

OraGrowth

TRIALS

oral therapy to increase natural GH secretion

Growth, IGF-1 and IGFBP-3 Responses to Oral LUM-201 in OraGrowthH210 and OraGrowthH212 Trials in Pediatric Growth Hormone Deficiency (PGHD) over 12 to 24 Months on Treatment

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ESPE European Society for
Paediatric Endocrinology

Liverpool, UK Nov 16-18,



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in Szczecin**

Disclosure

Dr. Petriczko is an investigator for LUM-201 clinical studies at the Szczecin Sonomed Centrum Medyczne (Sponsor - Lumos Pharma, Inc.) and is a lecturer for Sandoz.

LUM-201 is an investigational compound and is not approved for use by the FDA or any other regulatory agency. Some of the slides in this presentation are derived or copied from corporate presentations previously given by Lumos Pharma, Inc. These slides are used with permission.



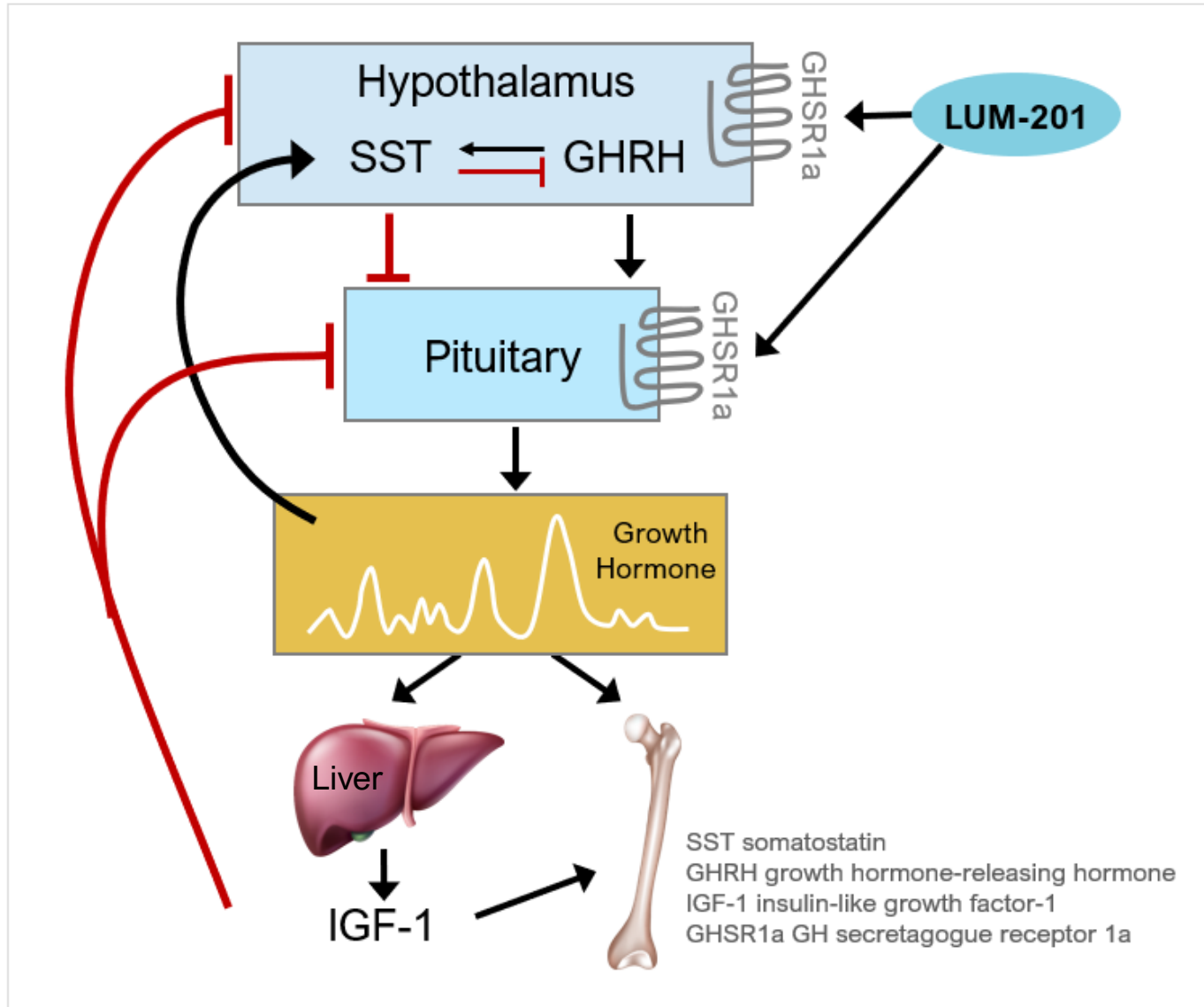
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LUM-201 Restores Natural Growth Hormone & IGF-1 Secretion



