Oral LUM-201 Restores Pulsatile Growth Hormone Secretion and Growth Response in Moderate Pediatric Growth Hormone Deficiency (PGHD) Key Discoveries from Phase 2 of OraGrowthH212 Trial

Fernando Cassorla, MD[1], Rossana Román, MD[1], Michael Linn Johnson, PhD[2], Alejandra Avila, RN[1], Germán Iñiguez, MD[1], Ingrid Baier, MD[1], Daniela Said, RN[1], Aleksandra Bruchey, PhD[3], Christopher Smith, MS[3], Erik L. Brincks, PhD[3], John C. McKew, PhD[3], Michael O. Thorner, MBBS, DSc[2,3], Pisit "Duke" Pitukcheewanont, MD[3]
[1]Institute of Maternal and Child Research, University of Chile, Santiago, Chile, [2]University of VA - Emeritus, Charlottesville, VA, USA, [3]Lumos Pharma, Inc., Austin, TX, USA.

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Conclusion

LUM-201 stimulates the secretion of endogenous GH by restoring the pulsatility of GH release within the standard physiological spectrum, resembling the pattern seen in normal children.

This approach preserves the normal GH-IGF-1 feedback mechanisms in moderate PGHD, offering an alternative to rhGH injections.

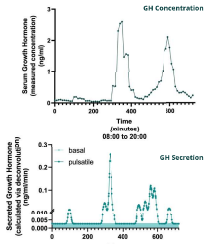
By providing an oral therapy that attains physiological GH profiles, investigational LUM-201 treatment aligns with the fundamental objectives of endocrine therapies — specifically, the restoration of normal hormonal homeostasis.

Deconvolution Analysis of Serum GH Pulsatility Provides a Measure of Pituitary Secretion of GH

Principles of Deconvolution Analysis*

Peaks of GH concentration are identified and analyzed by combining these features:
- a rapid increase representing secretion described by a Gaussian curve
- a slow decay representing elimination based on the half-life of GH in the circulation

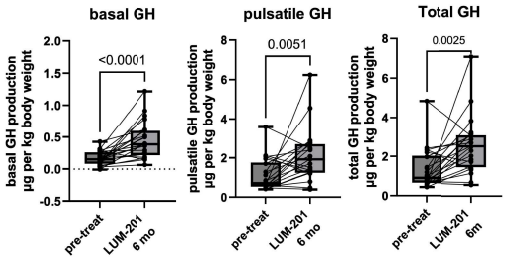
This generates episodes of GH secretion expressed as ng/ml/min.
The distribution volume of GH in plasma is used to define secretion over 12 hours per ml of blood, which is then converted into secretion from the pituitary as µg/kg body weight/12 hours.



*ML Johnson et al. "Signal-Response Modeling of Partial Hormone Feedback Networks", Journal of Diabetes Science and Technology 2009

GH Secretion of Oral LUM-201 Treatment at 0 vs 6 months

(1.6 & 3.2mg/kg/d combined)
All variables from deconvolution based on 72 samples in 12 hours



NOTE: box and whisker data plots represent median (bars), 75% (boxes), and individual subject data (whiskers)

Increasing 24-hour pulsatile secretion, LUM-201 stimulated GH pulsatile secretion approximating normal physiologic levels

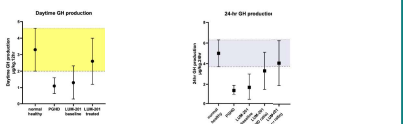
Time period	Normal healthy (IC-GH[‡])	Untreated GHD (IC-GH[‡])	LUM-201 (baseline GH)*	LUM-201 (treat 6M GH)*
	Zadik[A]		N = 22	
12h (day) µg/kg.12hr	3.3 ± 1.3	1.1 ± 0.5	1.3	2.6
24h** µg/kg.24hr	**5.0 ± 1.3**	1.4 + 0.5	1.7	**3.3 – 4.0**
Ratio 24:12(day)	1.52	1.27	1.27	1.27-1.52

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

*GH concentrations from the combined LUM-201 1.6 and 3.2 mg/kg/day cohorts

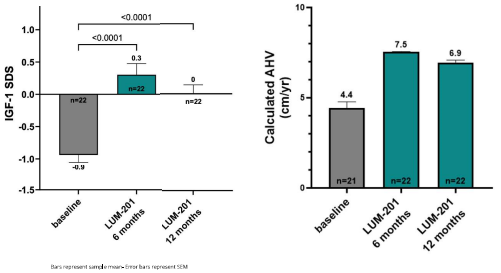
** 24 hour values were calculated by applying ratios described in Zadik

