LB17

The Majority of Children With Pediatric Growth Hormone Deficiency Treated With Lonapegsomatropin for up to 6 Years Met or Exceeded Average Parental Height SDS: Final Results of enliGHten

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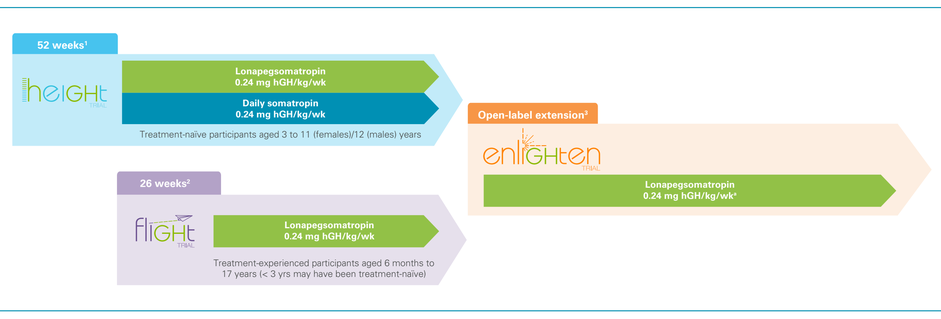
BACKGROUND

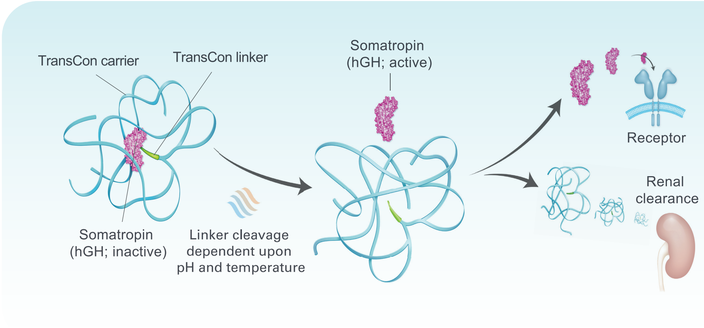
- The lonapegsomatropin (SKYTROFA®; TransCon™ hGH) phase 3 trial program evaluated dosing, efficacy and safety outcomes in pediatric growth hormone deficiency (GHD) across a range of pubertal stages **(Figure 1)**
  - Lonapegsomatropin demonstrated safety and efficacy in both treatment-naïve and treatment-experienced children in the 52-week heiGHt trial[1] and 26-week fliGHt trial,[2] respectively
- The enliGHten open-label extension trial enrolled participants from heiGHt and fliGHt for longer term investigation of safety and efficacy including children transitioning into puberty (more advanced Tanner stages)[3]
- Lonapegsomatropin (SKYTROFA®; TransCon® hGH), a prodrug of somatropin, is approved for once-weekly treatment of pediatric GHD by the FDA (pediatric patients 1 year or older and weighing at least 11.5 kg),[4] and by the EC (pediatric patients aged 3 years to 18 years)[5] **(Figure 2)**

Figure 1. Lonapegsomatropin Phase 3 Clinical Trials Overview



[a]Dose adjustments were allowed for weight change to next dosing bracket or to meet the goal of IGF-1 SDS between 0.0 and 2.0. If IGF-1 SDS was < 0.0 or > 2.0 (and clinically significant), dose could be increased or decreased to the next dose bracket, respectively, based on investigator or Medical Expert opinion.

Figure 2. Lonapegsomatropin (TransCon hGH) Design[3]



- Lonapegsomatropin is a prodrug of somatropin, administered once-weekly and designed to provide sustained release of active, unmodified somatropin[3,6]
- The unmodified, unbound somatropin released from lonapegsomatropin has the identical 191 amino-acid sequence and size (22 kDa) as endogenous growth hormone[3,6]

METHODS

OUTCOMES

- The primary objectives of enliGHten were to evaluate the long-term safety and efficacy of treatment with lonapegsomatropin
- enliGHten enrolled 298 participants from heiGHt and fliGHt
  - The full safety population includes all participants who enrolled in either heiGHt or fliGHt (n = 306)
- Results are reported through the participants' final visit (study end date: December 31, 2022), focusing on the subset (n = 81) that completed lonapegsomatropin treatment because it was determined by the investigator that treatment for pediatric GHD was no longer necessary ("treatment completers")

