to have fewer injections!*

Disclosure

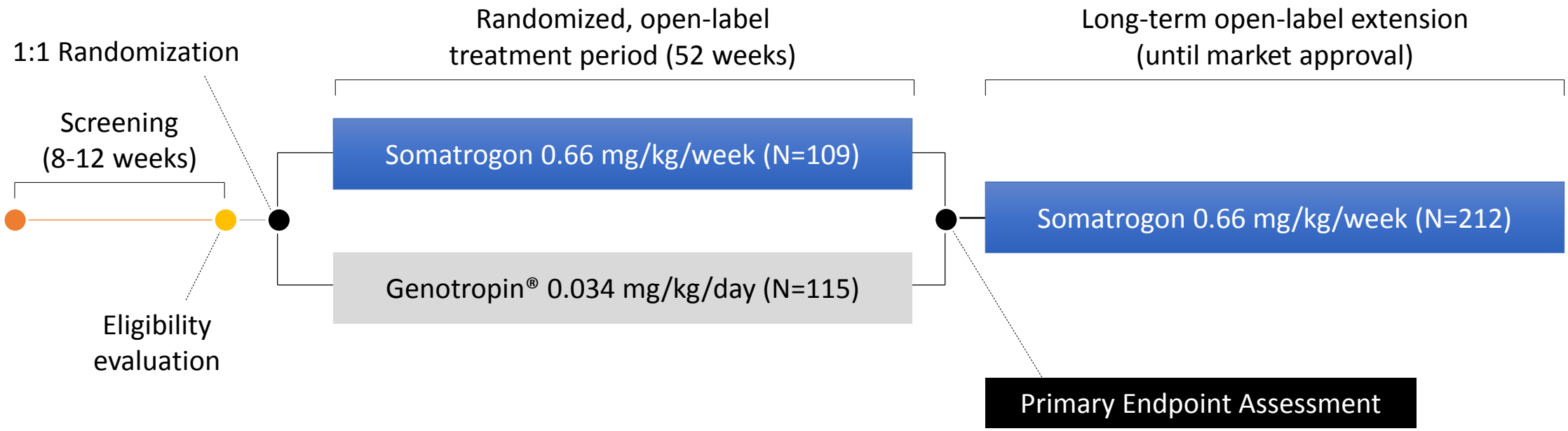
- I have received consultancy fees from Pfizer, Lilly, LUMOS, GLWL Research Inc, Neurocrine Bioscience
- I have received clinical trial support from Pfizer, Lilly, OPKO, EMD Serono, GLWL Research Inc, Levo Therapeutics, Millendo
- I have participated in speakers' bureaus for Ferring, Novo Nordisk, Pfizer, Lilly, Ascendis

Somatrogon: Long-Acting CTP-hGH Protein



- Long-acting somatrogon contains the amino acid sequence of human growth hormone (hGH) and three copies of the C-Terminal Peptide (CTP) 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
- Daily somatropin (recombinant human GH) has a well-established safety and efficacy profile in children with growth hormone deficiency (GHD)
- As such, the somatrogon phase 3 study was designed as a non-inferiority study of weekly somatrogon vs. daily somatropin in subjects with pediatric GHD