**LUM-201 mimics natural release of growth hormone (GH)
Different from injections of synthetic GH**

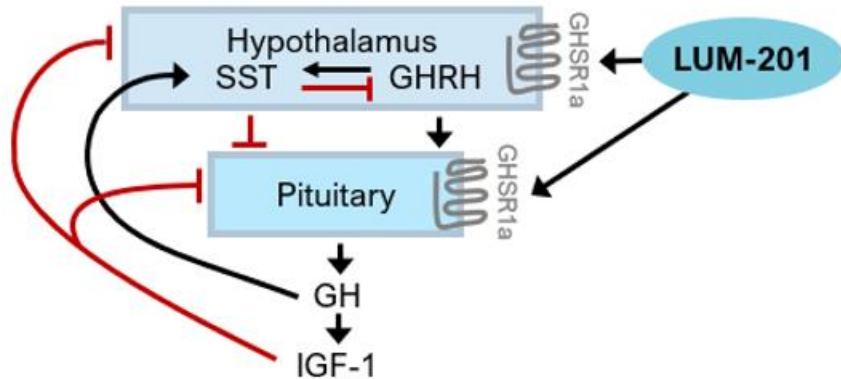
- LUM-201 is an oral GH secretagogue*
- Acts on specific receptors in hypothalamus and pituitary to stimulate release of GH¹
- Increases the amplitude of natural pulsatile GH secretion, ^{2,3} normalizing GH levels after 6 months on therapy⁴
- LUM-201 stimulated GH release regulated by natural GH/IGF-1 feedback mechanisms
- Differentiated mechanism versus exogenous injection of recombinant human growth hormone (rhGH) products

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

* GH secretagogue = molecule that stimulates the secretion of growth hormone (GH)

PEMs Enrich Trials for Patients Likely to Respond to LUM-201*

Moderate PGHD (PEM-Positive) Majority of PGHD population¹



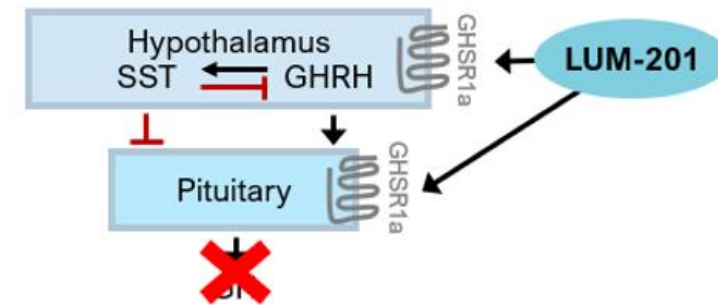
Responders to LUM-201²

Predictive Enrichment Marker Positive (PEM+)

- PGHD patients with baseline IGF-1 > 30 ng/ml
- Peak stimulated GH ≥ 5 ng/ml after a single 0.8 mg/kg dose of LUM-201
- Functional but reduced HP-GH axis

LUM-201
Single
Stimulation
Dose
(0.8 mg/kg)
Identifies
LUM-201
Responders

Severe PGHD (PEM-Negative) Small subset of PGHD population



Non-Responders to LUM-201

Predictive Enrichment Marker Negative (PEM-)

- PGHD patients with baseline IGF-1 < 30 ng/ml
- Peak stimulated GH < 5 ng/ml after a single 0.8 mg/kg dose of LUM-201
- Non-functional HP-GH axis

