# KOL Event

## Response to LUM-201 in Moderate PGHD

Fernando Cassorla, MD and
Michael Tansey, MD

June 21, 2023

# Forward Looking Statements

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This presentation contains forward-looking statements of Lumos that involve substantial risks and uncertainties. All such statements contained in this presentation are forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995.

We are passionate about our business, including LUM-201 and the potential it may have to help patients in the clinic. This passion feeds our optimism that our efforts will be successful and bring about therapeutics that are safe, efficacious, and offer a meaningful change for patients. Please keep in mind that actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make.

We have attempted to identify forward-looking statements by using words such as “projected,” "upcoming," "will," “would,” "plan," “intend,” "anticipate," "approximate," "expect," “potential,” “imminent,” and similar references to future periods or the negative of these terms. Not all forward-looking statements contain these identifying words. Examples of forward-looking statements include, among others, statements we make regarding progress in our clinical efforts including comments concerning screening and enrollment for our trials, momentum building in our LUM-201 program for PGHD, anticipated timing of interim analyses of trials, LUM-201’s therapeutic potential when administered to pediatric subjects with idiopathic or moderate growth hormone deficiency, that the interim sample size should be adequate to provide an initial indication of LUM 201’s impact, expecting the primary outcome data readout for our trials, market size potential for LUM-201, predictions regarding LUM-201, goals with respect to LUM-201, the potential to expand our LUM-201 platform into other indications, future financial performance, results of operations, cash position, cash use rate and sufficiency of our cash resources to fund our operating requirements through the primary outcome data readout from the OraGrowthH210 and OraGrowthH212 Trials, and any other statements other than statements of historical fact.

We wish we were able to predict the future with 100% accuracy, but that just is not possible. Our forward-looking statements are neither historical facts nor assurances of future performance. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make due to a number of important factors, including potential material differences between the interim results of our LUM-201 trials and the final results of the trials which are not known at this time, the effects of pandemics (including COVID-19), other widespread health problems, the Ukraine-Russia conflict, the outcome of our future interactions with regulatory authorities, our ability to project future cash utilization and reserves needed for contingent future liabilities and business operations, the ability to obtain the necessary patient enrollment for our product candidate in a timely manner, the ability to successfully develop our product candidate, the timing and ability of Lumos to raise additional equity capital as needed and other risks that could cause actual results to differ materially from those matters expressed in or implied by such forward-looking statements. You should not rely on any of these forward-looking statements and, to help you make your own risk determinations, we have provided an extensive discussion of risks that could cause actual results to differ materially from our forward-looking statements in the "Risk Factors" section and elsewhere in our Annual Report on Form 10-K for the year ended December 31, 2022, as well as other reports filed with the SEC including our Quarterly Reports on Form 10-Q filed after such Annual Report. All of these documents are available on our website. Before making any decisions concerning our stock, you should read and understand those documents.

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# Agenda

**Welcome & Overview**

- Rick Hawkins, *Chief Executive Officer & Chairman*

**Clinical Development Program Outlook**

- John McKew, PhD, *President & Chief Scientific Officer*

**ENDO Presentation on OraGrowtH212 Interim Data**

- Fernando Cassorla, MD, *University of Chile*

**ENDO Presentation on Combined OraGrowtH210 & '212 Interim Data**

- Michael Tansey, MD, *University of Iowa*

**Questions & Answers**

# Key Opinion Leaders in the Field of Pediatric Endocrinology

**Fernando Cassorla, MD** is currently Chief of Pediatric Endocrinology at the Institute of Maternal and Child Research of the University of Chile, a position he has held since 1993. Previously, Dr. Cassorla served as Senior Investigator at the Developmental Endocrinology Branch of the National Institute of Child Health and Human Development, rising to the position of Clinical Director of this Institute in 1990. He has authored numerous chapters in pediatric endocrinology, authored or co-authored over 200 original articles in peer reviewed journals, and has presented over 300 abstracts at scientific meetings. Dr. Cassorla received his MD from the University of Chile. He is Board Certified in both Pediatrics and Pediatric Endocrinology, having completed his residency in Pediatrics at the Albany Medical Center in New York and his fellowship in Pediatric Endocrinology at the Children´s Hospital of Philadelphia. Dr. Cassorla has received several international awards for his work including the European Society of Pediatric Endocrinology (ESPE) International Research Award, September 2022, and was elected to the Chilean Academy of Medicine for a lifetime position in 2003.

**Michael Tansey, MD** is currently Clinical Professor, Dept. of Pediatrics, Division of Pediatric Endocrinology and Diabetes, University of Iowa, Iowa City, a position he has held since 2012, having first served as Clinical Assistant Professor 2001-2006, then as Clinical Associate Professor 2006-2012. Dr. Tansey also serves as Clinical Director for Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics, University of Iowa. He has been a co-investigator for one of 5 clinical centers for the NIH-funded Diabetes Research in Children Network "DirecNet" group since 2001 and has co-authored numerous peer-reviewed scientific publications on brain function and growth in children with Type 1 diabetes. Dr. Tansey received his MD from Loyola Stritch School of Medicine, Maywood, Illinois, and completed his residency in Pediatrics at the University of Iowa Children's Hospital and his fellowship in Pediatric Endocrinology at the University of Iowa Hospitals and Clinics. He has received several awards including the Riesz Award, University of Iowa, and the Mary Tyler Moore and S. Robert Levine, MD, Excellence in Clinical Research Award.

