OraGrowtH210 TRIAL

Growth, IGF-1 and IGFBP-3 Responses to the Oral Growth Hormone (GH) Secretagogue, LUM-201, in Pediatric Growth Hormone Deficiency (PGHD) in the OraGrowtH210 Trial

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13th Biennial Scientific Meeting of APPES
New Delhi, India
October 3, 2024

Disclosure

Dr. Hofman is an investigator for clinical studies with LUM-201 at the University of Auckland (Sponsor - Lumos Pharma, Inc.).

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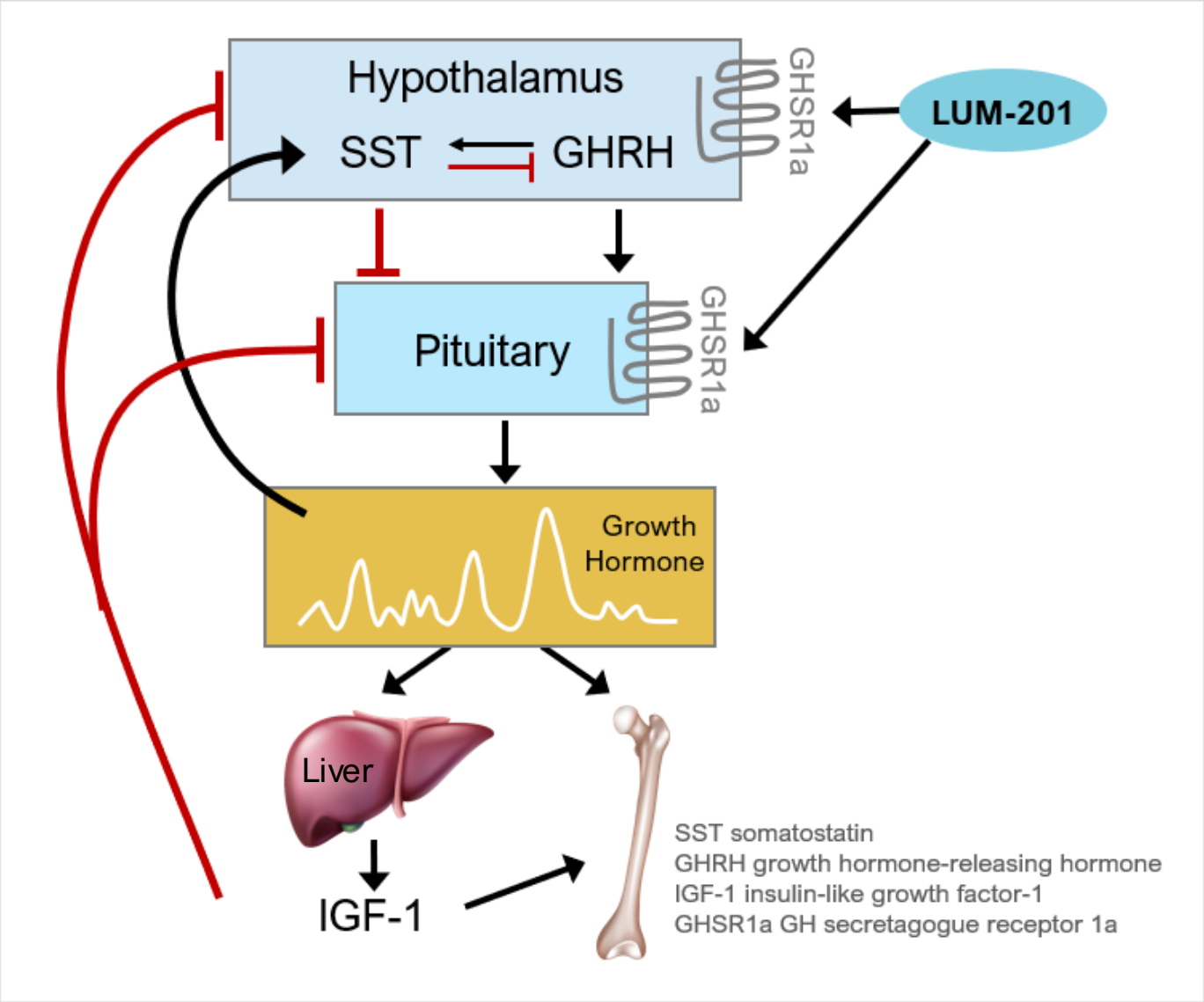
LUM-201 Restores Natural Growth Hormone & IGF-1 Secretion



