

OR21-06

“Growth Response of Oral LUM-201
in OraGrowthH210 and OraGrowthH212 Trials in
Idiopathic Pediatric Growth Hormone Deficiency (iPGHD):
Combined Analysis Interim Analysis Data”

Combined IA data

OraGrowthH210
TRIAL

+

OraGrowthH212
TRIAL



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Disclosure

Dr. Tansey is an investigator for clinical studies with LUM-201 at the University of Iowa (Sponsor - Lumos Pharma, Inc.). There are no additional disclosures for this presentation.

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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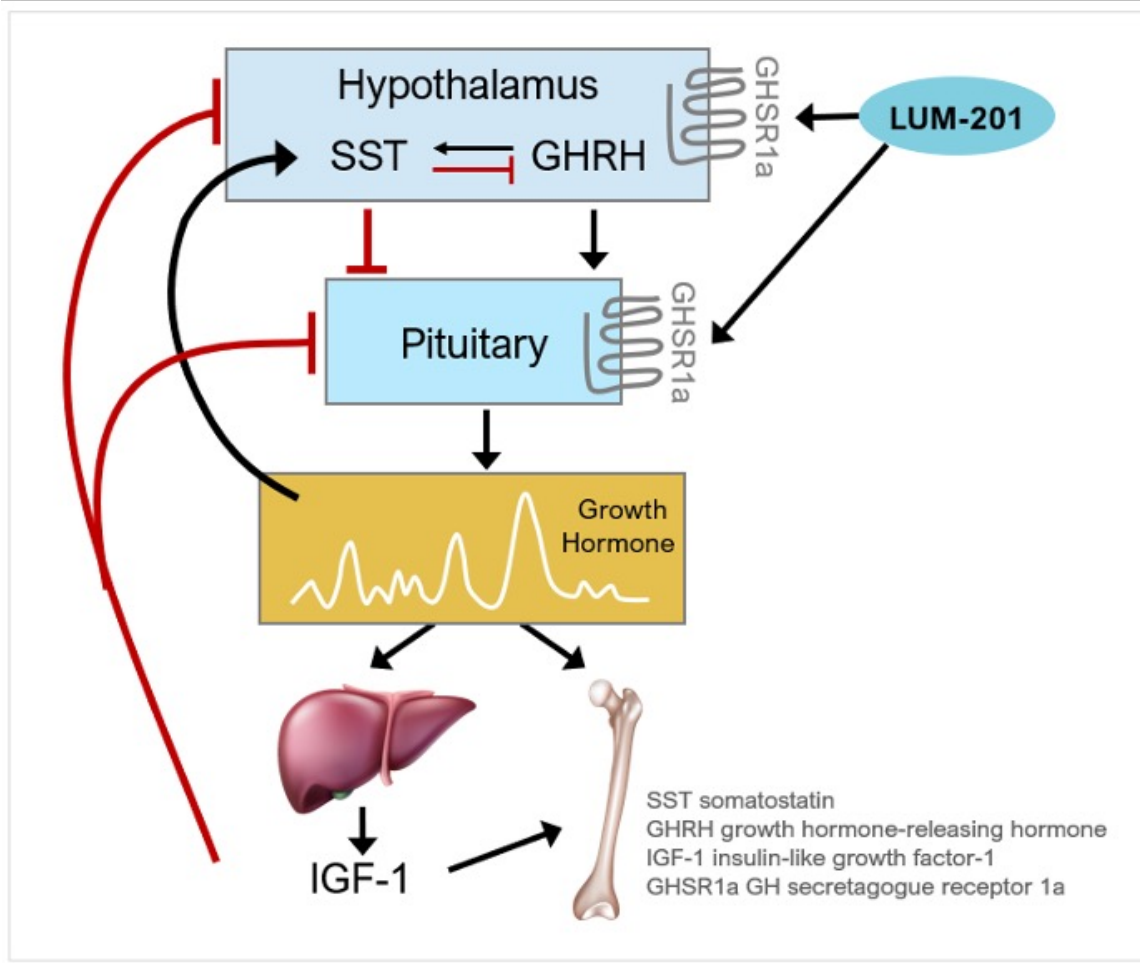
Objective of the Presentation

Report the growth response analyzing the combined interim analysis (IA) data from **two Phase 2 trials** studying LUM-201 at **two different doses** (1.6 mg/kg/day or 3.2 mg/kg/day).