# Overview
## *Lead asset targeting children with growth disorders*

| | |
|---|---|
| **Novel Oral Rare Disease Asset** | • Novel **oral** therapeutic asset, **LUM-201**, for growth hormone deficiency (GHD) disorders<br>• LUM-201 **acts within natural endocrine pathway**, differentiated from injectable therapies |
| **Pipeline in a Product** | • **Worldwide *injectable* market** for GHD disorders is **$3.4 billion**, excluding China*<br>• Market for initial oral LUM-201 indication, **Pediatric GHD (PGHD)**, is **$1.2 billion*** |
| **Late-stage Trials in PGHD** | • **Primary outcome data** for two Phase 2 OraGrowtH Trials expected **4Q 2023**<br>• PEM strategy **de-risks trials** by identifying and enrolling likely LUM-201 responders** |
| **Solid Financial Position** | • Cash balance of **$58.0 million** as of close of **1Q 2023**<br>• Cash runway **into 3Q 2024,** beyond Phase 2 OraGrowtH Trials primary outcome data |

PGHD = Pediatric Growth Hormone Deficiency
* USA, Germany, France, Italy, Spain, UK, Japan (Grandview Research, Growth Hormone Market Forecast, 2019)
** PEM (Predictive Enrichment Marker) strategy consists of screening for PEM+ PGHD patients = Baseline IGF-1 > 30 ng/ml & Peak stimulation GH ≥ 5 ng/ml from single oral dose of LUM-201

# Phase 2 OraGrowtH Trials – Primary Outcome Data Due Q4 2023

## OraGrowtH210 TRIAL

- **Dose-finding multi-site study**
- **N = 82** PEM+ PGHD subjects randomized
- 4 treatment arms
  - 0.8 mg/kg/day LUM-201
  - 1.6 mg/kg/day LUM-201
  - 3.2 mg/kg/day LUM-201
  - Standard dose rhGH control arm
- Primary outcome at 6 months on therapy
- On treatment for 24 months
- **To determine optimal Phase 3 dose**

## OraGrowtH212 TRIAL

- **Mechanistic single-site PK/PD study**
- **N = 22** PEM+ PGHD subjects randomized
- 2 treatment arms
  - 1.6 mg/kg/day LUM-201
  - 3.2 mg/kg/day LUM-201
- Q10 minute GH sampling for 12 hours
- Primary outcome at 6 months on therapy
- On treatment up to near-adult height
- **To demonstrate pulsatile LUM-201 MOA**

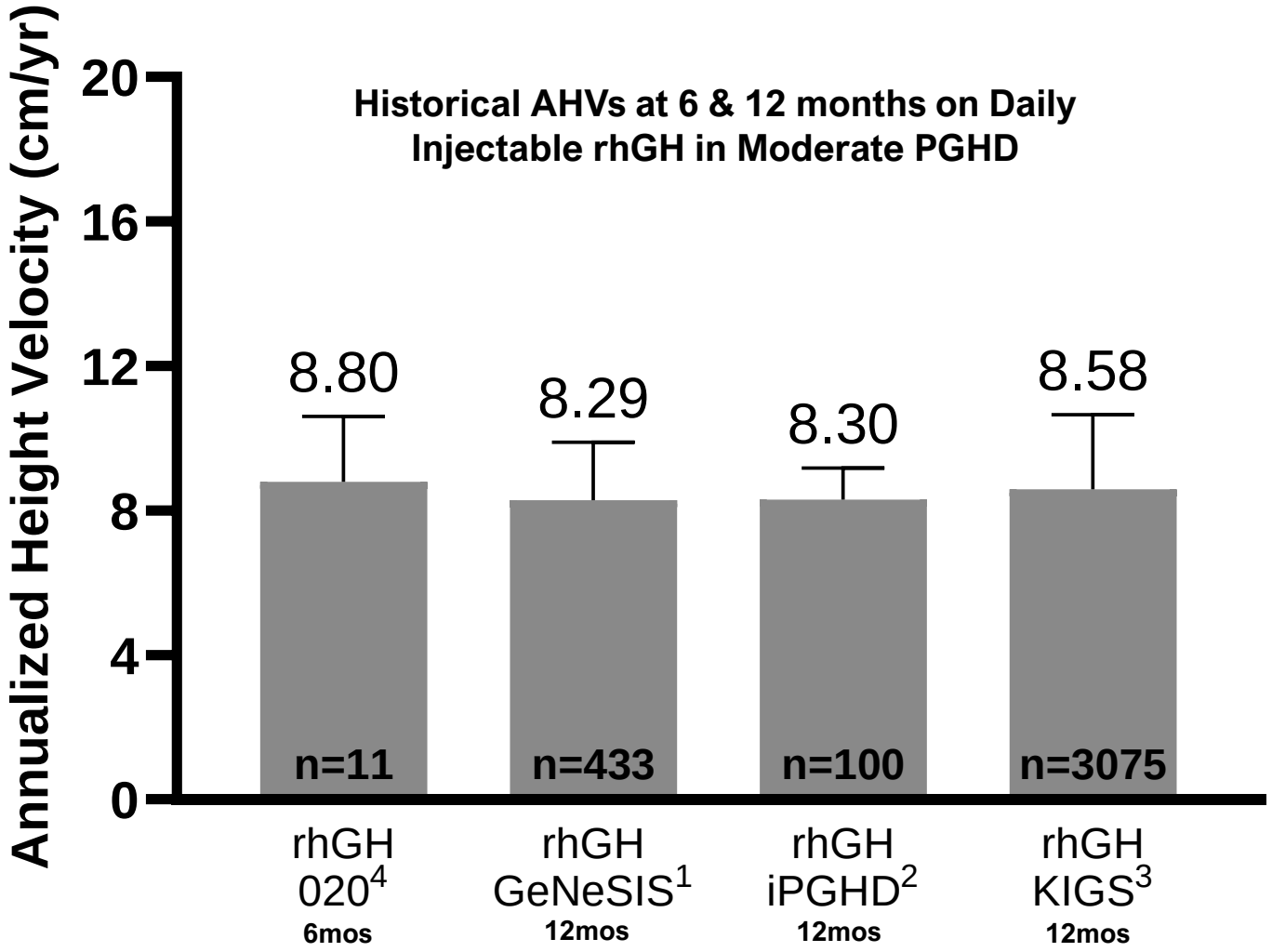
**Primary Outcome Readout: 6-month AHV for All Subjects**

