LUM-201 Restores Growth Hormone Secretion and Promotes Growth in Moderate Pediatric Growth Hormone Deficiency (PGHD): Phase 2 Topline Results from OraGrowtH210 and OraGrowtH212 Trials

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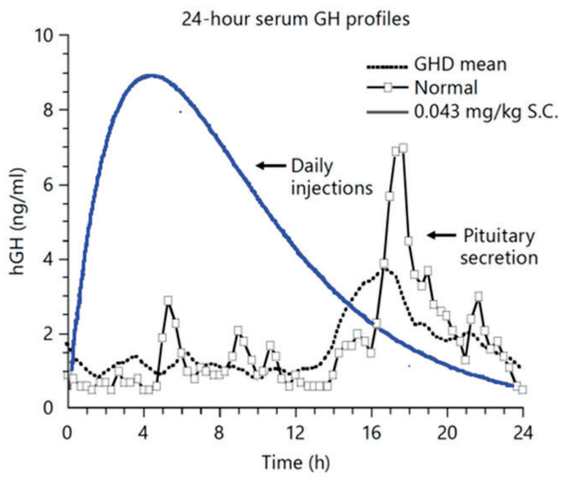
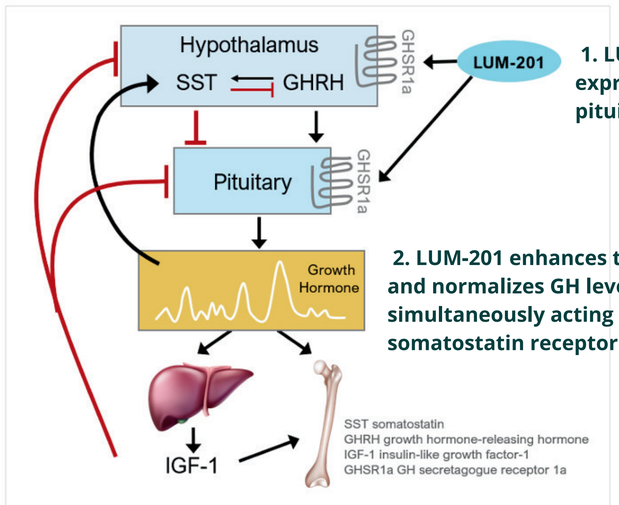
GH Profiles in a Normal and a GHD subject compared to exogenous GH injection over 24 hours



Advanced Therapies http://www.drugs.com/pro/nutropin.html Holl RW, et al. J Clin Endocrinol Metab, 77:216, 1993. Pediatric Endocrinology and Diabetology. Endocr Dev. Basel, Karger, 2016

What is LUM-201 (ibutamoren)

Oral Secretagogue: Agonist of the growth hormone (GH) Secretagogue Receptor 1a (GHSR1a)



1. LUM-201 acts on the GHSR1a which is expressed in the hypothalamus and anterior pituitary (ref 1).

2. LUM-201 enhances the amplitude of pulsatile releases of GH and normalizes GH levels after 12 months of therapy, while simultaneously acting as a functional antagonist at the somatostatin receptor (ref 2,3,4)

3. In turn, these effects increase the levels of IGF-1, which together with GH, reach the open growth plates and stimulate growth.

LUM-201 for Moderate GHD Children

Functional but reduced HP-GH axis necessary

Oral LUM-201 potentially helps stimulate a GHD child's own hypothalamic/pituitary gland to increase their own endogenous GH secretion.

