ENDO 2023 – Session OR21-06

Growth Response of Oral LUM-201 in OraGrowtH210 and OraGrowtH212 Trials in Idiopathic Pediatric Growth Hormone Deficiency (iPGHD): Combined Analysis Interim Analysis Data

Michael Tansey, MD
University of Iowa, Pediatric Endocrinology
Iowa City, Iowa

University of Iowa Health Care

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.

Abstract Contributors

***Andrew Dauber**, MD, MMSc, Children's National Hospital, Washington, DC, United States;*

***Beata Wikiera,** MD, PhD, Klinika Endokrynologii i Diabetologii Wieku Rozwojowego UM, Wroclaw, N/A, Poland;*

***Beata Pyrzak**, MD, Department of Pediatric and Endocrinology Medical University of Warsaw, Warsaw, N/A, Poland;*

***Artur Bossowski**, MD, Medical University in Białystok, Białystok, N/A, Poland;*

***Michael Tansey**, MD, University of Iowa, Iowa City, IA, United States;*

***Elzbieta Petriczko**, MD, Sonomed Clinic, Szczecin, N/A, Poland;*

***Renata Stawerska**, MD, Department of Paediatric Endocrinology, Medical University of Lodz, Lodz, N/A, Poland;*

***Sasigarn Bowden**, MD, Nationwide Children's Hospital, Columbus, OH, United States;*

***Alison Lunsford**, MD, Texas Tech HSC Amarillo, Amarillo, TX, United States;*

***Matthew Feldt**, DO, Children's Mercy Hospital and Clinics, Kansas City, MO, United States;*

***Michael Everett Gottschalk**, MD, PhD, Rady Children's Hospital, San Diego, CA, United States;*

***Monica Marin**, MD, Oklahoma Children's Hospital OU Health, Oklahoma City, OK, United States;*

***Sunil Nayak**, MD, Pediatric Endocrine Associates, Greenwood, CO, United States;*

***Bhuvana Sunil,** MD, Mary Bridge Children's Hospital and Health Center, Tacoma, WA, United States;*

***Elzbieta Moszczynska**, MD, Memorial Institute Children's Health Center, Warsaw, N/A, Poland;*

***David R Repaske**, MD, PhD, University of Virginia, Charlottesville, VA, United States;*

***Leslie Soyka**, MD, UMass Chan Medical School, Worcester, MA, United States;*

***John Fuqua**, MD, Indiana University School of Medicine, Indianapolis, IN, United States;*

***Oscar Escobar**, MD, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, United States;*

***Deborah Bowlby**, MD, Medical University of South Carolina, Charleston, SC, United States;*

***Patricia Y. Fechner**, MD, Seattle Children's/University of WA, Seattle, WA, United States;*

***Esko Wiltshire**, MBChB, MD, FRACP, University of Otago Wellington, Wellington, N/A, New Zealand;*

***Mark Harris**, MD, Queensland Children's Hospital, South Brisbane, N/A, Australia*

***Kupper Wintergerst**, MD, MBA, University of Louisville, Louisville, KY, United States;*

***Antony R Lafferty**, MD, Canberra Hospital and Australian National University Medical School, Canberra, Australia;*

***Bradley S Miller**, MD, PhD, University of Minnesota Medical School , Minneapolis, MN, United States;*

***Peter Simm**, MD, Royal Children's Hospital, Melbourne, N/A, Australia;*

Sponsor: Lumos Pharma, Inc., Austin, TX, United States : Aleksandra Bruchey, PhD; Christopher Smith, MS; David B Karpf, MD; John C McKew, PhD; Michael Thorner, BS, DSc, FRCP, MACP,