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 GH[1]
- Increases the amplitude of natural pulsatile GH secretion, [2,3] normalizing GH levels after 6 months on therapy[4]
- 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)

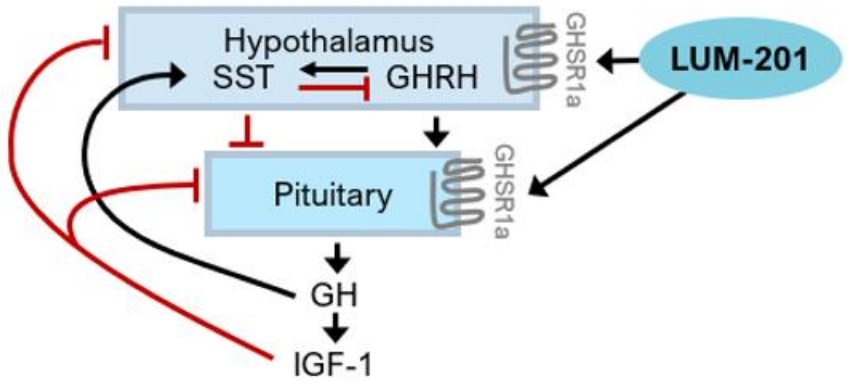
PEMs Enrich Trials for Patients Likely to Respond to LUM-201*

LUM-201

Single Stimulation Dose Identifies LUM-201 Responders

Moderate PGHD (PEM-Positive)

Majority of PGHD population[1]



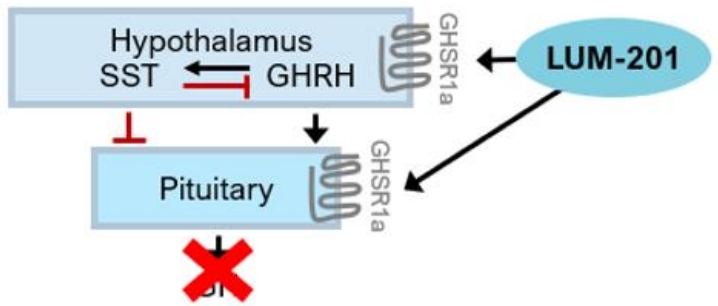
Responders to LUM-201[2]

Predictive Enrichment Marker Positive (PEM+)

- Baseline IGF-1 **>** 30 ng/ml
- Stimulation LUM-201 peak GH **≥** 5 ng/ml
- Functional but reduced HP-GH axis

Severe PGHD (PEM-Negative)

Small subset of PGHD population



Non-Responders to LUM-201

Predictive Enrichment Marker Negative (PEM −)

- Baseline IGF-1 **<** 30 ng/ml
- Stimulation LUM-201 peak GH **<** 5 ng/ml
- 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

HP-GH axis – hypothalamic pituitary growth hormone axis

Phase 2 - *Dose Finding Study* Design

Naive Moderate PGHD Patients

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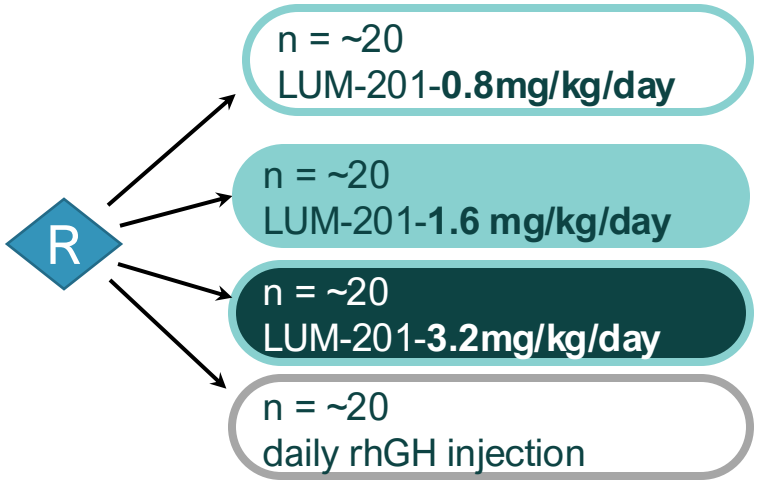
Screening