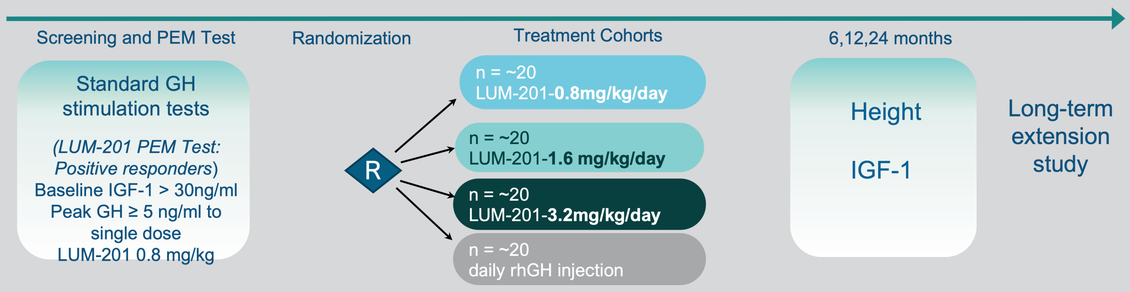
LUM-201 Predictive Enrichment Marker Strategy:

- Uses two common laboratory tests to help predict if a child is more likely to respond to oral investigational LUM-201 therapy (PEM positive/PEM+) or less likely (PEM negative/PEM-).
- The two tests are a pre-dose blood sample to evaluate baseline IGF-1 levels and post-dose blood sample to evaluate the GH response to a single oral dose of LUM-201 (0.8 mg/kg).

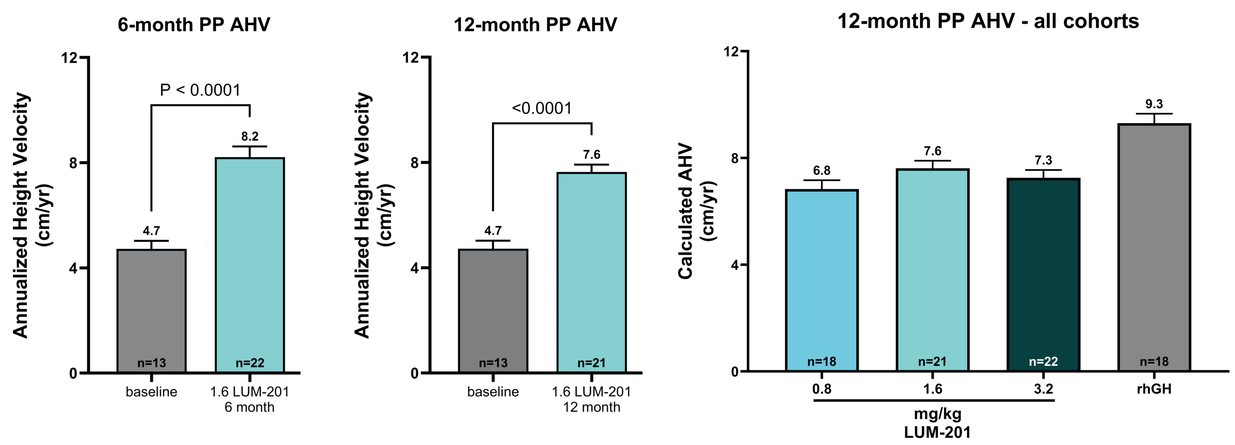
LUM-201 PEM positive (PEM +)
Baseline IGF-1 > 30 ng/ml
Stimulation LUM-201 peak GH ≥ 5 ng/ml