Abstract Contributors

***Fernando Cassorla**, MD, Institute of Maternal and Child Research, University of Chile, Santiago, Chile*

***Rossana Román,** MD, Institute of Maternal and Child Research, University of Chile, Santiago, Chile*

***Michael L Johnson,** PhD, Emeritus University of Virginia, Charlottesville, Virginia, USA*

***Alejandra Avila,** RN, Institute of Maternal and Child Research, University of Chile, Santiago, Chile*

***German Iñiguez,** MD, Institute of Maternal and Child Research, University of Chile, Santiago, Chile*

***Ingrid Baier,** MD, Institute of Maternal and Child Research, University of Chile, Santiago, Chile*

***Daniela Said,** MD, Institute of Maternal and Child Research, University of Chile, Santiago, Chile*

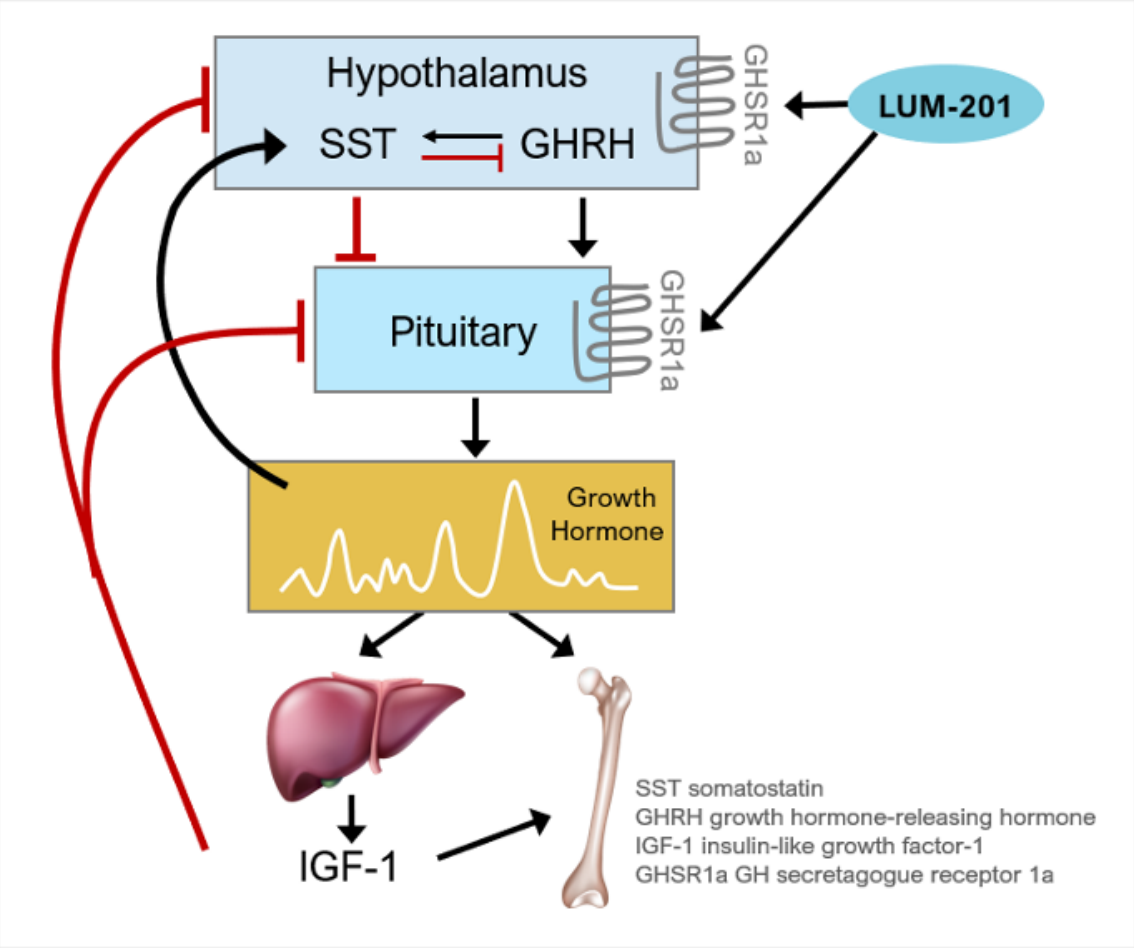
Sponsor: Lumos Pharma, Inc., Austin, TX, United States : Aleksandra Bruchey, PhD; Christopher Smith, MS; David B Karpf, MD; John C McKew, PhD; Michael Thorner, BS, DSc, FRCP, MACP,

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 release[1]
- 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

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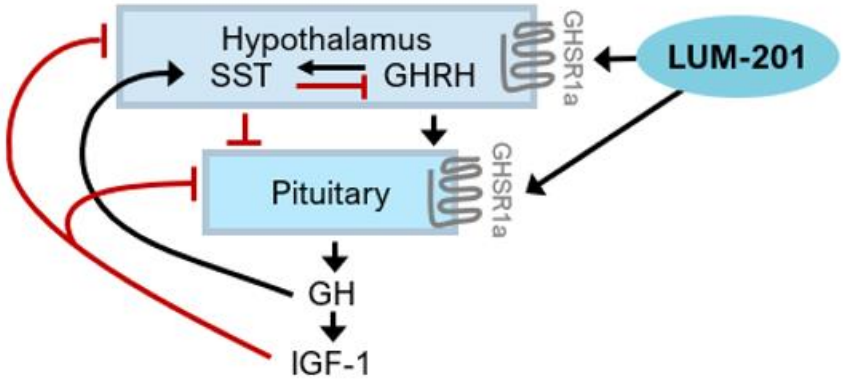
Single Stim Dose of LUM-201 Identifies PEM+ Responders