IA data from both studies were combined and analyzed for calculated annualized height velocity (AHV). Baseline demographics were analyzed for the two combined cohorts.



LUM-201 (ibutamoren) – Mechanism of Action



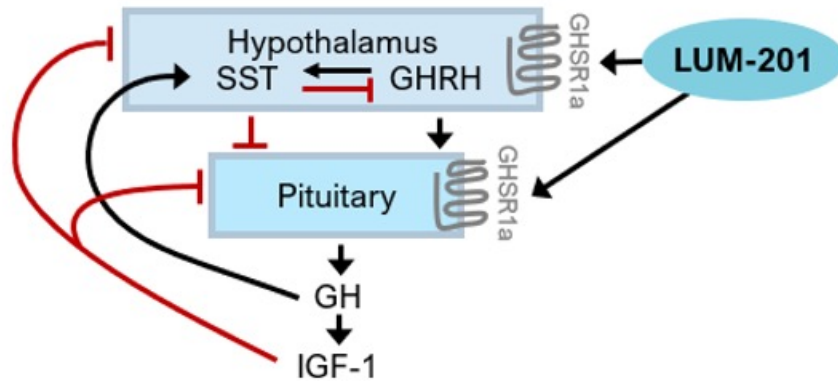
- Oral LUM-201 is a **growth hormone (GH) secretagogue**
- Acts as a durable agonist of GH Secretagogue Receptor (GHSR1a) to stimulate GH release¹
- LUM-201 has been observed to **increase the amplitude of endogenous, pulsatile GH secretion over 24 hours**^{2,3}
- Another differentiating feature vs rhGH is the **natural negative feedback mechanisms, which limit potential for hyperstimulation and excessive increases in IGF-1**
- LUM-201 promotes pulsatile GH secretion in a **selective PGHD population**

1. Howard 1996 Science 273:974-977
2. Nass 2008 Ann Intern Med 149:601-611
3. Chapman 1997 J Clin Endocrinol Metab 82:3455-3463

Single Stim Dose of LUM-201 Identifies PEM+ Responders

Predictive Enrichment Marker Positive (PEM+)

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



Responders to LUM-201

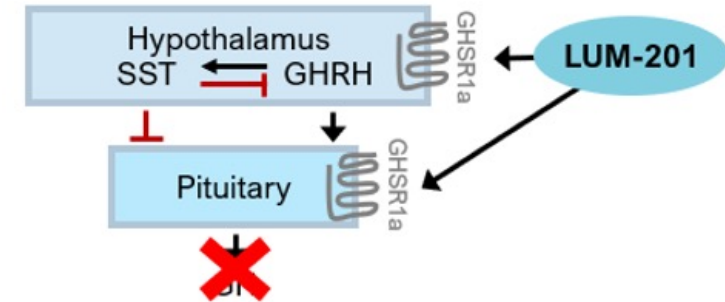
**Moderate / Idiopathic PGHD
PEM Positive**

~60% of total PGHD population¹



Predictive Enrichment Marker Negative (PEM -)

- Baseline IGF-1 ≤ 30 ng/ml
- Stim LUM-201 GH < 5 ng/ml
- Non-functional HP-GH axis