Somatrogon Phase 3 Design – Non-Inferiority to Daily GH



Somatrogon Phase 3 Design – Non-Inferiority to Daily GH

Primary Endpoint

- Annualized height velocity (HV) at month 12

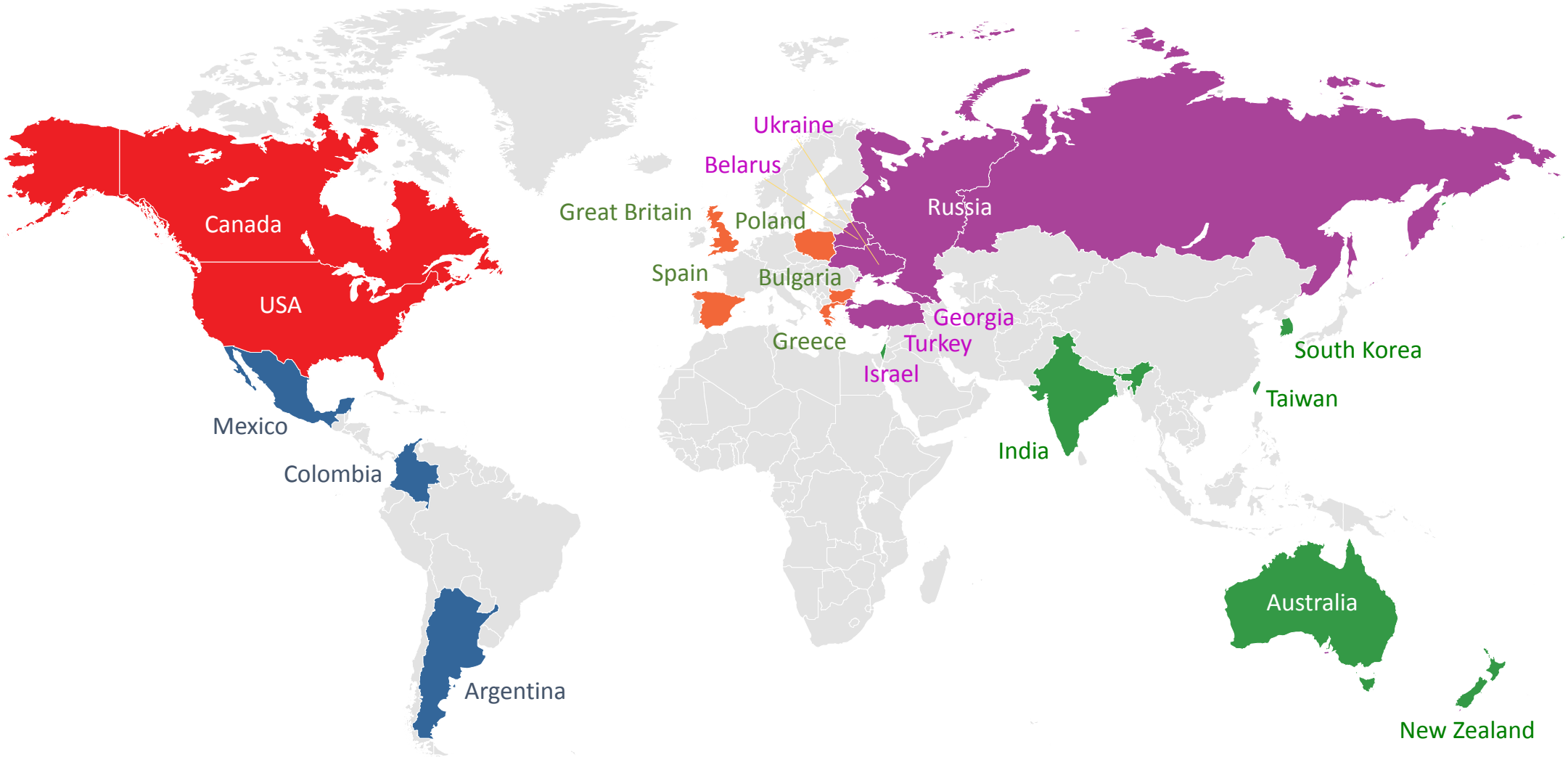
Key Secondary Endpoints

- Annualized HV at month 6
- Change in height standard deviation score (HT SDS) at months 6 and 12
- Change in bone maturation at month 12

Key Inclusion Criteria

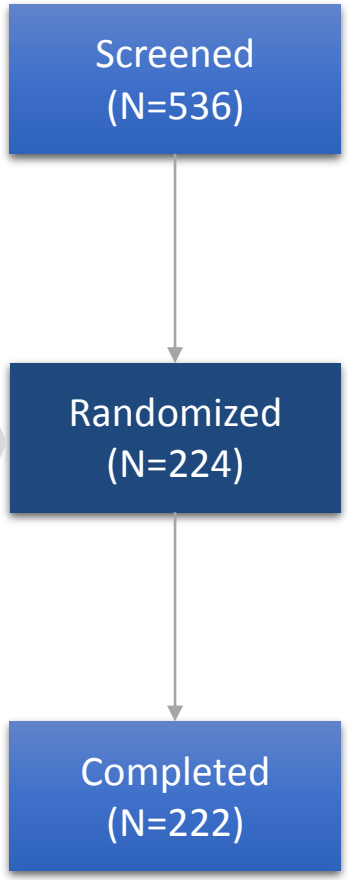
- GH-treatment naïve pre-pubertal children with GHD
- Age ≥ 3 years and < 11 (girls), < 12 (boys)
- Peak plasma GH level ≤ 10 ng/mL on two different provocative tests
- Bone age < 10 (girls), < 11 (boys)
- Normal karyotype for girls
- Annualized HV SDS < -0.7 (≤ 25th percentile for chronological age)
- IGF-1 SDS ≤ -1.0