Standard GH stimulation tests

Peak GH ≥ 5 ng/ml to single LUM-201 dose



6, 9, 12, 24 months

Height

IGF-1

Long-term extension study

Study Information

- N = 82 subjects
- Only PEM (+) pre-pubertal PGHD subjects that are rhGH-treatment naïve
- Inclusion: LUM- 201 stim GH ≥ 5 ng/mL & baseline IGF-1 > 30 ng/mL, Previous moderate PGHD diagnosis, Height < 2 SD, delayed bone age
- 45 trial sites US and International
- Trial duration: up to 24 months for LUM-201, rhGH cohort 12 months

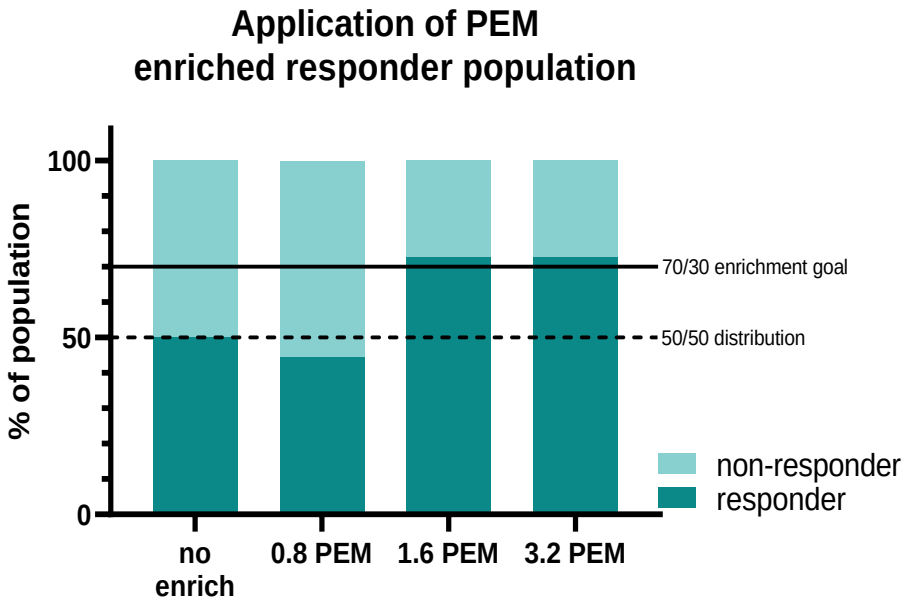
Primary Endpoints:

- Annualized Height Velocity (AHV)
- Confirm PEM strategy

Goal:

- Determine Optimal Phase 3 dose

OraGrowtH210 Met Primary & Secondary Statistical Objectives: PEM Test Enriches the Responder Population & Yields Highly Reproducible Results



PEM Test Reproducibility	
Subjects with Positive Agreement on PEM Tests	76/76
Reproducibility Rate	100%
95% Confidence Interval	(95.3%, 100%)

Highlights

- PEM test ensures patients enrolled in the study are capable of secreting GH in response to a single-dose of LUM-201
- PEM test is highly reproducible
- PEM-positive criteria:
  - 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

Enrichment strategy demonstrated that >70% of PEM+ subjects met pre-specified target growth in 1.6 and 3.2 mg/kg/day cohorts

PEM positive classification was 100% reproducible and exceeded pre-specified statistical objective

Full Data at 12 Months Demonstrate Significant Increase in Growth from Baseline, Durable Effect to 1 year, and Confirm Optimal LUM-201 Dose of 1.6 mg/kg/day