**Additional AHV Data for Subjects at 9, 12, and 18+ Months on Treatment**

****Phase 2 trials are NOT powered for efficacy****

* PEM-positive (PEM+) PGHD patients = PGHD patients with baseline IGF-1 > 30 ng/ml & peak GH ≥ 5 ng/ml from single oral 0.8 mg/kg dose of LUM-201

# Historical rhGH Data Set Expectations for Growth on Therapy in Moderate PGHD




## Historical Datasets for Moderate PGHD

- GeNeSIS[1], iPGHD[2], and KIGS[3] datasets demonstrating AHV at 12 months on rhGH
- Merck 020[4] AHV from 6 months of rhGH
- These trials set precedent for expected growth on rhGH in moderate idiopathic PGHD

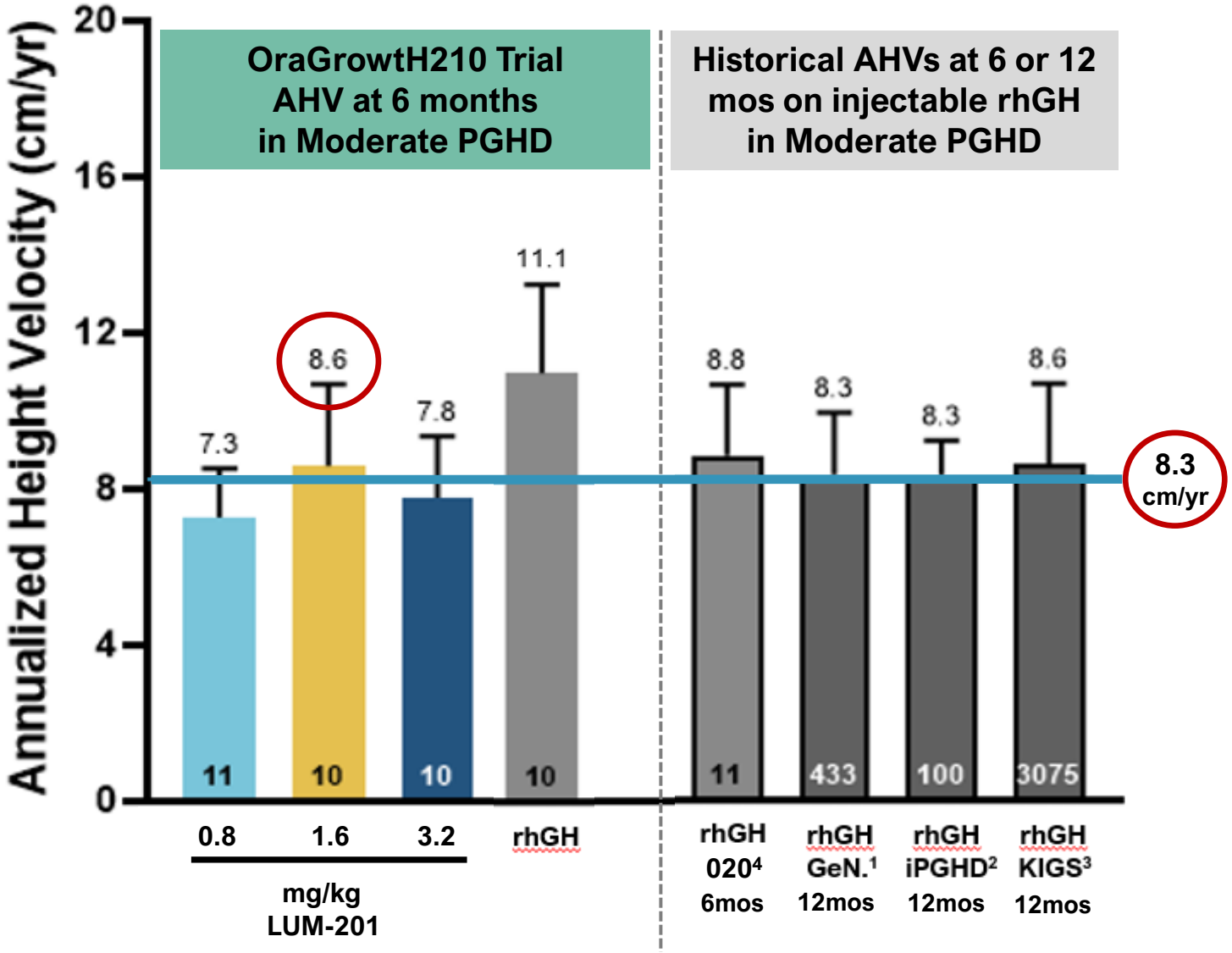
## Expected Growth in OraGrowthH210 Trial