Somatrogon Global Phase 3 Study
84 Clinical Sites in 21 Countries



Baseline Demographics and Disposition

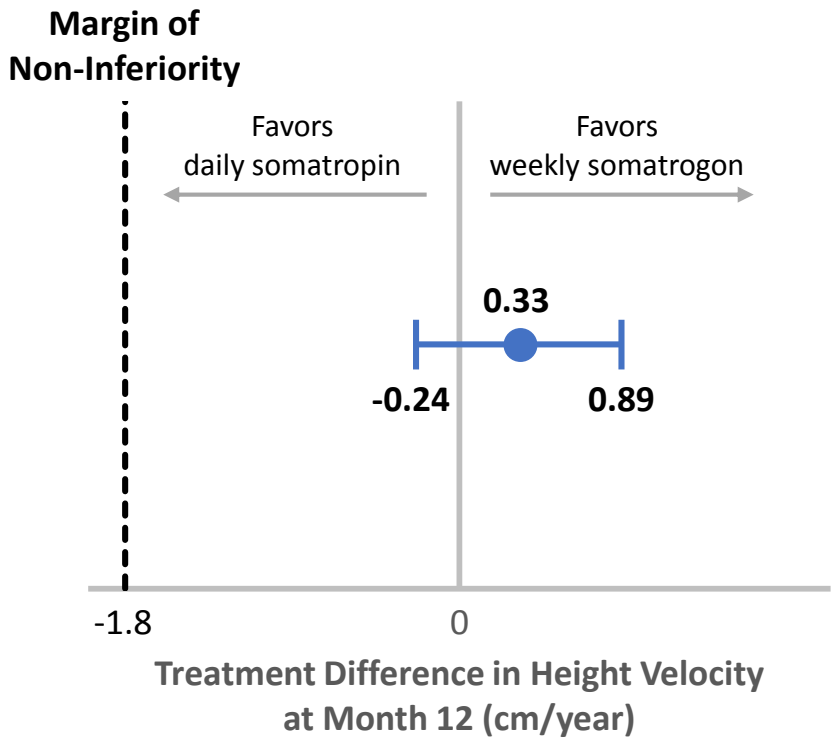
	Somatrogon (N=109)	Somatropin (N=115)
Age (years), mean (SD)	7.83 (2.66)	7.61 (2.37)
≥ 3 and ≤ 7	43 (39.4)	47 (40.9)
> 7	66 (60.6)	68 (59.1)
Male, n (%)	82 (75.2)	79 (68.7)
Race, n (%)		
White	81 (74.3)	86 (74.8)
Asian	24 (22.0)	21 (18.3)
Other	4 (3.7)	8 (6.9)
Hispanic or Latino, n (%)	11 (10.1)	13 (11.3)
Peak GH Level, n (%)		
≤ 3 ng/mL	22 (20.2)	21 (18.3)
> 3 ng/mL and ≤ 7 ng/mL	53 (48.6)	56 (48.7)
> 7 ng/mL and < 10 ng/mL	34 (31.2)	38 (33.0)
HT SDS, mean (SD)	-2.94 (1.29)	-2.78 (1.27)
IGF-1 SDS, mean (SD)	-1.95 (0.89)	-1.72 (0.90)
Other		
BMI SDS, mean (SD)	-0.28 (1.04)	-0.20 (1.01)
Gender-adjusted Target Height SDS	-0.94 (0.99)	-0.72 (1.01)