* PEM (Predictive Enrichment Marker) investigational strategy consists of screening for PEM-positive PGHD patients = Baseline IGF-1 > 30 ng/ml & Peak stimulation GH ≥ 5 ng/ml from single oral dose of LUM-201

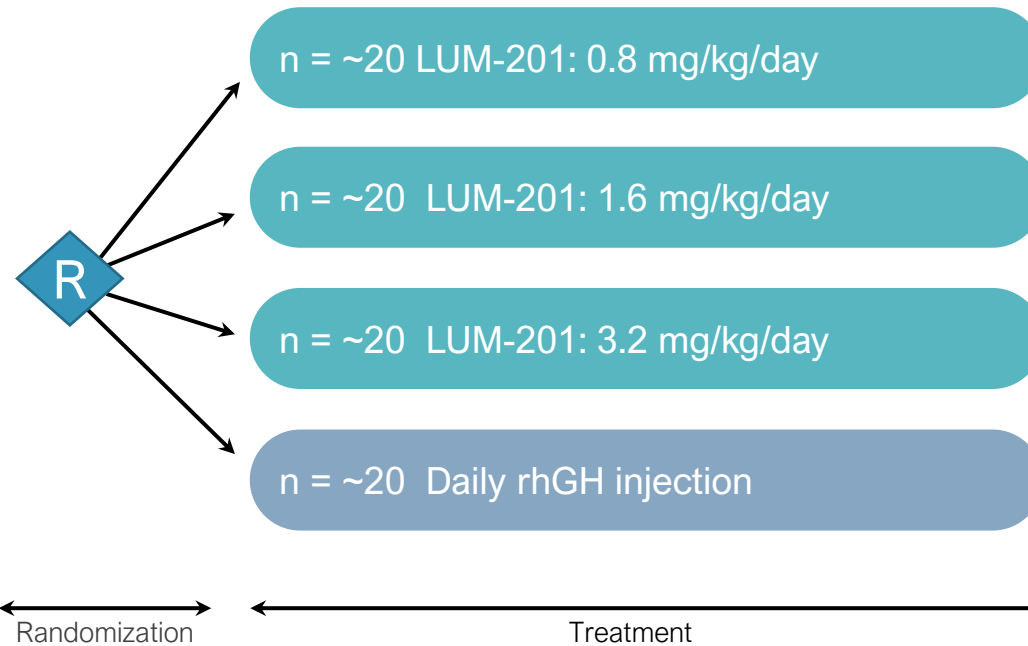
¹ Blum 2021 JES ² Bright 2021 JES

OraGrowthH210 Trial: Phase 2 Trial in Naïve Moderate PGHD

OraGrowthH210 TRIAL

- n = 82 PEM(+) PGHD subjects
- Inclusion: Ages : ≥ 3.0 years and ≤ 11.0 years for girls and ≤ 12.0 years for boys, Bone age delay, Height < 2 SD, rhGH treatment naïve
- ~45 trial sites US & International

Primary Outcome Data (n = 82) – at 6 months on therapy
Total Study Duration – 24 months



Objectives

Study Objectives:

- Prospectively confirm utility of PEM strategy
- Evaluate reproducibility of PEM classification
- Annualized Height Velocity (AHV)

Goals:

- Determine optimal dose for Phase 3

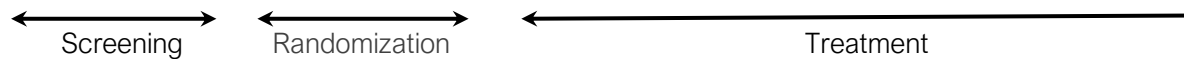
Study not powered to show statistical non-inferiority

OraGrowthH212 Trial: PK/PD Trial in Naïve Moderate PGHD

OraGrowthH212 TRIAL

- n = 22 PEM(+) PGHD subjects
- Open-label study
- rhGH-treatment naïve
- Dosing to near-adult height
- Single, specialized clinical site in Santiago, Chile
- Q10 minute GH sampling for 12 hours