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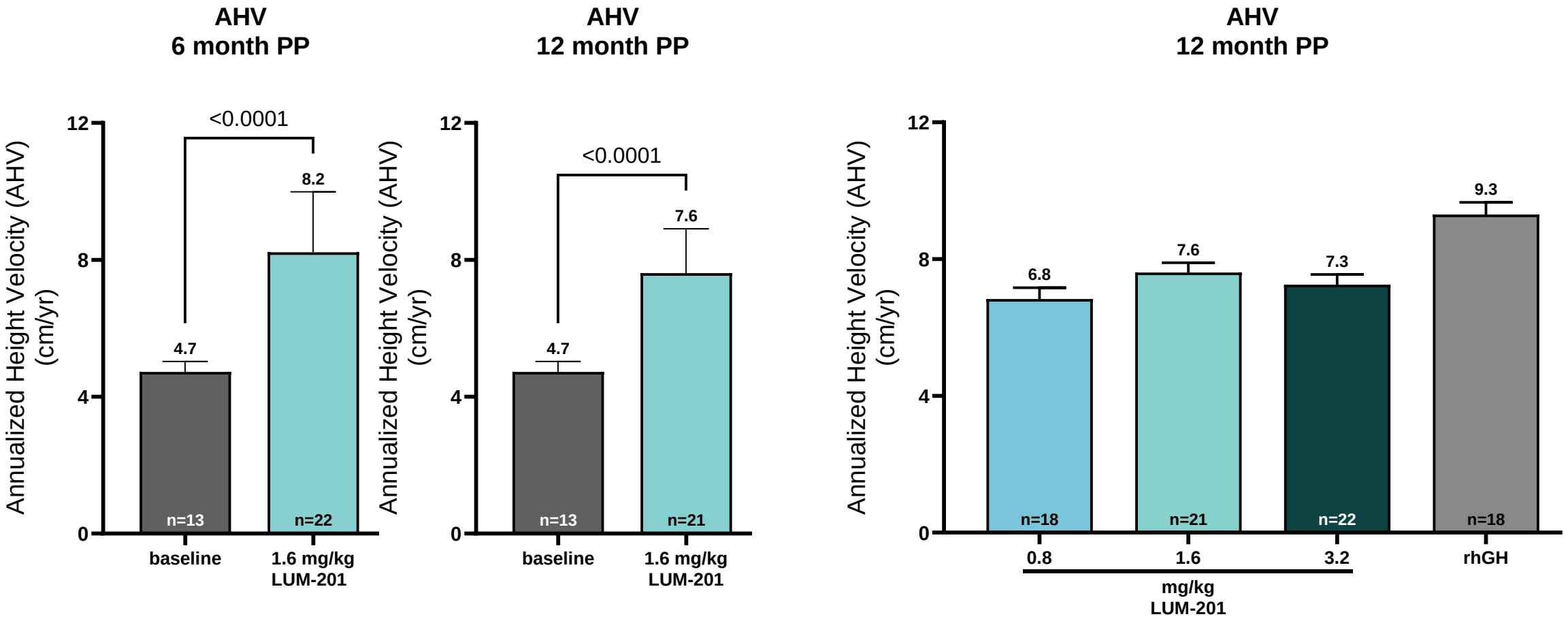
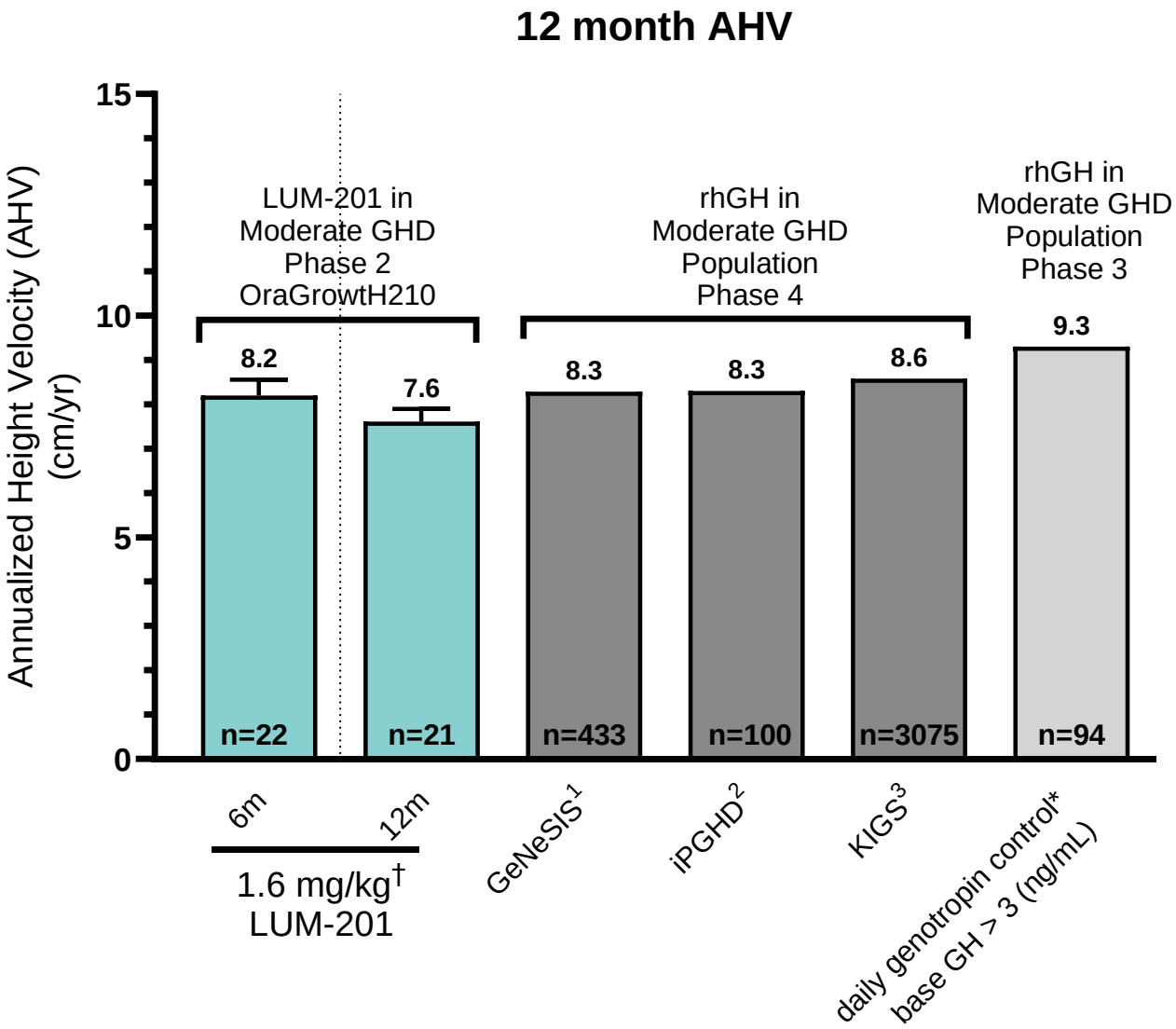


