

# OraGrowthH212

TRIAL

## Observed Serum IGF-1 Concentration Increase Within Normal Range After Prolonged Daily Oral LUM-201 Administration in Idiopathic Pediatric Growth Hormone Deficiency (iPGHD) from the OraGrowthH212 Trial: Interim Analysis Data

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### LUM-201 (ibutamoren)

- **Oral Secretagogue:** Agonist of the growth hormone (GH) Secretagogue Receptor 1a (GHR1a)
- **Mechanism of Action:** Figure 1: LUM-201 acts on the GHR1a which is expressed in the hypothalamus and anterior pituitary. LUM-201 enhances the amplitude of pulsatile releases of GH over 24 hours, while simultaneously acting as a functional antagonist at the somatostatin receptor. In turn, these effects increase the levels of IGF-1, which together with GH, reach the open growth plates and stimulate growth.

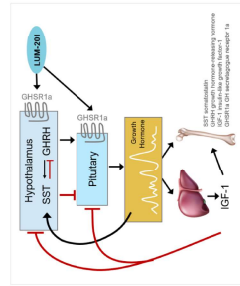
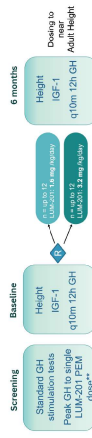


Figure 1: Mechanism of Action of LUM-201, an orally administered GHR1a agonist

### LUM-201 (ibutamoren) in OraGrowthH212 Trial

Pulsatility and PK/PD Clinical Study Design of LUM-201 in Naive iPGHD patients



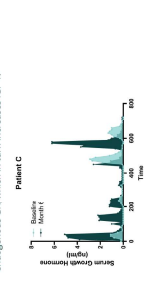
#### Baseline Demographics Table

Subjects (15)	1.6mg/kg (N=8)	3.2mg/kg (N=7)
Age (mes)	95.5 (10.5)	82.7 (22.7)
Height (cm)	115.2 (6.5)	113.1 (9.9)
Height SDS	-2.29 (0.30)	-2.31 (0.30)
IGF-1 SDS	-0.90 (0.69)	-0.46 (0.46)
MPH (cm)	105.24 (7.58)	105.5 (6.5)
MPH SDS	-1.36 (0.62)	-1.7 (0.46)
BA Delay (yrs)	1.50 (0.26)	1.83 (0.88)
BMI SDS	-0.74 (0.91)	-0.77 (1.09)
Male/Female (%)	0/97	7/29

- Study Objective:** To evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) of oral LUM-201 (ibutamoren) in children with idiopathic pediatric growth hormone deficiency (iPGHD)
- Study Information:**
- Open-label study; N = 22
  - iPGHD patients that are GH-treatment naive
  - \*Inclusion Criteria: Height < 2 SD, delayed bone age; serum IGF-1 below the mean for age, and peak GH response to a condense stimulation test
  - \*Exclusion Criteria: Height > 2 SD, previous GH treatment, or any other condition that may affect growth
  - \*Dosing to near adult height
  - \*Single, specialized clinical site
  - University of Chile, Santiago
- Primary Endpoints:**
- Assess LUM-201 effect on endogenous GH pulsatility and Annualized Height Velocity (AHV)
  - Evaluate PK/PD in children
- Goals:**
- Confirm prior PK/PD data in adults & subset of Merck 020 trial
  - Support future regulatory filings & commercialization
- Baseline Demographics:**
- Differences between the two groups:
    - Slight imbalance in age and gender
    - Slightly higher BMI in the 1.6mg/kg iPGHD SDS, BMI-SDS, and bone age delay

### Interim Analysis: IGF-1 Values, 6-12 month AHV, Pulsatility and Safety Data

**Pulsatility Data**  
The below pulsatility graphs and GH-1 and GH AUC tables, show the increase in GH pulsatility and GH release of endogenous GH which in turn increases IGF-1.



IGF-1 (ng/ml)	IGF-1 SDS (ng/ml)	% change 6 months IGF-1 SDS baseline**
109.7	1.6	69%
272.8	3.2	185%

IGF-1 (ng/ml)	IGF-1 SDS (ng/ml)	% change 6 months IGF-1 SDS baseline**
133.7	1.6	113%
343.8	3.2	185%

### Conclusions

LUM-201, at doses of 1.6 mg/kg/day and 3.2 mg/kg/day, increases the natural pulsatile release of GH in children with iPGHD. These increases in GH AUC in turn stimulate an increase in IGF-1 and IGF-1 SDS, which increases growth in children with iPGHD; all subjects demonstrate an increase in AHV.

Both of the doses of LUM-201 showed acceptable safety and tolerability.

The preliminary optimal dose, based on the controlled dose range finding study, OraGrowthH210 Trial, is 1.6 mg/kg/day, as it produced increases in AHV that were comparable to the higher dose of 3.2 mg/kg/day.

Given the modest imbalance in baseline demographics, including baseline AHV, between the two dose groups in the OraGrowthH212 Trial interim analysis, the 6, 9, and 12-month AHV values appear to be comparable in the trial.

Due to the nature of negative feedback mechanisms, even doubling the dose of LUM-201 may not result in lower baseline AHV than to be comparable in the trial.

The increase in AHV over 6 months in the OraGrowthH212 Trial appears to be primarily related to lower baseline AHV than to dose.

Pending the final analysis in Q4R-2023, the optimal dose currently appears to be 1.6 mg/kg/day.

**References:**  
1. Journal of Clinical Endocrinology and Metabolism  
2. Journal of Clinical Endocrinology and Metabolism  
3. Current Pediatric Endocrinology



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