- Prediction for growth in OraGrowthH210 is AHV of ~8.3-8.6 cm/yr on both LUM-201 and rhGH based on historical data

Sources: 1 Blum et al JES 2021, 2 Lechuga-Sancho et al JPEM 2009, 3 Ranke et al JCEM 2010, [4] Bright et al JES 2021.

# Interim OraGrowtH210 Data: LUM-201 Growth in Line with Historical Norms

*rhGH growth not in line with historical norms for moderate PGHD*




**OraGrowtH210 Trial Interim Results**

- LUM-201 1.6 mg/kg/day growth of **8.6 cm/yr** in line with historical data
- rhGH cohort grew faster than expected due to outliers
- Cohort baseline differences contributed to growth variances[1,3]
- Converging baseline characteristics seen at full enrollment should lead to better AHV balance

**AHV disparities should narrow at full data readout**

Sources: [1] Blum et al JES 2021, [2] Lechuga-Sancho et al JPEM 2009, [3] Ranke et al JCEM 2010, [4] Bright et al JES 2021.

# OraGrowtH210 Trial Baseline Characteristics at 50% & 100% Enrollment

| | At 50% enrollment | | | At 100% enrollment* | |
|---|---|---|---|---|---|
| | **LUM-201 1.6 mg** Mean (SD) **N=10** | **rhGH** Mean (SD) **N=10** | | **LUM-201 1.6 mg** Mean (SD) **N=22** | **rhGH** Mean (SD) **N=20** |
| **Age (months)** | 99.3 (28.3) | 90.3 (26.7) | | 95.2 (27.3) | 91.4 (23.3) |
| **Height (cm)** | 114.6 (9.6) | 111.6 (11.9) | | 113.0 (11.0) | 112.3 (10.5) |
| **Height SDS** | -2.35 (0.62) | -2.29 (0.43) | | -2.42 (0.68) | -2.23 (0.41) |
| **IGF-1 SDS** | -1.17 (0.72) | -1.37 (0.48) | | -1.40 (0.57) | -1.39 (0.47) |
| **MPH (cm)** | 166.98 (7.15) | 168.78 (8.85) | | 165.4 (7.4) | 169.1 (8.26) |
| **MPH SDS Δ** | 1.76 (0.60) | 1.76 (0.73) | | 1.69 (0.81) | 1.91 (0.65) |
| **BA Delay (yrs)** | 1.9 (0.5) | 1.8 (1.0) | | 1.8 (0.9) | 1.9 (0.9) |
| **BMI SDS[1]** | -0.35 (0.79) | +0.31 (1.05) | | -0.27 (0.90) | +0.01 (0.95) |

Imbalance between LUM-201 & rhGH arms narrows at full enrollment, which we expect will diminish the rhGH outlier impact

* Preliminary assessment

[1] Yang, et al. Nature Sci Rep 2019, 9(1); 16181

SDS = Standard deviation score MPH = Mid-parental height (Child's target height) MPH SDS delta = (MPH SDS) – (Height SDS) BA = Bone age BMI = Body mass index

# Expectations for a Registrational Phase 3 Trial in Moderate PGHD

*Based on recent peer registrational trials in PGHD*

| | |
|---|---|
| **Projected Design for Phase 3 Trial** | • International multi-center trial<br>• ~200 PEM-positive (PEM+) moderate idiopathic PGHD subjects*<br>• Subjects randomized 2:1 daily oral LUM-201 vs daily injectable rhGH<br>• Stratification by age and 2-3 other factors based on Phase 2 data<br>• 12-month treatment period |
| **Anticipated Endpoints for Phase 3 Trial** | • Primary endpoint: AHV at 12 months on treatment<br>• Non-inferiority AHV margin of ~2 cm between LUM-201 & rhGH arms at 12 months |