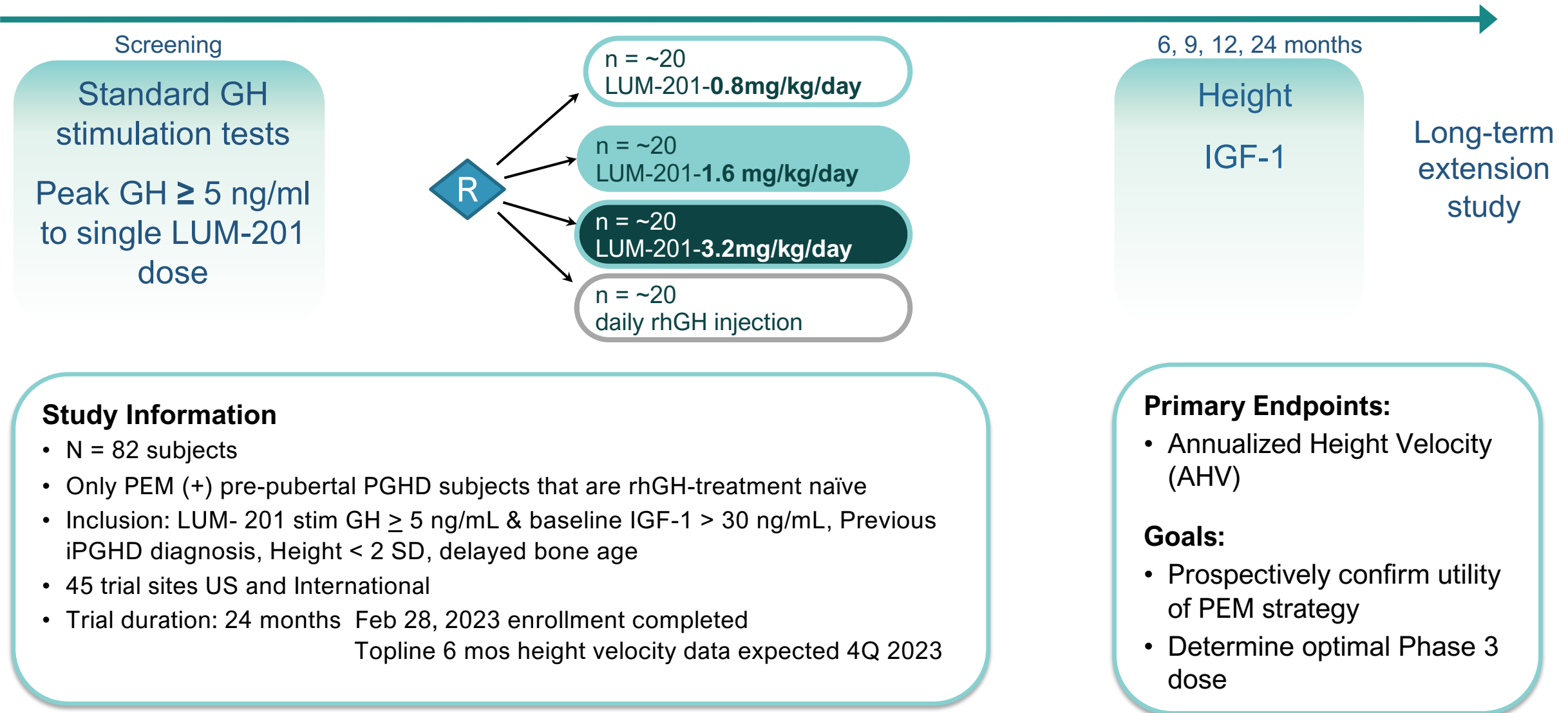
Non-Responders to LUM-201

**Severe / Organic PGHD
PEM Negative**

~40% of total PGHD population

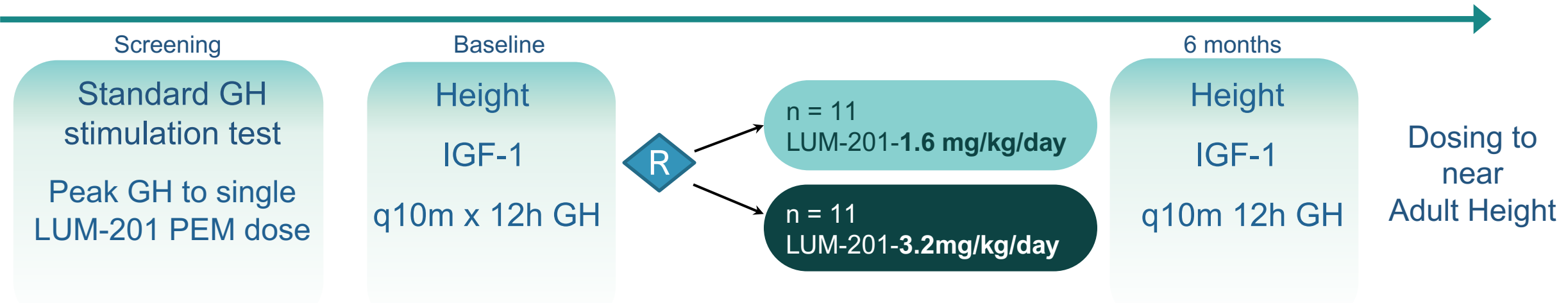
Phase 2 - Dose Finding Study Design

Naive Idiopathic PGHD Patients



Phase 2 - Pulsatility and PK/PD Study Design

Naive Idiopathic PGHD Patients



Study Information

- Open-label study: N = 22
- Pre-pubertal PGHD subjects that are rhGH-treatment naïve
- Inclusion: Height < 2 SD, delayed bone age, peak GH response to a clonidine stimulation test between 3 and 10 ng
- 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 for OraGrowthH210 and OraGrowthH212

OraGrowthH210 TRIAL

Subjects N=20	1.6 mg N=10	3.2 mg N=10
	Mean (SD)	
Age (mos)	99.3 (28.3)	96.1 (21.7)