Primary Endpoint: Annual Height Velocity at Month 12

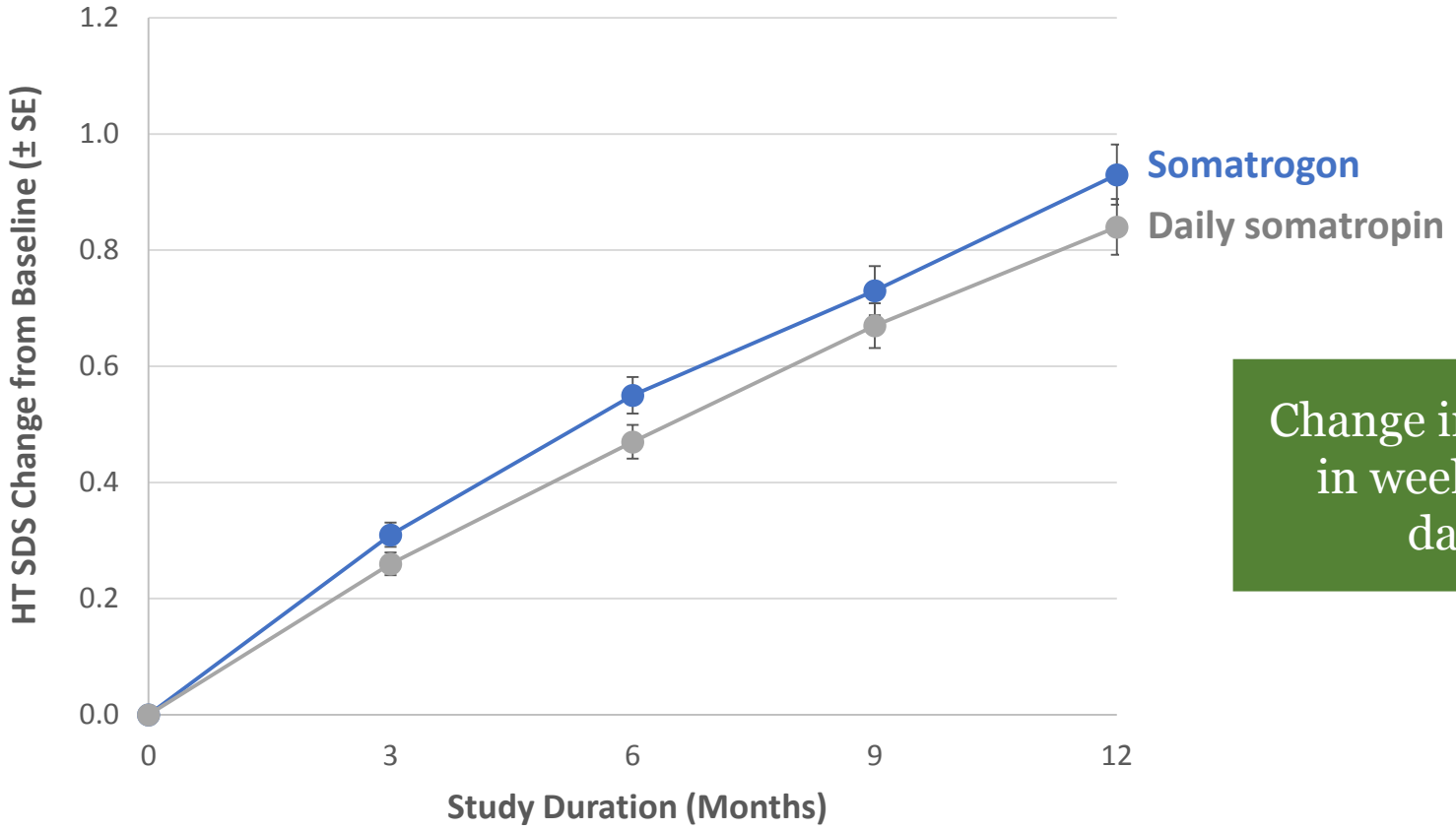
Primary Endpoint: Annualized Height Velocity (cm/year)