Primary Outcome Data (n = 22) – at 6 months on therapy
Total Study Duration – Subjects on therapy to near adult height



Objectives

Study 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

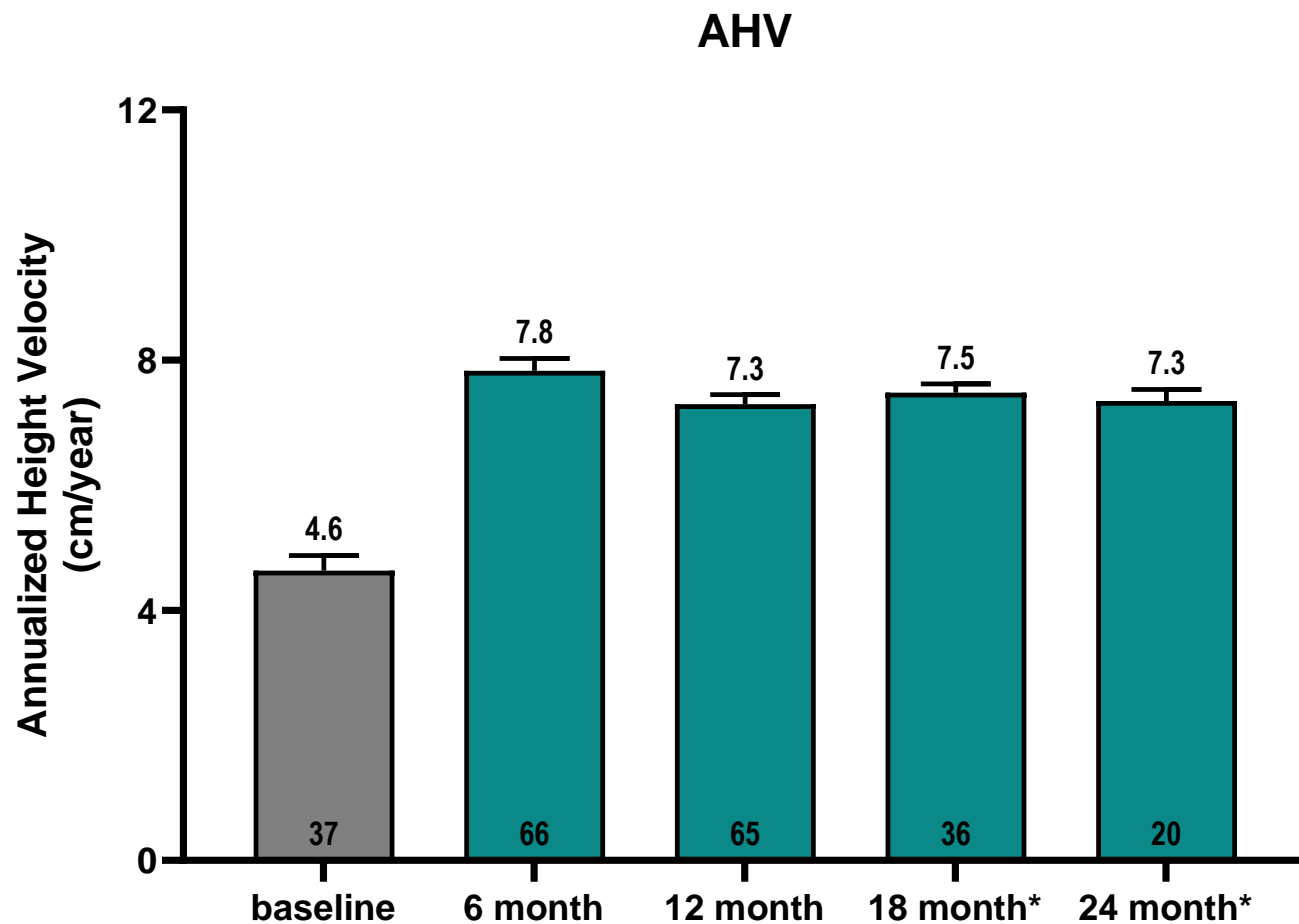
OraGrowthH212 was a single-site trial with a more homogenous patient population than larger international OraGrowthH210 Trial