Height (cm)	114.6 (9.6)	113.8 (8.8)
Height SDS	-2.35 (0.62)	-2.30 (0.48)
IGF-1 SDS	-1.17 (0.72)	-1.39 (0.61)
MPH (cm)	166.98 (7.15)	166.20 (8.06)
MPH SDS Δ	1.76 (0.60)	1.96 (0.83)
BA Delay (yrs)	1.91 (0.53)	2.19 (0.86)
BMI (SDS)	-0.35 (0.79)	-0.70 (0.48)
Male/Female%	60/40	40/60

OraGrowthH212 TRIAL

Subjects N=15	1.6 mg N=8	3.2 mg N=7
	Mean (SD)	
Age (mos)	96.9 (11.9)	95.0 (22.7)
Height (cm)	115.2 (4.57)	113.1(9.97)
Height SDS	-2.12 (0.29)	-2.34 (0.45)
IGF-1 SDS	-1.1 (0.535)	-0.8 (0.377)
MPH (cm)	161.8 (6.98)	160.82 (5.73)
MPH SDS Δ	0.73 (0.47)	0.81 (0.43)
BA Delay (yrs)	1.50 (0.26)	1.83 (0.88)
BMI (SDS)	-0.18 (0.96)	+0.48 (1.02)
Male/Female%	63/37	71/29

These data represent the patient data that had been collected at time of Interim Analysis calculation.