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



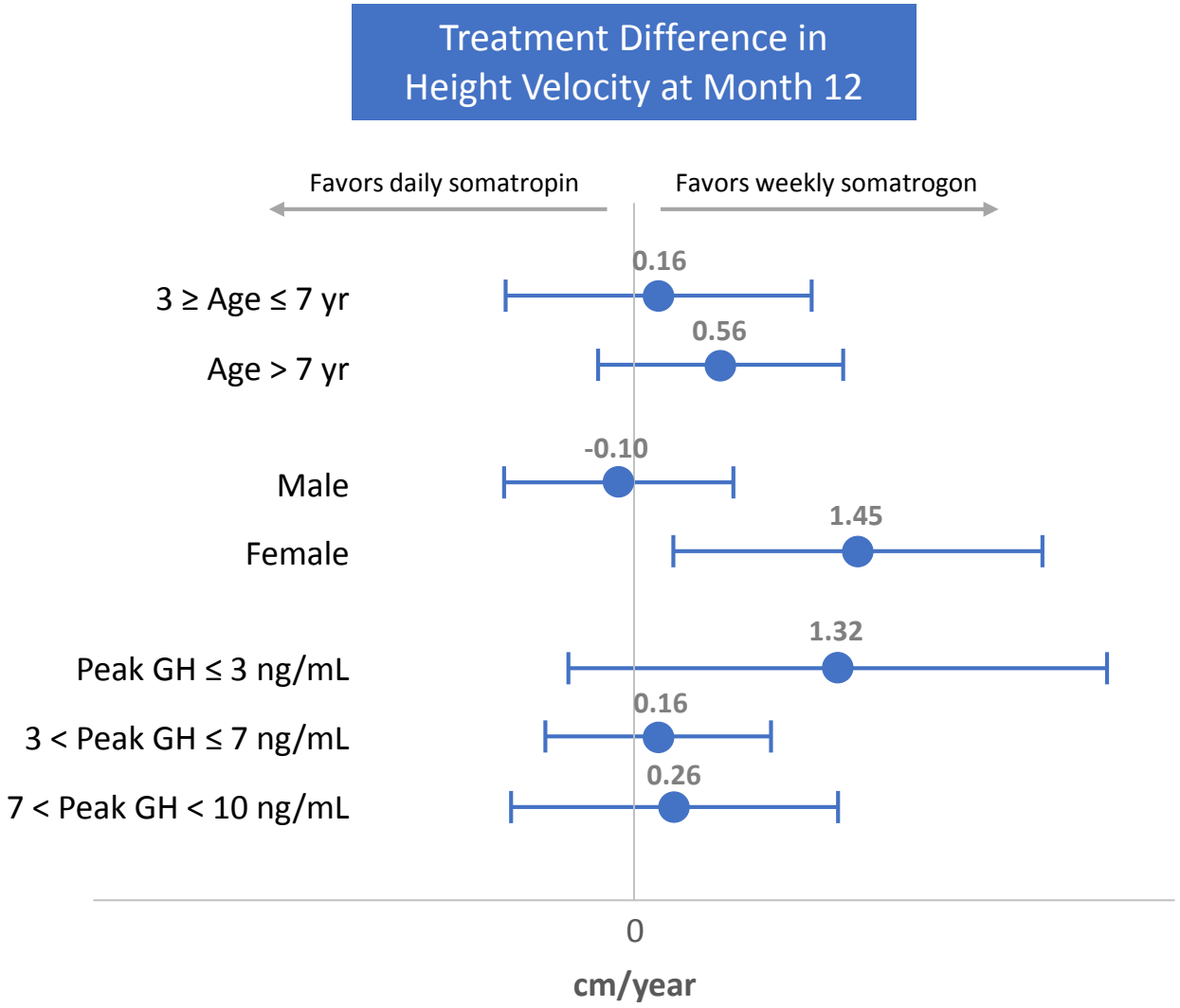
Once weekly somatrogon was non-inferior to daily GH with respect to annualized HV after 12 months of treatment in subjects with pediatric GHD

Secondary Endpoint: Change in HT SDS from Baseline at Month 12



Change in HT SDS increased over time in weekly somatrogon-treated and daily GH-treated subjects

Weekly Somatrogon is Comparable to Daily Growth Hormone



- Age, gender, and peak GH groups show similar height velocity responses to weekly somatrogon and daily GH
- Mean change in bone maturation (BA/CA) at month 12 was also comparable between somatrogon (0.05) and daily GH (0.06) groups

