### RESULTS

• Three doses of weekly TransCon hGH1 compared to daily Genotropin, for Growth Hormone Deficiency (GHD) Treated with Lonapegsomatropin

### METHODS

• Objective: predict an average weekly IGF-1 at steady state from a single IGF-1 sample任何时候 during a 7-day dosing week

### BACKGROUND

• Once-weekly prodrug release unfolds IGF-1 designed to mimic daily hGH

• Tissue Distribution

• Pharmacokinetics levels

• Therapeutic efficacy, efficacy, and tolerability

### Figure 1. TransCon hGH (lonapegsomatropin) Design

### Figure 2. Dense Proportional IGF-1 Response in a Phase 2 Study

### Figure 3. IGF-1 Profile at Week 13 (n=11)

### Figure 4. Comparing ∆(d) of IGF-1 SDS From The Mixed Model With Taylor Series, And From Boxplots of Simulation From The Population PD Model at Week 52

### Figure 5. Average IGF-1 SDS From an IGF-1 Sample at Steady State: Results From a Linear Mixed Model With Taylor Series

### Figure 6. Average IGF-1 Concentration From an IGF-1 Sample at Steady State: Results From a Linear Mixed Model With Taylor Series

### Conclusions

• A simple linear mixed model was established to predict weekly average IGF-1 for children with GHD on lonapegsomatropin based on a single sample at steady state using either IGF-1 SDS or concentration data

• This prediction has good accuracy from a single sample anytime during the dosing interval, with lowest estimation errors between days 2.5 and 5

• A mathematical nonlinear model was developing using IGF-1 data from the phase 2 trial and the heiGHt trial to predict full IGF-1 profiles and support calculation of average weekly IGF-1 concentration for single pediatric subjects from the heiGHt trial

• An innovative step function model with simultaneous zeros and first order of stimulation of IGF-1 production, first order clearance, and proportional error was selected as the final model

### Key Inclusion Criteria

• Prepubertal children with GHD

• Height SDS ≤-2.0

• IGF-1 SDS ≤-1.0

• A 2 GH stimulation tests (GH ≤10 ng/mL)

• Bone age ≥6 months behind chronological

• IGF-1 SDS ≤-1.0

• 2 GH stimulation tests (GH ≤10 ng/mL)

• Separate linear regressions were utilized to bridge baseline (pre-dose) IGF-1 data before and after steady state

### Statistical Analysis to Predict Average IGF-1 From a Single Sample of IGF-1

• A non-compartmental analysis (NCA) on the simulated profiles from the heiGHt trial

• An endogenous 1-compartment model with simultaneous

• Late IGF-1 profiles and support calculation of average weekly IGF-1

• Standard covariates were tested, e.g. age, weight, height, and sex. No significant covariates were identified as model parameters

• A non-parametric bootstrap approach was employed to verify that the final model adequately predicted both the central tendency and variability of the observed data

• A non-parametric bootstrap approach was employed to verify that the final model accurately predicted and with the observed data

### Population Nonlinear Mixed-effect PD Model for IGF-1

• For an IGF-1 sample drawn 2.5 days post-dose, divide the sample concentration by 0.68

• For an IGF-1 sample drawn 5 days post-dose, add the measured value by 0.03

### Conclusions

• For an IGF-1 sample drawn 2.5 days post-dose, divide the sample concentration by the ratio of 0.68

• For an IGF-1 sample drawn 5 days post-dose, divide the sample concentration by the ratio of 0.68

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