Baseline Demographics for 1.6mg/kg and 3.2 mg/kg cohorts

OraGrowthH210 TRIAL	LUM-201 1.6 mg Mean (SD) N=22	LUM-201 3.2 mg Mean (SD) N=22	OraGrowthH212 TRIAL	LUM-201 1.6 mg Mean (SD) N=11	LUM-201 3.2 mg Mean (SD) N=11
Age (months)	95.2 (27.3)	94.5 (21.1)	Age (months)	99.7 (15.2)	100.9 (21.1)
Height (cm)	113.6 (11.0)	113.8 (9.2)	Height (cm)	116.5 (5.5)	116.6 (9.5)
Height SDS	-2.27 (0.51)	-2.20 (0.59)	Height SDS	-2.12 (0.28)	-2.22 (0.37)
IGF-1 SDS	-1.38 (0.61)	-1.40 (0.54)	IGF-1 SDS	-1.02 (0.62)	-0.85 (0.47)
MPH (cm)	164.9 (7.4)	167.4 (7.7)	MPH (cm)	162.6 (7.0)	160.3 (8.7)
BA Delay (yrs)	1.9 (0.84)	2.0 (0.96)	BA Delay (yrs)	1.7 (0.86)	1.8 (0.96)
BMI SDS	-0.18 (0.87)	-0.54 (0.99)	BMI SDS	-0.07 (0.87)	0.29 (0.97)