AHV data are ANCOVA values representing an analysis of covariates incorporating multiple baseline demographic terms. LUM-201 at 6m PP and 12m PP (PP = Per Protocol) Bars represent Least Squares Mean (LSM); Error bars represent the Standard Error of LSM.

LUM-201 Generates AHVs Comparable to Reported Historical Phase 4 rhGH Studies

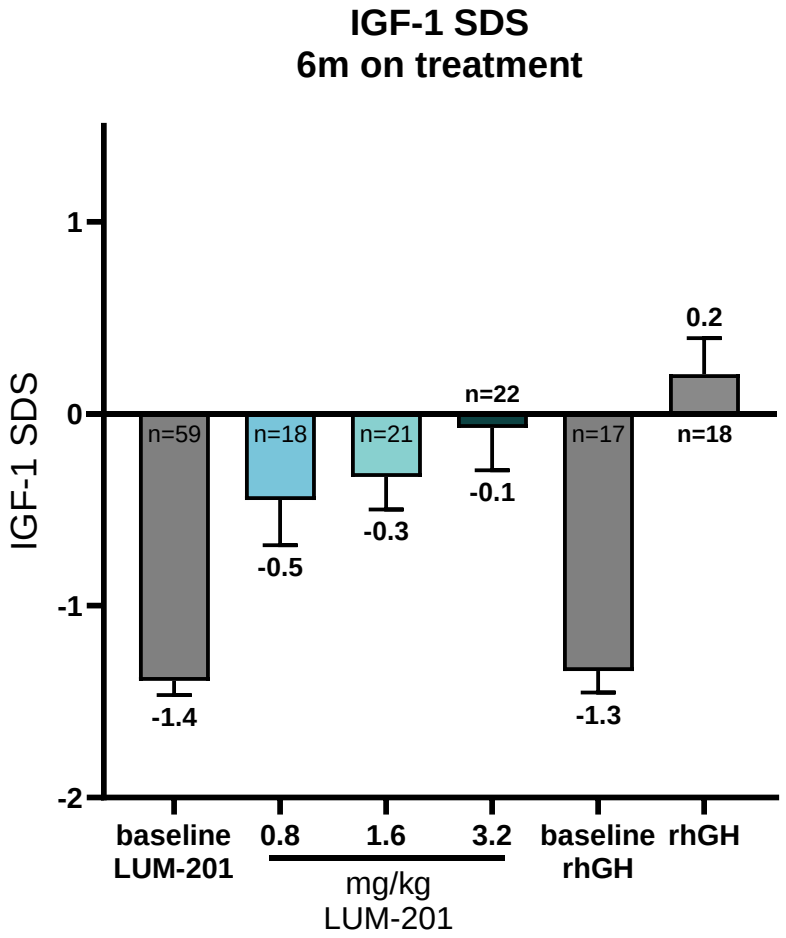


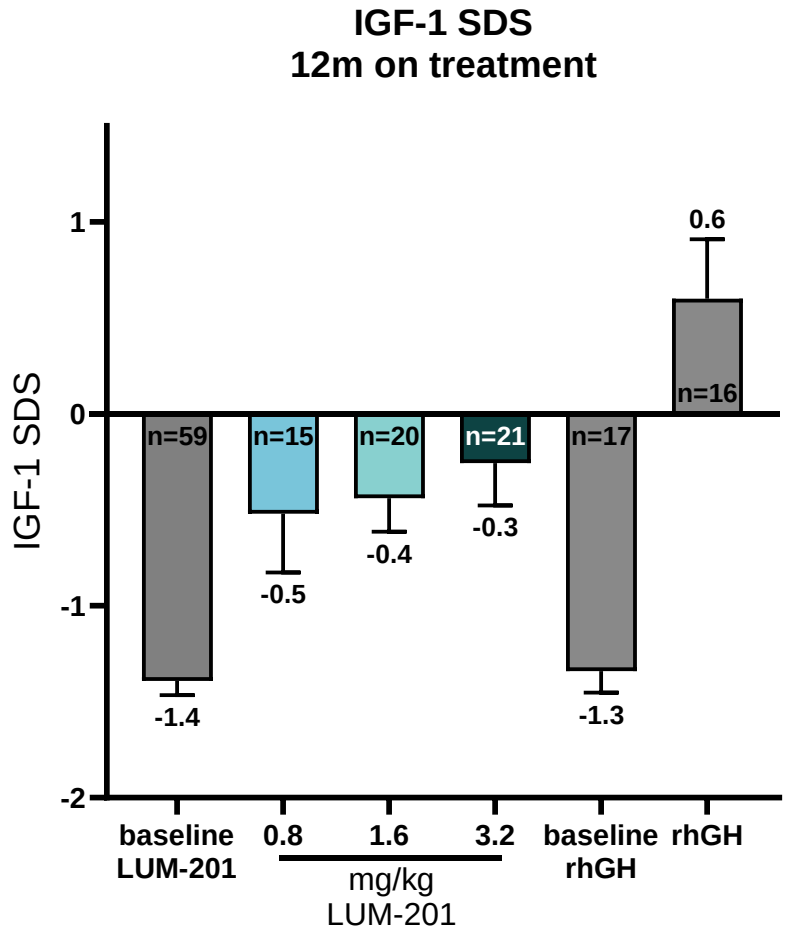
- AHVs range from 8.3-9.3 cm/yr in historical datasets of moderate PGHD patients treated with daily rhGH
- LUM-201 AHVs of 8.2 and 7.6 cm/yr at 6 and 12 months, respectively, were in line with these historical rhGH growth rates in similar moderate patient populations