OraGrowtH210 TRIAL

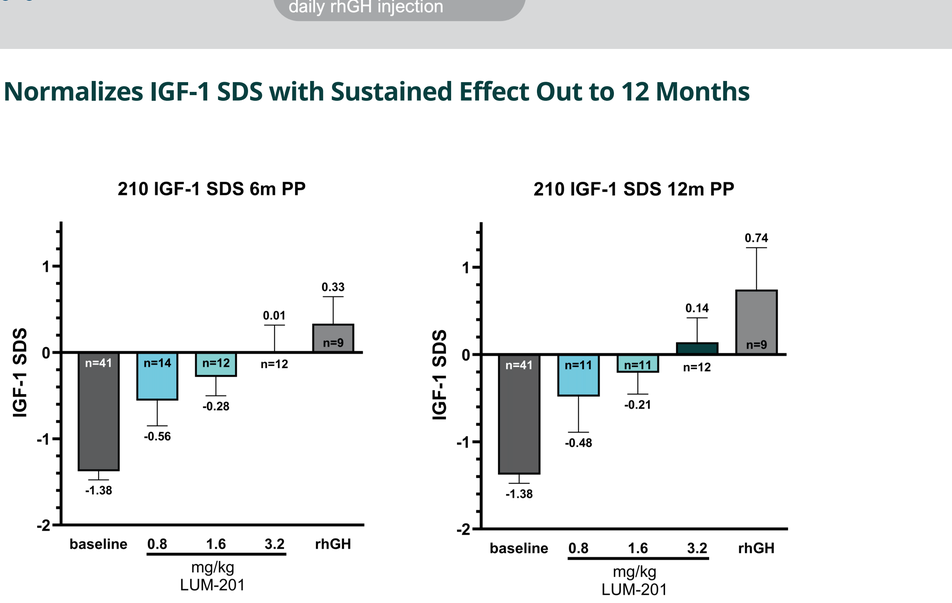
International dose finding study- 4 cohorts, N=82
Objectives: Confirm PEM strategy, Assess Height velocity
(Not powered for non-inferiority)