Summary of Treatment-Emergent Adverse Events (TEAEs)

	Somatrogon (N=109)	Somatropin (N=115)
TEAEs	95 (87.2%)	97 (84.3%)
TEAEs Related to Study Drug	59 (54.1%)	45 (39.1%)
Serious TEAEs	3[a] (2.8%)	2[b] (1.7%)
Severity Mild to Moderate Severe	 86 (78.9%) 9 (8.3%)	 91 (79.1%) 6 (5.2%)
TEAEs Leading to Study Discontinuation	1 (0.9%)	0

[a] Chronic tonsillitis, gastroenteritis, and pneumonia; [b] Tonsillitis and ureterolithiasis
Note: none of the SAEs were related to the study drug; N = number of subjects

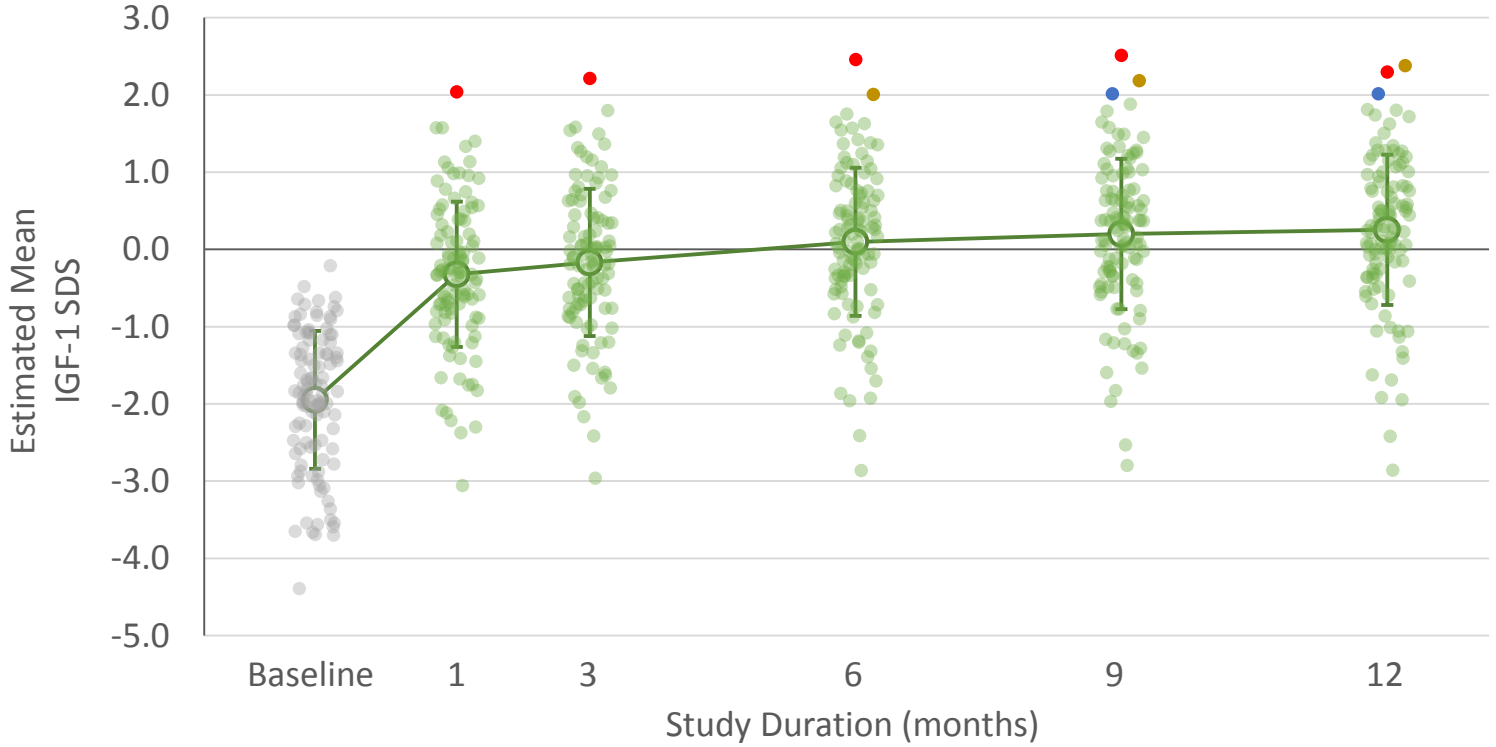
TEAEs ≥ 5% of Subjects

Preferred Term	Somatrogon (N=109)	Somatropin (N=115)
Injection site pain	43 (39.4%)	29 (25.2%)
Nasopharyngitis	25 (22.9%)	29 (25.2%)
Headache	18 (16.5%)	25 (21.7%)
Pyrexia	18 (16.5%)	16 (13.9%)
Cough	9 (8.3%)	9 (7.8%)
Injection site erythema	9 (8.3%)	0
Vomiting	8 (7.3%)	9 (7.8%)
Anaemia	7 (6.4%)	7 (6.1%)
Hypothyroidism	7 (6.4%)	3 (2.6%)
Pharyngitis	7 (6.4%)	5 (4.3%)
Arthropod bite	6 (5.5%)	1 (0.9%)
Injection site pruritus	6 (5.5%)	0
Oropharyngeal pain	6 (5.5%)	4 (3.5%)
Rhinitis	6 (5.5%)	1 (0.9%)
Arthralgia	5 (4.6%)	8 (7.0%)
Tonsillitis	5 (4.6%)	6 (5.2%)
Otitis media	4 (3.7%)	7 (6.1%)
Bronchitis	3 (2.8%)	9 (7.8%)
Abdominal pain upper	2 (1.8%)	6 (5.2%)
Blood creatine phosphokinase increased	2 (1.8%)	8 (7.0%)
Ear Pain	2 (1.8%)	7 (6.1%)

Note: N = number of subjects

IGF-1 SDS Profile Over Time in Somatrogon-Treated Patients

- IGF-1 was to be measured on day 4 (96 hrs) post dose, as this interval has been shown to provide the best estimate of the mean IGF-1 value over the dosing interval of 1 week (Fisher et al, 2017)
- Study subjects had samples drawn at variable days post-dose
