The Pivotal Phase 3 heiGHt Trial of Weekly TransCon™ hGH vs. Daily hGH in Treatment-Naïve Subjects with Pediatric Growth Hormone Deficiency

**BACKGROUND**

TransCon™ hGH is a long-acting prodrug designed for patients with growth hormone deficiency (GHD). TransCon™ hGH consists of a parent drug, hGH, that is transiently bound to a carrier via a proprietary linker. The carrier extends hGH circulation time in the body allowing elimination from the body. The carrier and linker are cleared primarily by renal filtration and to a minor extent by hepatobiliary excretion.

TransCon™ hGH is a long-acting prodrug consisting of parent drug, unmodified hGH, transiently bound to a carrier, mPEG (40 kDa), via a proprietary TransCon™ linker (Figure 1). Over one week, TransCon™ hGH releases fully unmodified hGH and mimic daily hGH: allowing elimination from the body. The carrier extends hGH circulation time in the body allowing elimination from the body. The carrier and linker are cleared primarily by renal filtration and to a minor extent by hepatobiliary excretion.

**OBJECTIVES**

- To compare the efficacy and safety of TransCon™ hGH 0.24 mg/kg/week compared to Genotropin® 0.034 mg/kg/day (ie, 0.24 mg/kg/week) for 52 weeks
- Males and females (aged 3-11 years, respectively) in Tanner stage 1 diagnosed with isolated GHD (or as part of multiple pituitary defects) and growth velocity ≤ 2.0 SDS
- Bone Age (BA)(years) 8.51
- Chronological Age (CA)(years) 8.51
- Treatment naïve and naïve to hGH treatment
- Height was a global, pivotal, phase 3 randomized, open-label, study to evaluate the non-inferiority and superiority of TransCon™ hGH vs. daily Genotropin® height SDS at Weeks 1, 13, 26, 39, and 52

**METHODS**

- Key secondary objectives included:
  - Change in IGF-1 SDS and IGFBP-3 SDS
  - ADverse Event Reporting
  - Bone age at baseline and follow-up visits
  - Laboratory assessments at baseline and follow-up visits
  - Safety data collected for 52 weeks

**RESULTS**

Table 3: Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TransCon™ hGH (n=56)</th>
<th>Genotropin® (n=56)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>8.51 (2.5)</td>
<td>8.51 (2.5)</td>
<td>0.99</td>
</tr>
<tr>
<td>Sex</td>
<td>56</td>
<td>56</td>
<td>0.88</td>
</tr>
<tr>
<td>Male</td>
<td>28</td>
<td>28</td>
<td>0.88</td>
</tr>
<tr>
<td>Female</td>
<td>28</td>
<td>28</td>
<td>0.88</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>111.4 (18.0)</td>
<td>112.0 (18.0)</td>
<td>0.48</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>16.06 (2.4)</td>
<td>15.89 (2.4)</td>
<td>0.34</td>
</tr>
<tr>
<td>IGF-1 SDS (SDS)</td>
<td>-2.04 (1.2)</td>
<td>-2.01 (1.2)</td>
<td>0.71</td>
</tr>
<tr>
<td>IGFBP-3 SDS (SDS)</td>
<td>-0.25 (1.2)</td>
<td>-0.25 (1.2)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

At Week 52, the AHV for TransCon™ hGH was 11.2 cm while that for Genotropin® was 10.3 cm. The treatment difference was 0.86 cm in favor of TransCon™ hGH. Indirect comparison of TransCon™ hGH vs. daily Genotropin® showed a similar trend as AHV, with the difference in LS Mean Change from Baseline for equivalent doses of TransCon™ hGH and Daily Genotropin®: 1.2 cm in favor of TransCon™ hGH (p=0.0088). Further, baseline IGF-1 SDS values were similar and within the normal range for both arms.

**IMPLICATIONS**

- Availability of a safe and well-tolerated long-acting hGH therapy has been long awaited and elusive
- The standard of care for pediatric GHD for over the past 30 years has been intermittent hGH administered daily. Weekly hGH has both an excellent safety profile and satisfactory efficacy, the frequency of its administration causes a significant burden on daily life for both children with GHD and their caregivers
- The heiGHt Trial results represent another step closer to development of a safe, well-tolerated, and effective long-acting treatment for pediatric GHD