RESULTS

Table 1. enliGHten Baseline[a] Demographics

	Full Analysis Set (N = 298)	Treatment Completers (n = 81)
Age, years		
Mean (SD)	10.3 (3.4)	13.3 (1.8)
Min, max	1.7, 17.8	8.8, 17.4
Sex, male, n (%)	235 (78.9)	66 (81.5)
Height SDS, mean (SD)	-1.6 (0.9)	-1.6 (0.7)
Δ Average parental height SDS, mean (SD)[b]	-1.8 (1.2)	-1.2 (0.9)
IGF-1 SDS, mean (SD)	1.0 (1.3)	0.8 (1.5)
Tanner Stage, n (%)		
Stage I	214 (71.8)	22 (30.1)
Stage II	40 (13.4)	17 (23.3)
Stage III	25 (8.4)	28 (38.4)
Stage IV	16 (5.4)	6 (8.2)
Stage V	3 (1.0)	0

The trial of origin for treatment completers were:

- heiGHt (lonapegsomatropin arm), n = 8
- heiGHt (daily somatropin arm), n = 10
- fliGHt (lonapegsomatropin), n = 63

[a]Baseline indicates last non-missing measurement before first dose of lonapegsomatropin.
[b]Δ average parental height SDS is the difference between the patient's height SDS and the average parental height SDS where average parental height SDS = (height SDS^{mother} + height SDS^{father})/2.

Figure 3. Height SDS by Visit for Treatment Completers

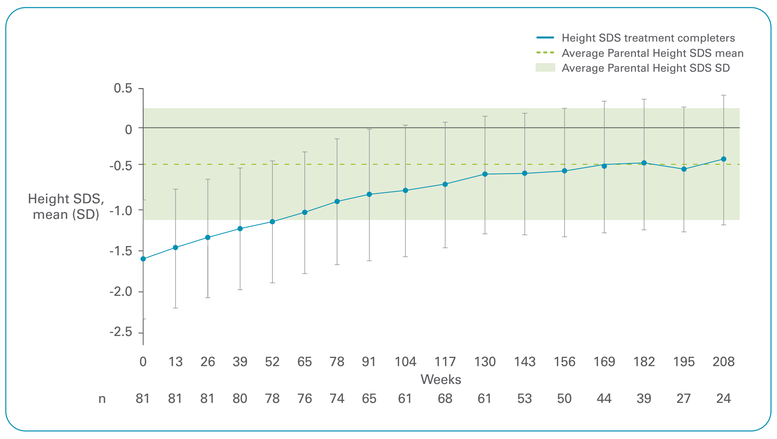
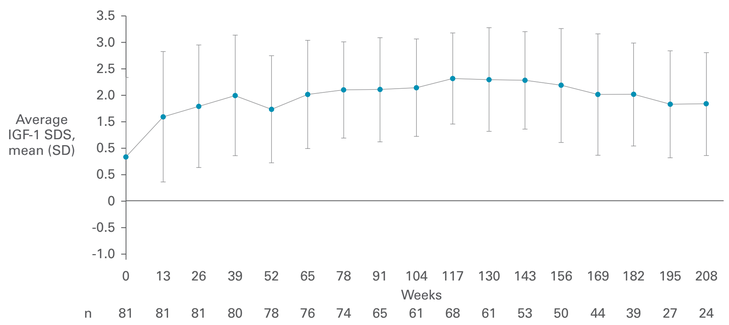


Figure 4. Average IGF-1 SDS by Visit for Treatment Completers



- IGF-1 SDS remained stable over time in a population that included older participants in more advanced Tanner stages

Table 2. Key Data at Last Visit

Growth Outcomes for Treatment Completers at Last Visit	Treatment Completers (n = 81)
Height SDS, mean (SD)	-0.4 (0.7)
Δ Average parental height SDS, mean (SD)[a]	-0.1 (0.7)
% met or exceeded average parental height	59.3

Additional Data for Treatment Completers at Last Visit	Treatment Completers (n = 81)
Age, years, mean (SD)	16.5 (1.4)
Min, max	13.0, 18.6
Female (n = 15), mean (SD)	14.5 (1.0)
Male (n = 66), mean (SD)	16.8 (1.0)
Bone age, years, mean (SD)	15.7 (1.3)
Min, max	13.0, 17.0
Female (n = 15), mean (SD)	14.2 (0.8)
Male (n = 66), mean (SD)	16.0 (1.1)
Duration of lonapegsomatropin Treatment, mean (SD)	3.2 (1.1)
Min, max	0.5, 5.3
Average IGF-1 SDS, mean (SD)	1.8 (1.1)
Tanner Stage, n (%)	
Stage I	0
Stage II	0
Stage III	0
Stage IV	23 (28.4)
Stage V	58 (71.6)

[a]Δ average parental height SDS is the difference between the patient's height SDS and the average parental height SDS where average parental height SDS = (height SDS^{mother} + height SDS^{father})/2.