† ANCOVA values represent an analysis of covariates incorporating multiple baseline demographic terms. LUM-201 at 6m PP and 12m PP. Twelve-month LUM-201 AHV updated to include preliminary analysis of full 12-month dataset. Bars represent Least Squares Mean (LSM); Error bars represent the Standard Error of LSM. Sources: 1 Blum et al JES 2021, 2 Lechuga-Sancho et al JPEM 2009, 3 Ranke et al JCEM 2010 *Daily Genotropin control group for Somatrogon Ph3 dosed at 0.034 mg/kg/day (equates to 0.24 mg/kg/wk); subjects were stratified based on GH production during a standard stim test. JCEM Volume 107, Issue 7, July 2022, Pages e2717–e2728.

LUM-201 Normalizes IGF-1 SDS with Durable Effect out to 12m

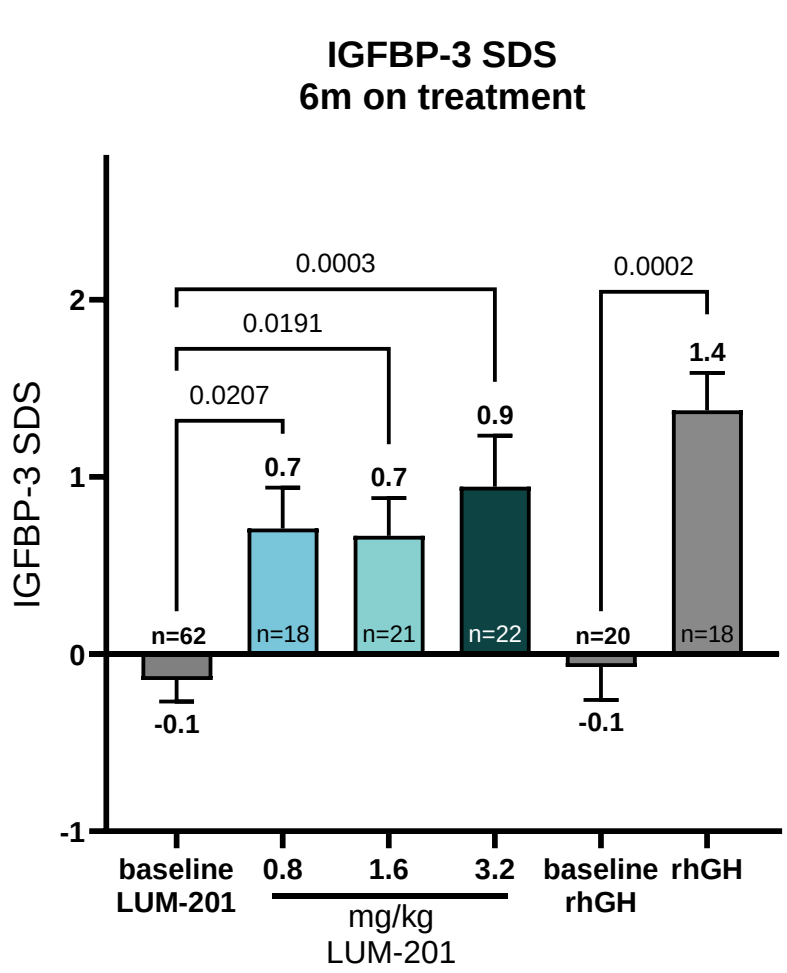
LUM-201 treatment normalizes serum IGF-1 SDS values in every dose cohort.
Normalization is sustained through 12 months of treatment.