* PEM-positive (PEM+) PGHD patients = PGHD patients with baseline IGF-1 > 30 ng/ml & peak GH ≥ 5 ng/ml from single oral 0.8 mg/kg dose of LUM-201

# ENDO 2023 – Session OR21-03

## Dose Responsiveness of LUM-201 as Measured by Acute GH Response and IGF-1 and Annualized Height Velocity (AHV) Measured at 6 Months in the Interim Analysis of the OraGrowtH212 Study in Idiopathic Pediatric Growth Hormone Deficiency (iPGHD)

Cassorla F[1], MD; Román R[1], MD; Johnson M[2], PhD; Smith C[2], MS; Avila A[1], RN; Iñiguez G[1], PhD; Baier I[1], MD; Said D[1], RN; Karpf DB[2], MD; McKew JC[2], PhD; Thorner M[2], MB BS, DSc

OraGrowtH212 TRIAL

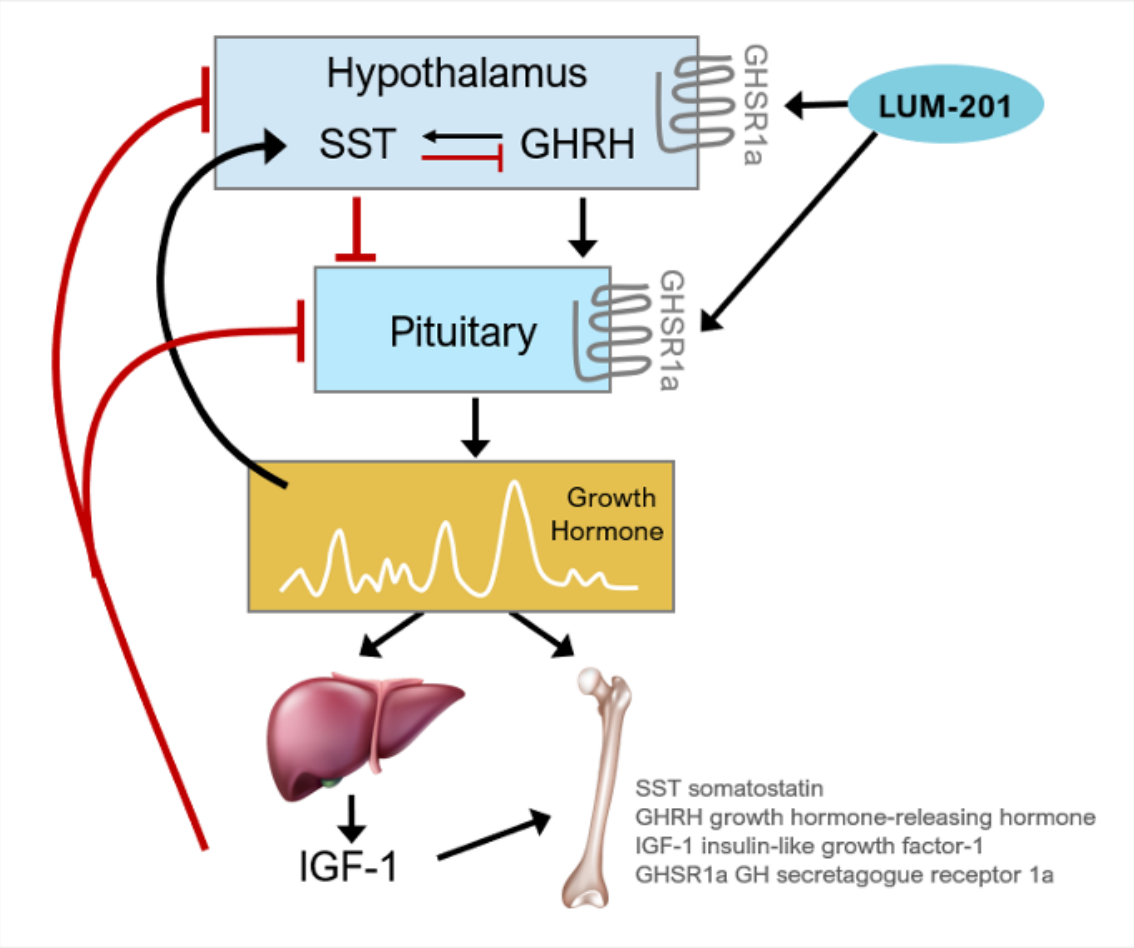
[1]University of Chile, Santiago, Chile
[2]Lumos Pharma, Austin, TX

# Disclosure

Dr. Cassorla is an investigator for clinical studies with LUM-201 at the University of Chile (Sponsor - Lumos Pharma, Inc.) and has previously acted as a consultant for Debiopharm, Pfizer, Merck, Novo Nordisk and 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.