- The majority of treatment completers (59.3%) had met or exceeded average parental height at last visit and all were in Tanner stage IV or V

Figure 5. TEAEs for Treatment Completers

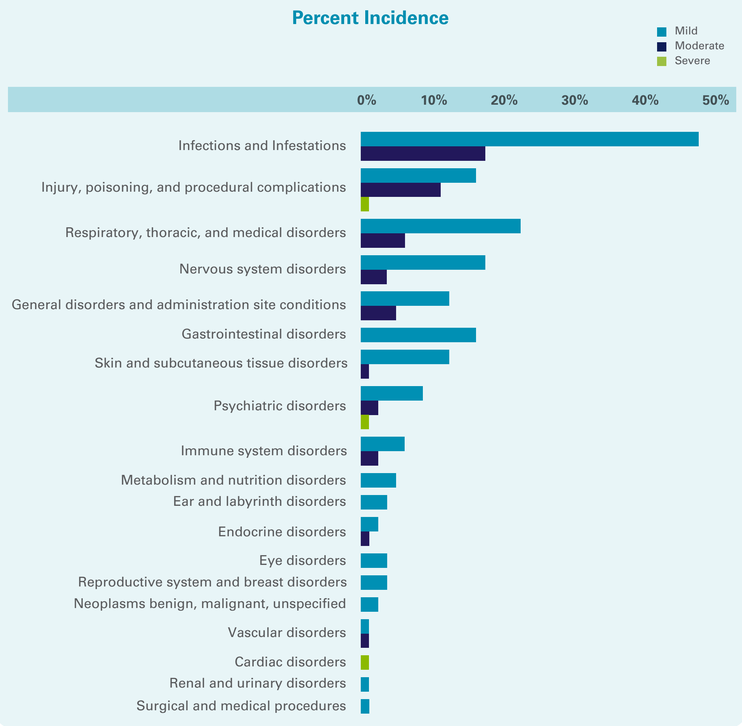


Table 3. Adverse Event Summary in Treatment Completers

	n = 81
Treatment emergent adverse events (TEAE)	67 (82.7)
Related TEAE	7 (8.6)
Serious TEAEs	2 (2.5)
Serious Related TEAEs	0
Severe TEAEs	3 (3.7)
Severe Related TEAEs	0
TEAEs leading to discontinuation of study drug	0

- There were no TEAEs that led to discontinuation of study drug in treatment completers (n = 81) or in the full safety population (n = 306)

Table 4. Overview of Outcomes for Full enliGHten Population at Final Visit

	n = 298
Lonapegsomatropin treatment duration, years, mean (SD)	4.1 (1.1)
Min, max	0.5, 6.0
Duration 4 - < 5 years, n (%)	140 (47.0)
Duration 5 - < 6 years, n (%)	52 (17.5)
% met or exceeded average parental height	53.4
Tanner Stage, n (%)	
Stage I	89 (29.9)
Stage II	32 (10.7)
Stage III	28 (9.4)
Stage IV	63 (21.1)
Stage V	86 (28.9)

CONCLUSIONS

- Long-term safety was demonstrated in participants treated with lonapegsomatropin for pediatric GHD for up to 6 years
- The majority of all participants (n = 298), including those who by study end date had completed treatment with lonapegsomatropin (n = 81), met or exceeded average parental height SDS without a mean dose increase over time

ABBREVIATIONS

GHD = growth hormone deficiency; **hGH** = human growth hormone; **SD** = standard deviation; **SDS** = standard deviation score; **TEAE** = treatment-emergent adverse event

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1. Thornton PS, Maniatis AK, Aghajanova E, et al. Weekly Lonapegsomatropin in Treatment-Naive Children With Growth Hormone Deficiency: The Phase 3 heiGHt Trial. *J Clin Endocrinol Metab.* 2021;106(11):3184-3195. **2.** Maniatis AK, Nadgir U, Saenger P, et al. Switching to Weekly Lonapegsomatropin from Daily Somatropin in Children with Growth Hormone Deficiency: The fliGHt Trial. *Horm Res Paediatr.* 2022;95(3):233-243. **3.** Maniatis AK, Casella SJ, Nadgir UM, et al. Safety and Efficacy of Lonapegsomatropin in Children With Growth Hormone Deficiency: enliGHten Trial 2-Year Results. *J Clin Endocrinol Metab.* 2022;107(7):e2680-e2689. **4.** SKYTROFA. US Prescribing Information (USPI). Ascendis Pharma; 2022. Accessed March 29, 2023. https://ascendispharma.us/products/pi/skytrofa/skytrofa_pi.pdf. **5.** SKYTROFA. SmPC. EPAR product information. EMA. https://www.ema.europa.eu/en/medicines/human/EPAR/skytrofa-previously-lonapegsomatropin-ascendis-pharma. Accessed March 29, 2023. **6.** Sprogoe K, Mortensen E, Karpf DB, Leff JA. The rationale and design of TransCon Growth Hormone for the treatment of growth hormone deficiency. *Endocr Connect.* 2017;6(8):R171-R181.

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