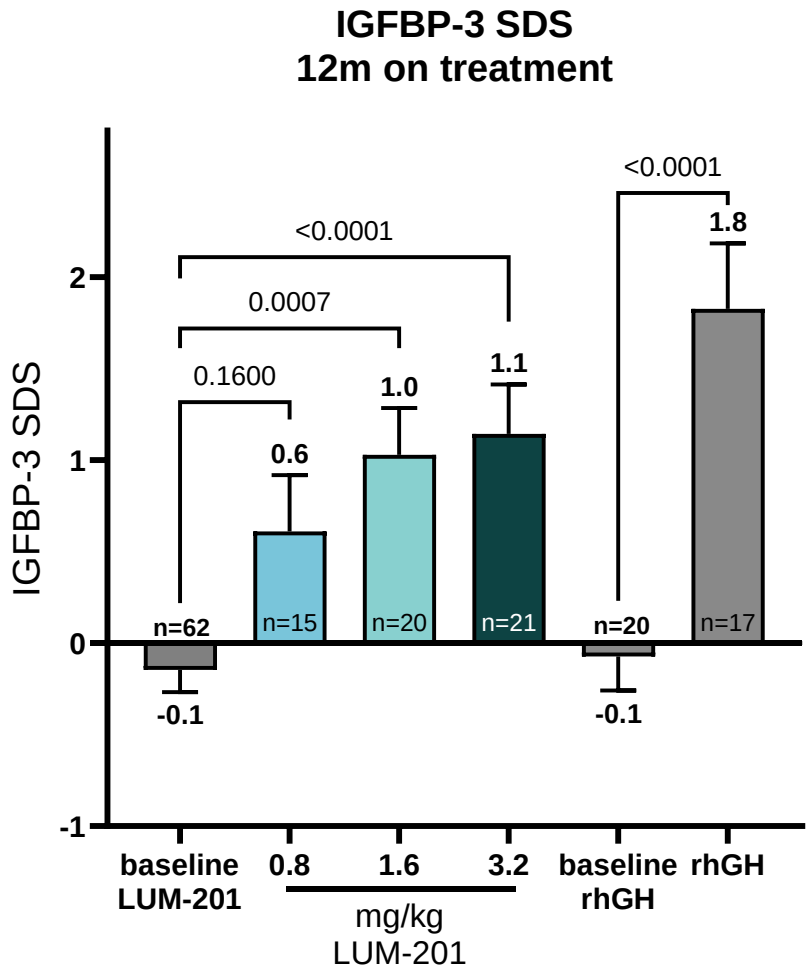




LUM-201 1.6mg/kg Significantly Increases IGFBP-3 at 12m

IGFBP-3 increases are sustained in LUM-201 1.6mg/kg through 12 months of treatment.





LUM-201 Favorable Investigational Safety Profile to Date

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	PEM**	0.8 mg/kg	1.6 mg/kg	3.2 mg/kg	rhGH
	N =104	N =18	N =22	N=22	N =20
Number of AEs	37	73	132	115	77
Subjects with AE (%)	23 (22.1%)	14 (77.8%)	21 (95.5%)	20 (90.9%)	17 (85.0%)
Treatment Related AEs *	7	3	2	4	10
Subjects with Treatment Related AEs (%)	4 (3.8%)	2 (11.1%)	2 (9.1%)	3 (13.6%)	6 (30.0%)
Subjects with SAEs (%)	#1 (1.0%)	1 (5.6%)	1 (4.5%)	0 (0%)	##1 (5.0%)
Subject with Treatment Related SAEs (%)	0 (0%)	0 (0%)	0 (0%)	0 (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 (2), Pain in extremity (2), Arthralgia (2)

Subject had SAE between PEM dose and randomized dose

Subject had SAE after PEM and rhGH dose on Day 1

**PEM cohort captures AEs from time of PEM dose to start of randomized treatment

Data on File

LUM-201 Summary

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- LUM-201 1.6mg/kg dose shows the highest AHV comparable to daily rhGH treatment
- LUM-201 normalizes IGF-1 level at 6m with durable effect at 12m
- Favorable investigational safety profile to date

Conclusions

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