LUM-201

Single Stimulation Dose

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

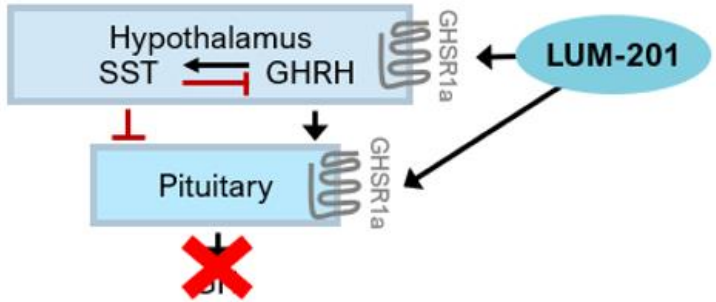


Responders to LUM-201

Moderate / Idiopathic PGHD
PEM Positive
~60% of total PGHD population[1]

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

1 Blum 2021 JES

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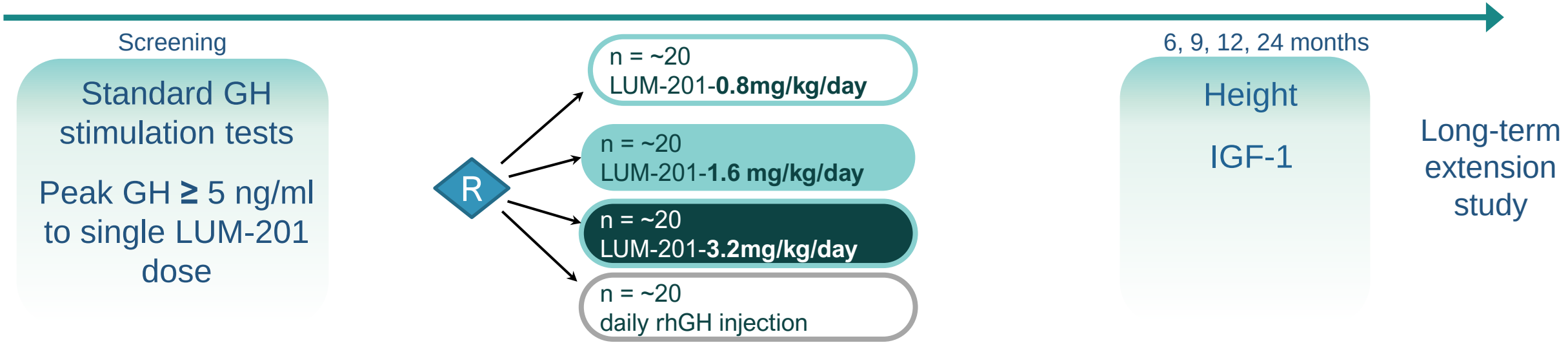
Phase 2 - *Dose Finding Study* Design

Naive Idiopathic PGHD Patients

OraGrowtH210 TRIAL



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 iPGHD diagnosis, Height < 2 SD, delayed bone age
- 45 trial sites US and International
- Trial duration: 24 months Feb 28, 2023 enrollment completed
  Topline 6 mos height velocity data expected 4Q 2023

Primary Endpoints:

- Annualized Height Velocity (AHV)

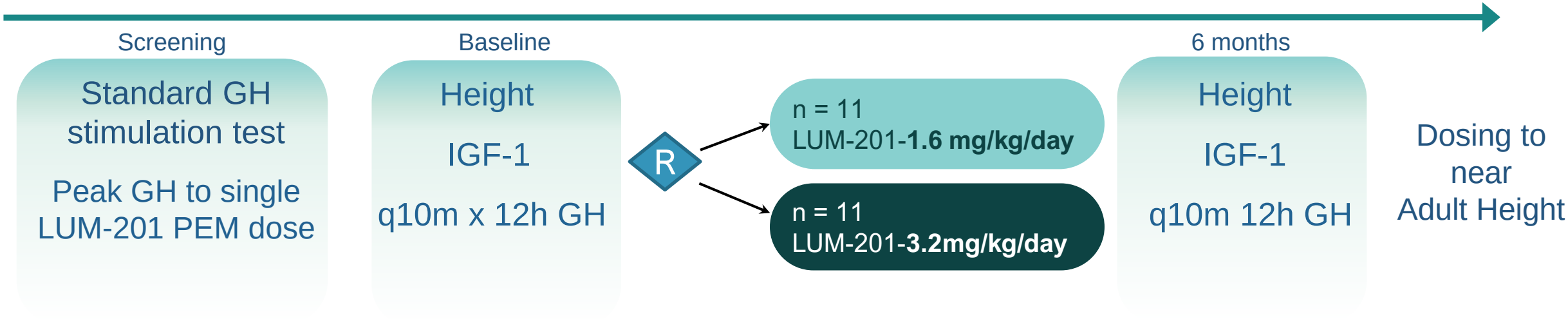
Goals:

- Prospectively confirm utility of PEM strategy
- Determine optimal Phase 3 dose

Phase 2 - *Pulsatility and PK/PD Study* Design

Naive Idiopathic PGHD Patients

OraGrowtH212 TRIAL



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 OraGrowtH210 and OraGrowtH212

OraGrowtH210 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

OraGrowtH212 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

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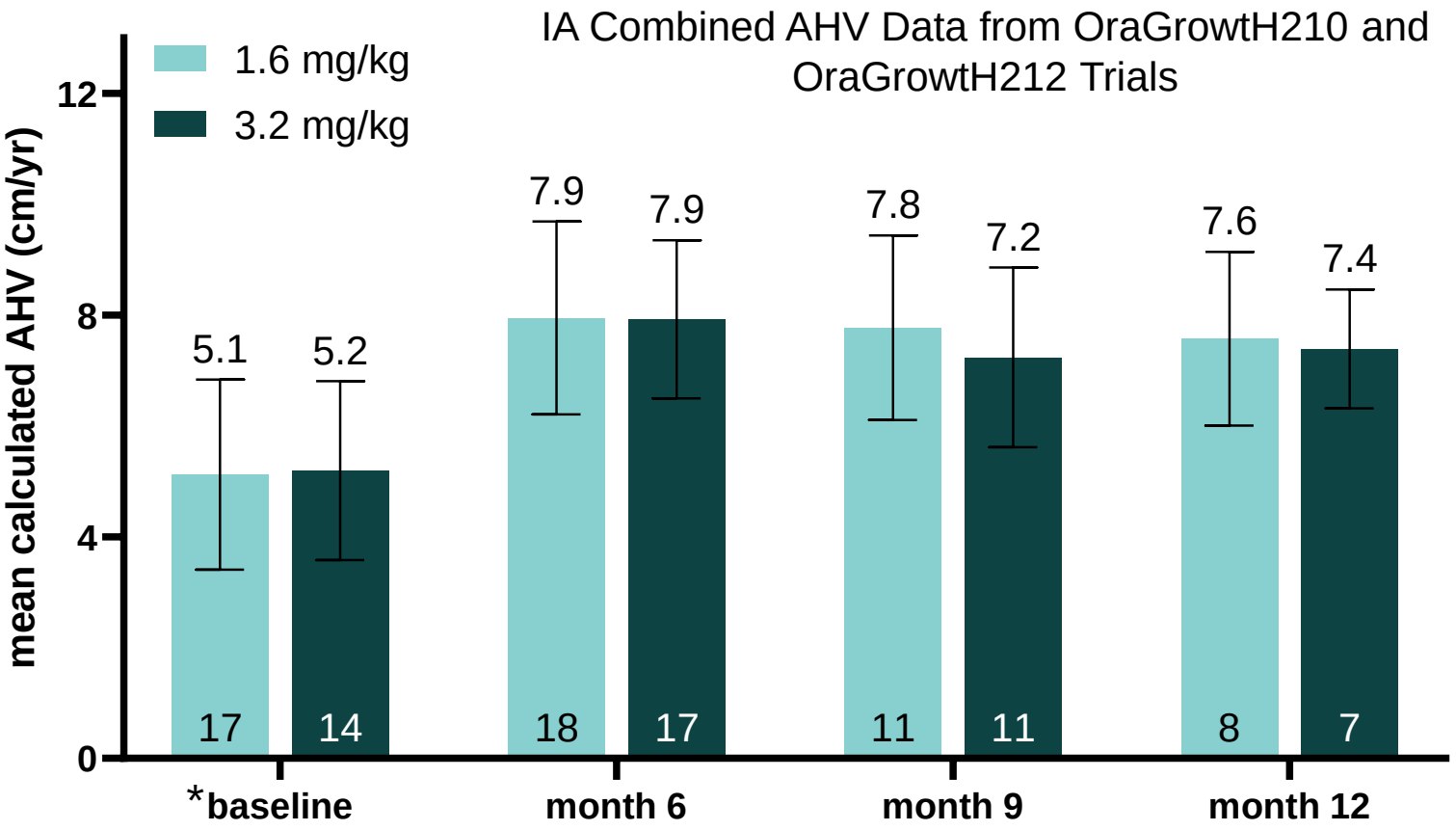
Annualized Height Velocity of 2 Doses Show Durable Response from 6-12 Months



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.

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