# 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 the potential for hyperstimulation and excessive increases in IGF-1***
- LUM-201 promotes pulsatile GH secretion in a ***selective PGHD Population***

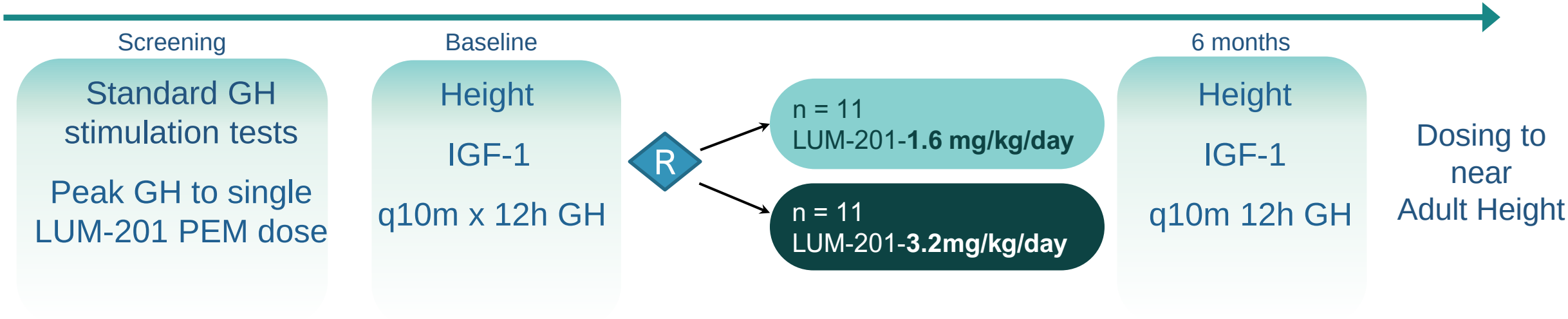
☑ Moderate Idiopathic PGHD - Axis Responsive


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

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

## Naive Idiopathic PGHD Patients

OraGrowth212 TRIAL




**Study Information**

- Open-label study: N = 22
- 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

# Questions

1. Does LUM-201 dose-dependently augment endogenous GH pulses in patients with Idiopathic Pediatric Growth Hormone Deficiency (iPGHD)?

2. Will increased amplitude of GH pulsatility and increase in IGF-1 within normal range improve height velocity?

3. Is the effect on AHV durable out to 12 months?

# Baseline Demographics

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 |

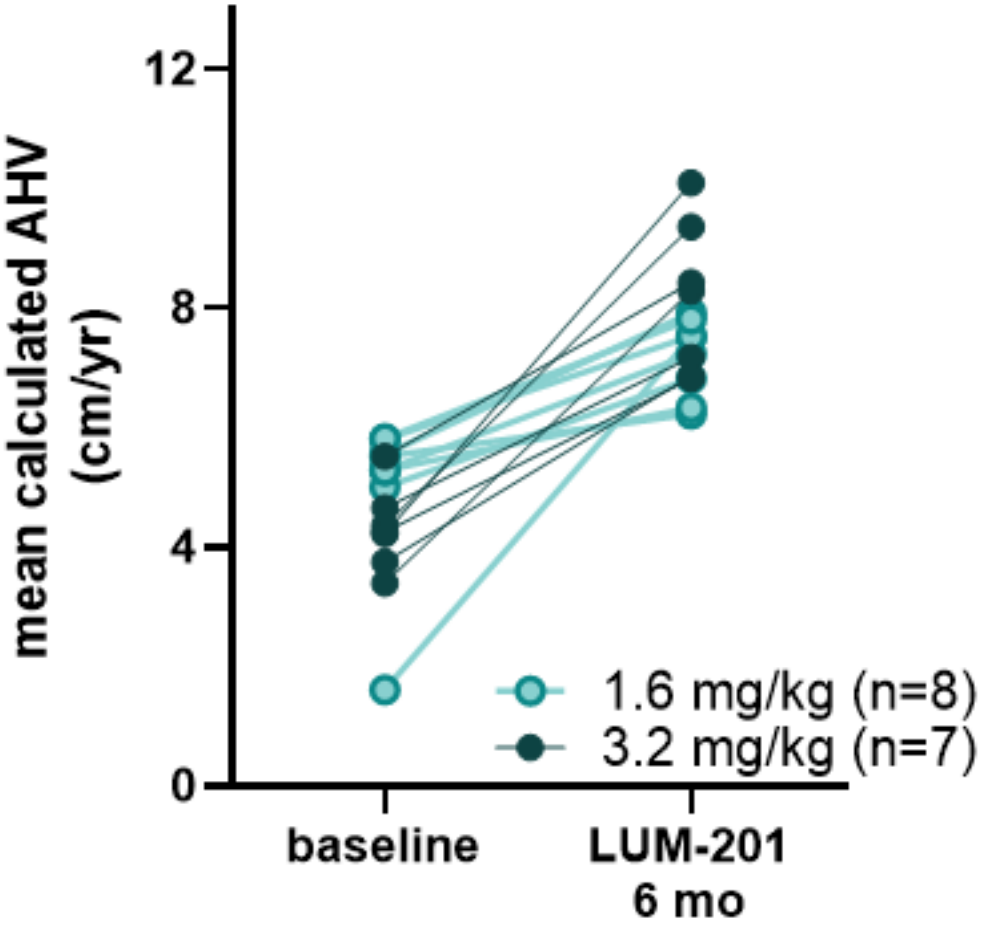
**Differences between the two groups:**

- Slight imbalance in age and gender
- Slight imbalance in delta below MPH, BMI, and bone age delay