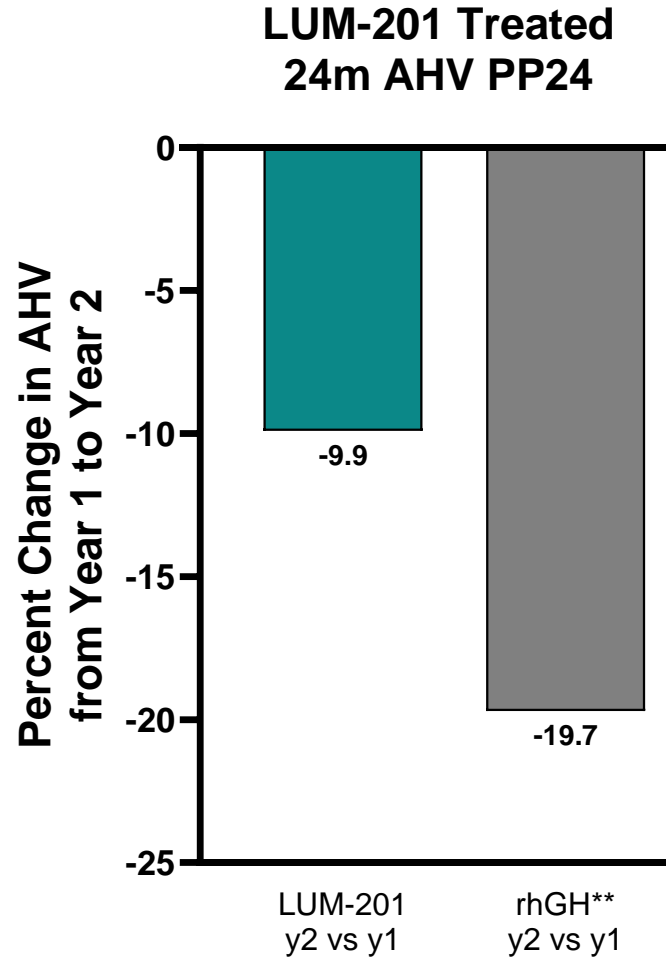
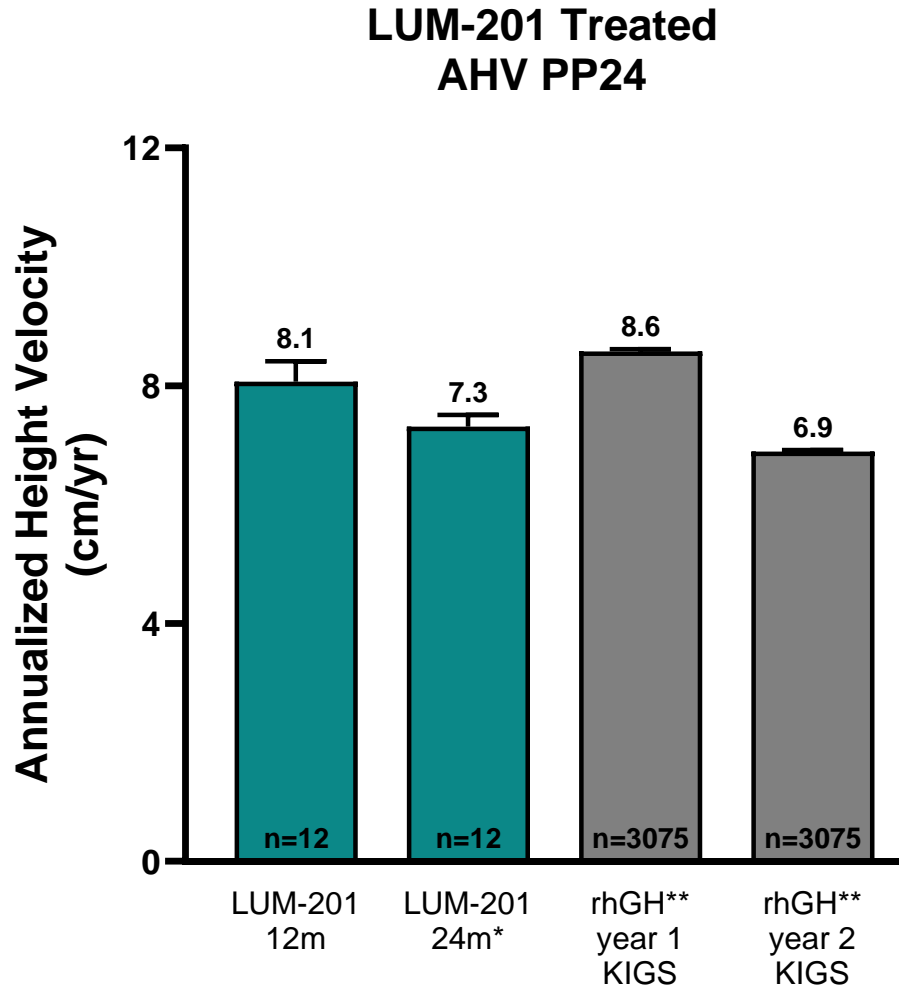
No statistically significant differences between cohorts in each trial (unpaired t-test comparing baseline mean/SD).

LUM-201 Demonstrates Significant Increases in Growth from Baseline with a Durable Effect to 24 Months (Combined 1.6 mg/kg and 3.2 mg/kg doses)



* At 18 and 24 months, data include a subset of subjects from OraGrowthH210 trial who met protocol criteria to continue past 12 months. Data represent all subjects for whom AHV data was available at time of interim read.

Combined LUM-201(1.6 mg/kg and 3.2 mg/kg doses) Data Suggest Sustained Durability LUM-201 Response vs Historical SOC rhGH at 24 months