OraGrowtH210 12 Month Data Confirms Optimal LUM-201 Dose of 1.6 mg/kg/day

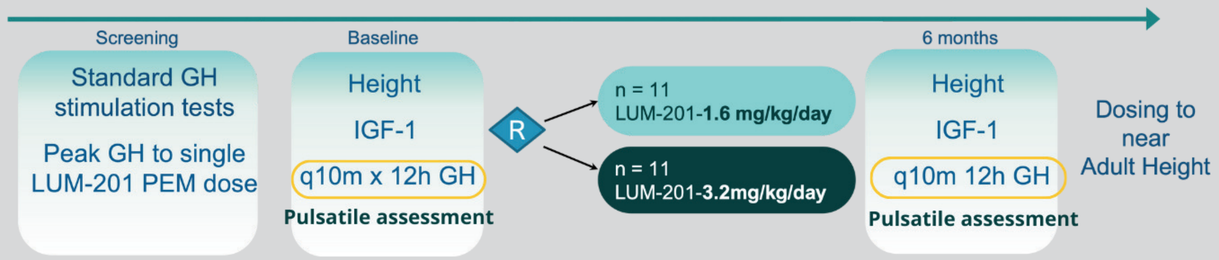


Normalizes IGF-1 SDS with Sustained Effect Out to 12 Months

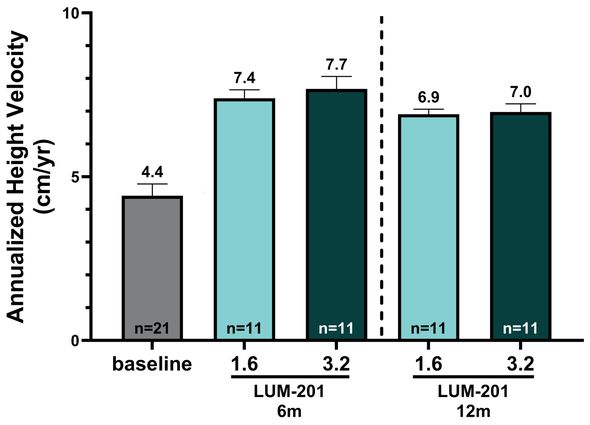


OraGrowtH212 TRIAL

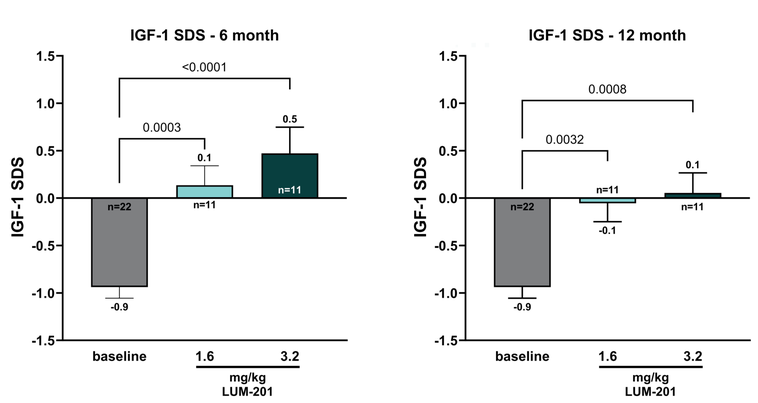
PK/PD study conducted at Univ of Santiago, Open label LUM-201 1.6 & 3.2mg/kg daily, N=22,
Objectives: Assess LUM-201 effect on endogenous GH pulsatility,Assess Height Velocity, Evaluate PK/PD



OraGrowtH212 12 Month AHV Data Demonstrate Meaningful Growth



Normalizes IGF-1 SDS with Durable Effect Out to 12 Months



LUM-201 Normalizes GH Concentrations in Moderate PGHD

Increasing 24-hour pulsatile secretion, LUM-201 achieves comparable growth to exogenous injectable rhGH, with only 20% of GH concentration levels

	Normal Healthy (IC-GH‡)	Untreated GHD (IC-GH‡)	LUM-201 (baseline GH)*	LUM-201 (treat 6M GH)*	Comparator arm rhGH 34µg/kg/day
	Zadik†		N=22		Albertsson-Wiklandtt
12h (day) µg/kg.12h	3.3 ± 1.3	1.1 ± 0.5	1.3 ± 1.0	2.6 ±1.4	--
24h µg/kg.24h¥	**5.0 ±1.3**	1.4 ± 0.5	1.7 ± 1.3	**3.3 – 4.0**	**~20**
Ratio 24:12 (day)	1.52	1.27	1.27	1.27-1.52	--

‡ IC-GH: integrated concentration of Growth Hormone; data represent mean + standard deviation

* GH concentrations from the combined 1.6 and 3.2 mg/kg/day cohorts of the OraGrowtH212 Trial

¥ 24-hr GH concentration for LUM-201 calculated from 12-hr data using published conversion ratios

† Zadik et al Horm Res 1992

†† Adapted from data in Albertsson-Wikland et al JCEM 1994; 24h exposures listed reflect absorbance/bioavailability of ~60% of the administered dose

Combined Safety Data from OraGrowtH210 and OraGrowtH212 Trial

- No meaningful treatment-related Serious Adverse Events (SAEs)
- No drop-outs due to SAEs or AEs
- No meaningful safety signals observed in laboratory values, adverse events data, or in EKG values to date
- Treatment related AEs: 1.6 mg/kg dose: Increased appetite (12), Pain in extremity (2), Arthralgia (2), 3.2 mg/kg dose: Increased appetite (11), Pain in extremity (5), Arthralgia (3)

References
1. Howard 1996 Science
2. Nass 2008 Ann Intern Med
3. Chapman 1997 J Clin Endocrinol Metab
4. Supported by Lumos Pharma Topline Phase 2 Data (Nov 2023) and recent updates (July 2024 Corporate Presentation)

Learnings from the LUM-201 Phase 2 Trials

At 6 and 12 months, LUM-201 restored GH pulsatile secretion and normalized IGF-1, promoting growth with a lower GH secretion rate than that observed with daily rhGH administration.

The 1.6 mg/kg dose showed the highest AHV, with a normalized IGF-1 which persisted at 12 months.

LUM-201 Summary

- Restoration of approximately normal pulsatile endogenous GH secretion
- Similar growth to that achieved with daily pharmacological rhGH
- Maintenance of normal IGF-I levels
- Favorable investigational safety profile to date