KEY: SDS = Standard deviation score MPH = Mid-parental height (Child's target height) MPH SDS Δ = MPH SDS-Ht SDS BA = Bone age BMI = Body mass index

# AHV Before and After 6 months of LUM-201 Treatment



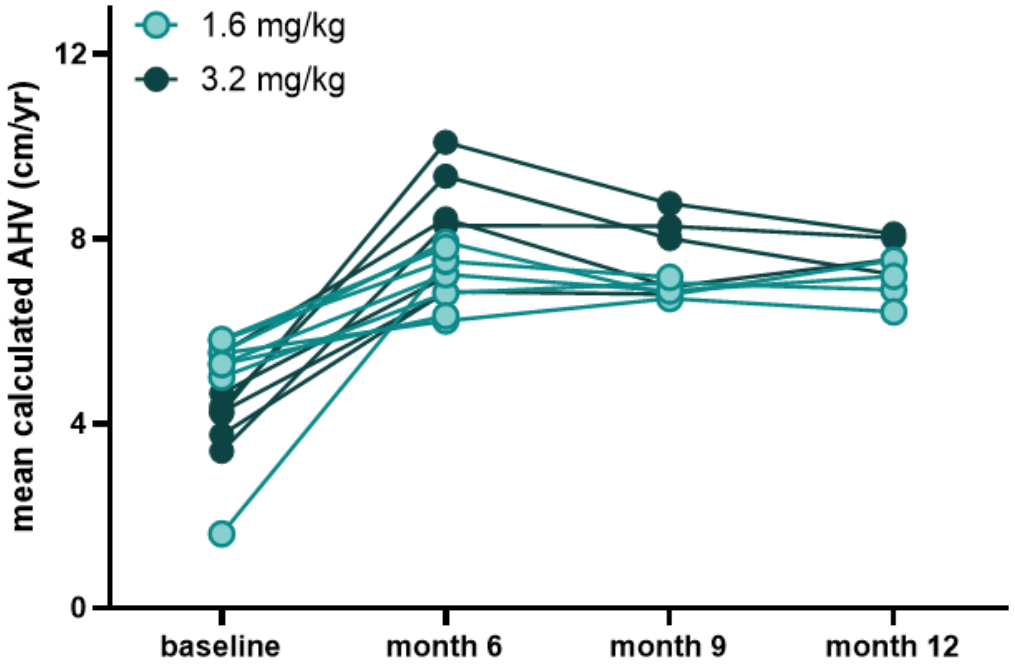

**6-month observations:**

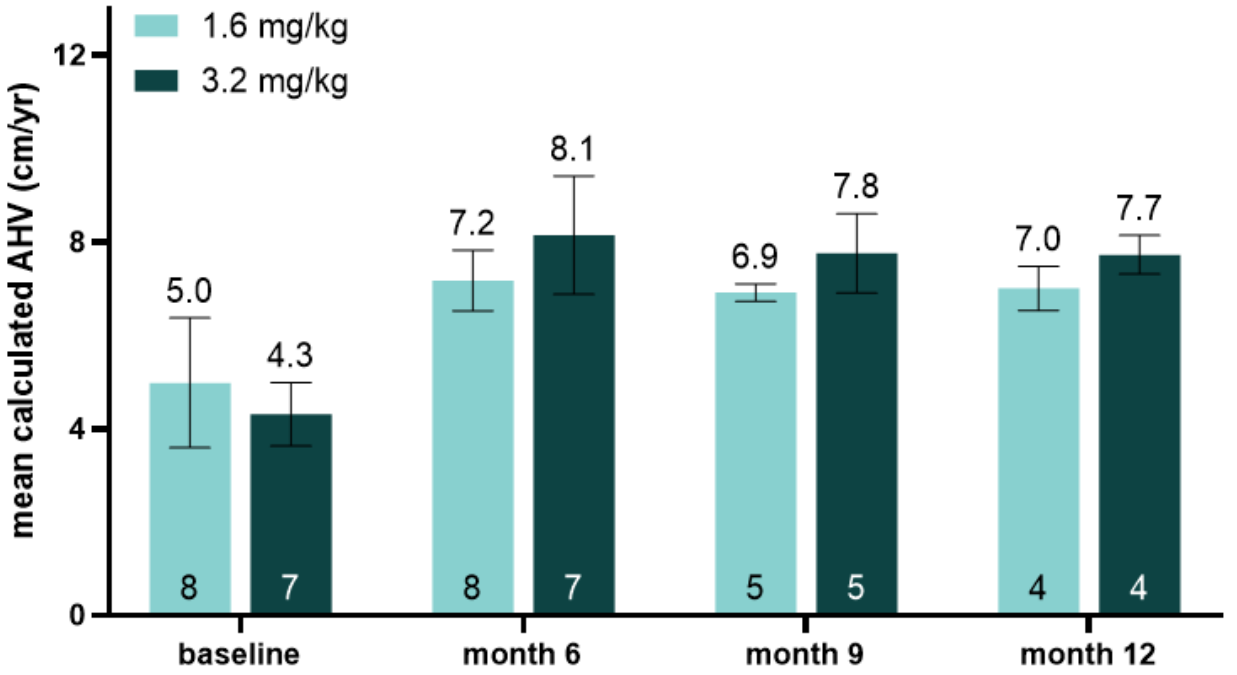
- LUM-201 raised the AHV (growth rate) from baseline after 6 months on therapy for both the 1.6 mg/kg cohort ($p = 0.0006$) and the 3.2 mg/kg cohort ($p < 0.0001$)
- No statistical difference exists between the two cohorts at each timepoint
- As expected, greater growth response was observed in patients with lower baseline height velocity