Highlights

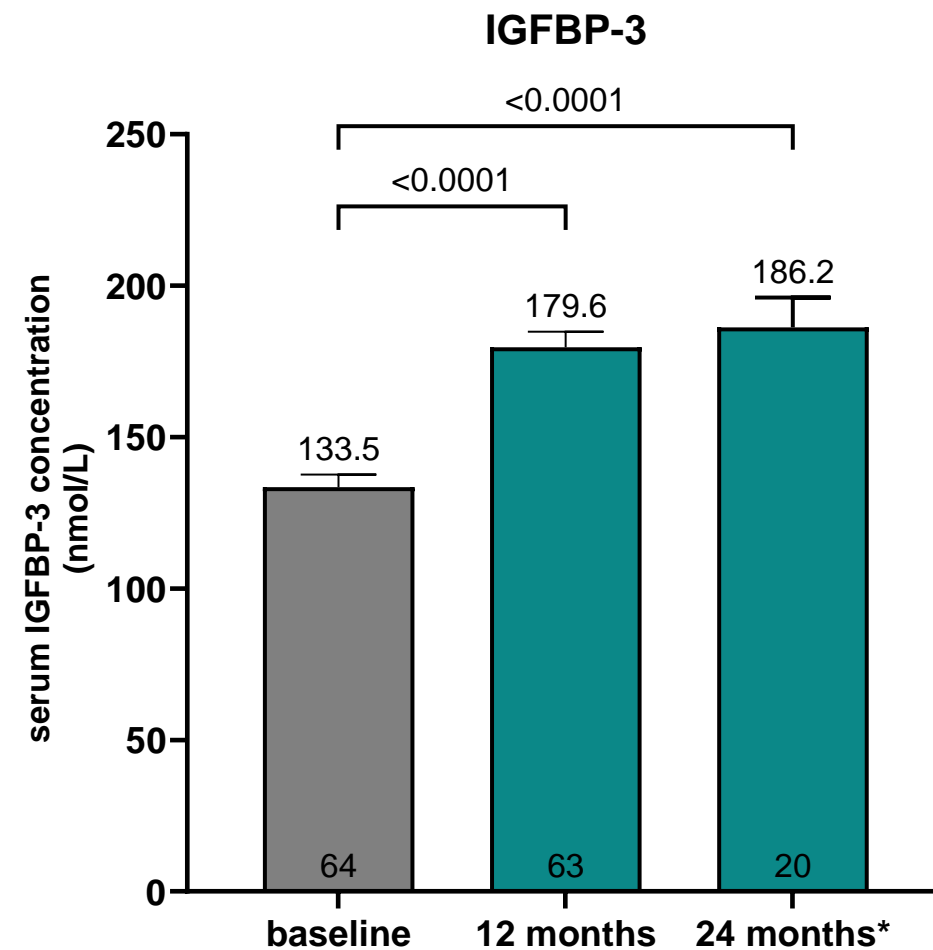
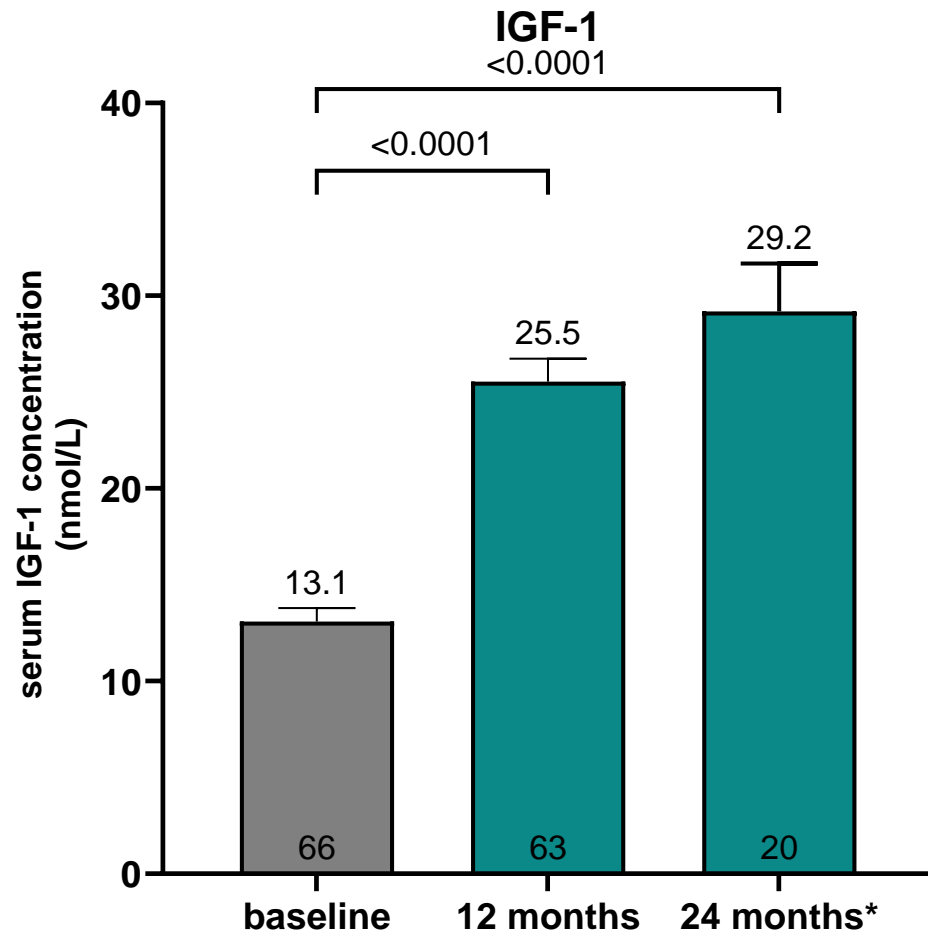
- Preliminary data demonstrated LUM-201 AHV durable to 24 months
- More moderate year 2 AHV decline than rhGH likely due to LUM-201 restoration of GH and IGF-1 to normal levels via pulsatile secretion