- Model was developed to calculate estimated mean IGF-1 SDS values over the dosing interval (1 week), regardless of the timing of IGF-1 measurement since last dose



- 3 individual subjects had mean IGF-1 SDS ≥ 2 and none had IGF-1 SDS ≥ 3

Subject 1 Subject 2 Subject 3

Glucose Metabolism Remained Stable and Within the Normal Range

Time Point	HbA1c (%)		Fasting Glucose (mmol/L)	
	Somatrogon (N=109)	Somatropin (N=115)	Somatrogon (N=109)	Somatropin (N=115)
Baseline	5.20 (0.29)	5.21 (0.25)	4.60 (0.51)	4.58 (0.60)
Month 3	5.23 (0.30)	5.28 (0.47)	4.76 (0.44)	4.77 (0.53)
Month 6	5.34 (0.29)	5.30 (0.31)	4.80 (0.45)	4.82 (0.51)
Month 9	5.37 (0.29)	5.32 (0.30)	4.88 (0.37)	4.83 (0.44)
Month 12	5.38 (0.31)	5.34 (0.28)	4.84 (0.40)	4.71 (0.46)

Conclusions

- The study met the primary objective of non-inferiority of weekly somatrogon compared to daily GH; annualized HV at month 12 for once weekly somatrogon was 10.10 cm/year vs. 9.78 cm/year for daily GH
- Change in HT SDS and various sensitivity analyses for the primary endpoint (including sub-group analyses) were higher for the weekly somatrogon group compared to the daily GH group
- Over 95% of the patients achieved estimated mean IGF-1 SDS levels within the normal range of ±2 SDS
- Low numbers of SAEs were reported in both the weekly somatrogon and daily GH groups and the majority of AEs were mild to moderate in severity
- Weekly somatrogon administration was generally well-tolerated in patients with pediatric GHD

Take-Home Message

Treatment with once-weekly somatrogon resulted in a robust and non-inferior improvement in height velocity and height SDS while raising IGF-1 and maintaining it within the normal range

Thank you for your attention and
for your participation in ENDO 2020!