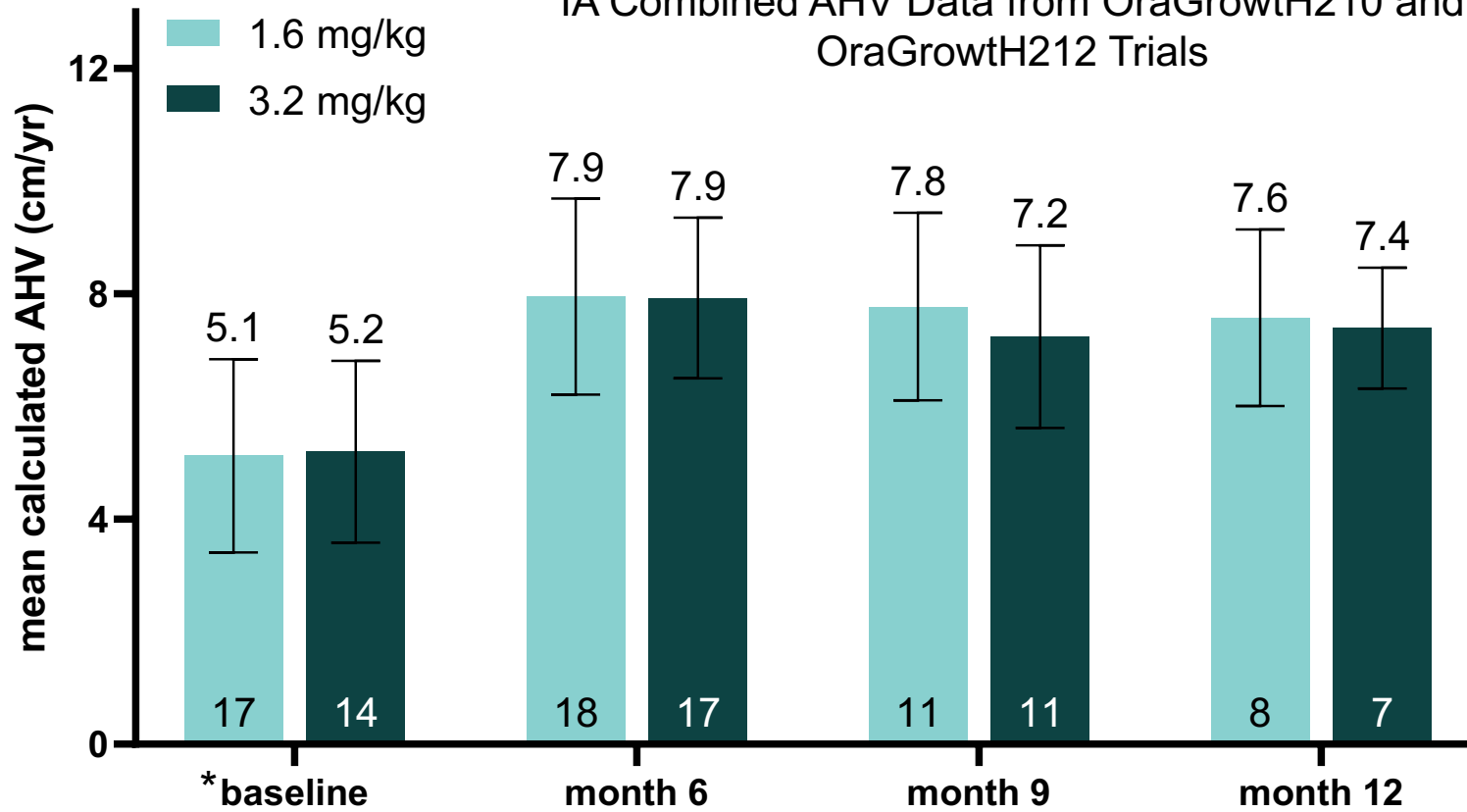
No statistically significant differences between cohorts in each trial (unpaired t-test comparing baseline mean/SD)

SDS = Standard deviation score MPH = Mid-parental height MPH SDS Δ = MPH SDS-Ht SDS BA = Bone age BMI = Body mass index

Annualized Height Velocity of 2 Doses Show Durable Response from 6-12 Months



IA Combined AHV Data from OraGrowthH210 and OraGrowthH212 Trials



Interim Analysis (IA) Results

- Interim data demonstrate LUM-201 produces durable AHV response from 6 to 12 months in moderate PGHD
- LUM-201 at both 1.6 mg/kg and 3.2 mg/kg produces a clinically meaningful increase in AHV from baseline

*Pre-treatment baseline AHV was not required for this study but available data shown

IA Safety Data from Combined Trials



	1.6 mg/kg	3.2 mg/kg
	N =33	N=33
Number of AEs	105	110
Subjects with AE (%)	29 (87.9%)	30 (90.9%)
Treatment Related AEs *	17	19
Subjects with Treatment Related AEs (%)	12 (36.4%)	13 (39.4%)
Subjects with SAEs (%)	0 (0%)	0 (0%)

Interim Analysis (IA) Results

- No 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
- * Treatment related AEs in both groups: Increased appetite (21), Arthralgia (6), Pain in extremity (6), Abdominal pain (2), Bone pain (1)

Conclusion

- As the growth velocity was comparable for the two doses of oral LUM-201, this analysis of the combined IA data suggests 1.6 mg/kg/day as the optimal dose for the Phase 3 trial, as doubling the dose appeared to offer no meaningful improvement in efficacy.
- Final dose determination will await final full data set analysis of both studies
- No treatment-related Serious Adverse Events, no discontinuation due to AEs, and no meaningful safety signals observed in either laboratory values, adverse event data, or in electrocardiogram values.