* At 24 months, data include a subset of subjects from OraGrowthH210 trial who met protocol criteria to continue past 12 months. Data presented are the subset of subjects that remained pre-pubertal through the 24 month timepoint. Only subjects for whom a 24-month AHV reading was available are presented.

** Ranke et.al. 2010 – Pfizer KIGS database rhGH treated cohort of moderate prepubertal GHD children; mean AHV for the moderate GHD cohorts were 8.58 cm/yr in year 1 and 6.89 cm/yr in year 2.

LUM-201 Significantly Increases IGF-1 and IGFBP-3 levels

With full 12m data set and continues to 24m



* At 24 months, data include a subset of subjects from OraGrowthH210 trial who met protocol criteria to continue past 12 months. Data represent all subjects for whom AHV data was available at time of interim read.

LUM-201 Favorable Investigational Safety Profile to Date

	1.6 mg/kg	3.2 mg/kg
	N =33	N=33
Number of AEs	258	233
Subjects with AE (%)	32 (97.0%)	31 (93.9%)
Treatment Related AEs *	16	19
Subjects with Treatment Related AEs (%)	13 (39.4%)	13 (39.4%)
Subjects with SAEs (%)	#1 (3.0%)	0 (0%)
Subject with Treatment Related SAEs (%)	0 (0%)	0 (0%)

Safety Results

- 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 in 1.6 and 3.2 groups: Increased appetite (23), Pain in extremity (7), Arthralgia (5)

The 1.6 subject had unrelated SAE of Left Thigh Pain

LUM-201 Summary

- LUM-201 shows a significant increase in AHV at 6m and the effect continues with a minimal decrease in AHV through 24m
- Compared to historical rhGH (KIGS), LUM-201 has a smaller drop in AHV from 12m to 24m
- LUM-201 significantly increases IGF-1 and IGFBP-3 levels at 12m which continues to 24m
- Favorable investigational safety profile to date



Conclusions

- Oral LUM-201 1.6mg/kg is the optimal dose for a Phase 3 trial in moderate PGHD
- Oral LUM-201 may provide an innovative way to treat children with moderate PGHD

Phase 2 OraGrowth Trial Investigators



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Sasigarn Bowden, MD, Columbus, OH
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Leslie Soyka, MD, Worcester, MA
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Monica Marin, MD, Oklahoma City, OK
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Oscar Escobar, MD, Pittsburgh, PA
Jennifer Abuzzahab, MD, Minneapolis, MN
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Peter Simm, MD, Melbourne, Australia
Paul Hofman, MD, Auckland, New Zealand
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Announcement:

Late Breaking Free Communication

Monday Monday Nov 18
Session Time: 09:30 - 10:30
Location- Hall 1
Presented by Peter Clayton, MD

“The Amount and The Pattern of Pulsatile GH Secretion Induced by the Oral GH Secretagogue LUM-201 Is Related to Growth and IGF-1 Responses In Moderate Pediatric Growth Hormone Deficiency (PGHD)”