A. Zadik et al Horm Res 1992



LUM-201 Normalizes IGF-1 Levels with Durable Effect out to 12 months

(1.6 & 3.2mg/kg/d combined)

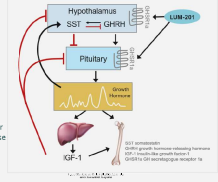


Bars represent sample mean ± error bars represent SEM

Background, Objectives and Methodology

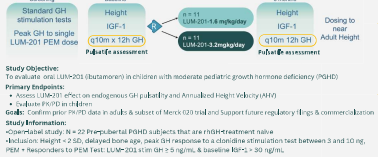
LUM-201 (ibutamoren)

- **Oral Secretagogue:** Agonist of the growth hormone (GH) Secretagogue Receptor 1a (GHSR1a)
- **Mechanism of Action:** Figure 1: LUM-201 acts on the GHSR1a which is expressed in the hypothalamus and anterior pituitary (ref 1). LUM-201 enhances the amplitude of pulsatile releases of GH and normalizes GH levels after 6 months of therapy, while simultaneously acting as a functional antagonist at the somatostatin receptor (ref 2,3,4). In turn, these effects increase the levels of IGF-1, which together with GH, reach the open growth plates and stimulate growth.



LUM-201 in OraGrowthH212 Trial

Phase 2 Pulsatility and PK/PD Study Design Moderate PGHD patients- Clinical Design



Study Objective:
To evaluate oral LUM-201 (ibutamoren) in children with moderate pediatric growth hormone deficiency (PGHD)

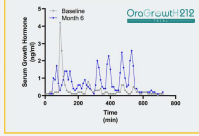
Primary Endpoints:
- Assess LUM-201 effect on endogenous GH pulsatility and Annualized Height Velocity (AHV)
- To assess PK/PD in children

Goals: Confirm prior PK/PD data in adults & subset of Merck 020 trial and Support future regulatory filings & commercialization

Study Information:
•Open-label study, N = 22 Pre-pubertal PGHD subjects that are rhGH-treatment naive
•Inclusion: Height < 2 SD, delayed bone age, peak GH response to a clonidine stimulation test between 3 and 10 ng, PEM + Responders to PEM Test: LUM-201 stim GH ≥ 5 ng/mL & baseline IGF-1 > 30 ng/mL

Example of an individual subject's GH profile

Q10m-12 hour : Baseline vs Treatment



Individual GH Serum Secretion Profile Table Values		Baseline	6 months LUM-201 3.2 ng/kg/d
Q10m 12h GH	AUC_{0-12} (ng*hr/ml)	252.9	481.8
	% change from baseline**		↑1%
IGF-1 (ng/ml)		48	↑11
	% change from baseline**		↑31%
Height velocity (cm/yr)		4.4	3.4

**Percent change from baseline calculated as (treatment value – baseline value) / baseline value

Baseline Characteristics OraGrowthH212 Trial	LUM-201 1.6 mg/kg Mean (SD) N=11	LUM-201 3.2 mg/kg Mean (SD) N=11
Male/Female	7/4	7/4
Age (months)	99.7 (15.2)	100.9 (21.1)
Height SDS	-2.15 (0.28)	-2.26 (0.38)
BMI SDS	-0.07 (0.85)	0.28 (0.97)
MPH SDS Δ	-0.85 (0.53)	-0.73 (0.51)
BA Delay (yrs)	1.7 (0.86)	1.8 (0.96)
Baseline Peak GH Stim Test	7.69 (2.1)	7.33 (1.8)
IGF-1 SDS	-1.01 (0.64)	-0.85 (0.50)

Safety Data LUM-201 OraGrowthH212 Trial	LUM-201 1.6 mg/kg N=11	LUM-201 3.2 mg/kg N=11
Number of AE's	76	75
Subjects with AE (%)	11 (100%)	11 (100%)
Treatment Related AEs	15	15
Subjects with Treatment Related AEs (%)	11 (100%)	10 (90.9%)
Subjects with SAEs (%)	0 (0.0%)	0 (0%)
Subject with Treatment Related SAEs (%)	0 (0%)	0 (0%)

No meaningful treatment-related Serious Adverse Events (SAEs) to date.

No drop-outs due to SAEs or AEs to date.

No meaningful safety signals observed in laboratory values, adverse events data, or in EKG values to date.

Treatment related AEs in 1.6 and 3.2 groups:
Increased appetite (21) with no significant changes
in BMI after 12 months. Pain in extremity (5), Arthralgia (3), Abdominal Pain (1) to date.

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4. Supported by Lumos Pharma Septre Maine 2 Data