# Durable Response After 12 Months of LUM-201 Administration

OraGrowtH212 TRIAL

## Mean AHV's in OraGrowtH212 Trial




[1]Ranke, et.al. 2010 JCEM 95(3):1229-1237.

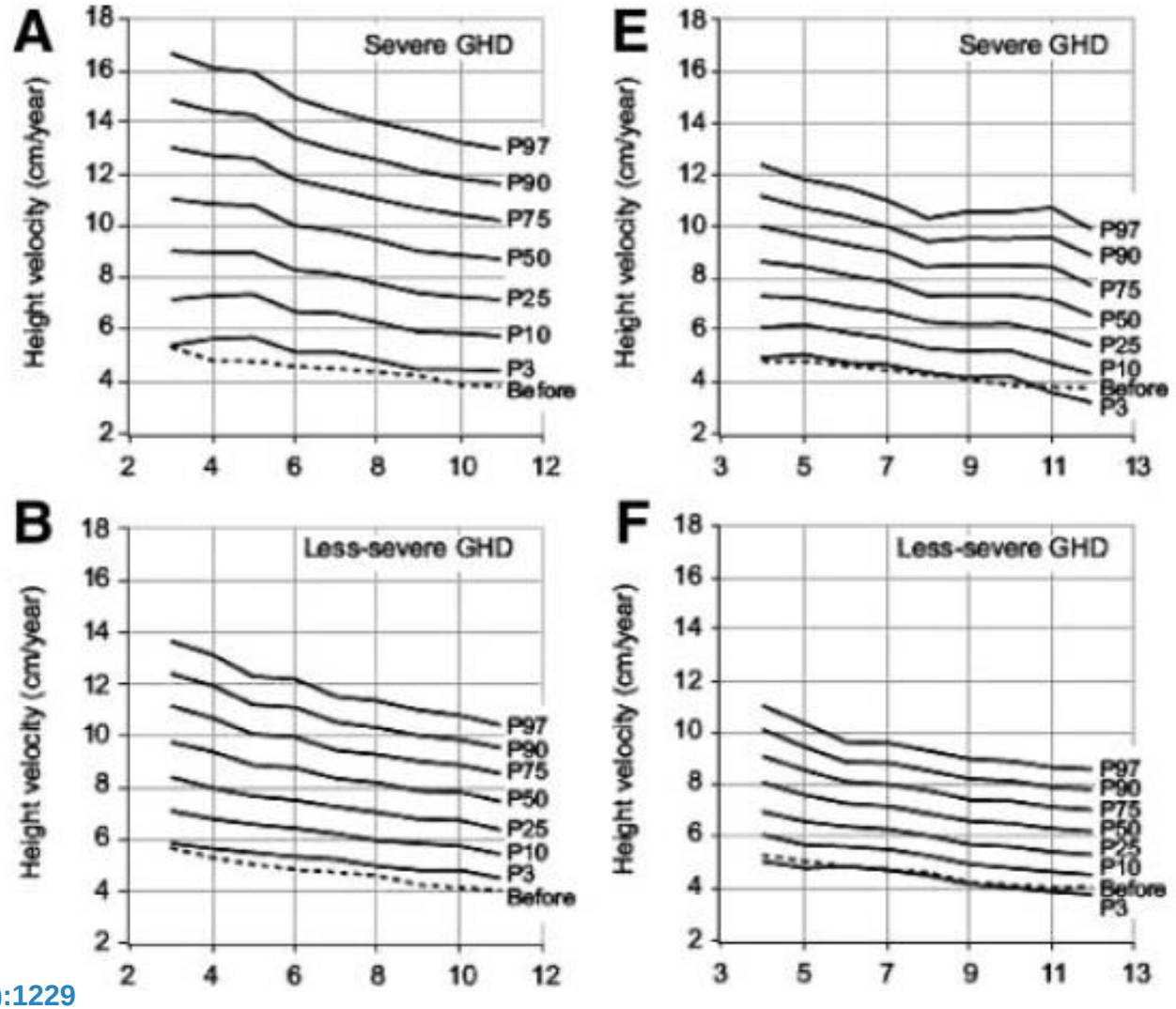
# Height Velocity During Daily rhGH Therapy

OraGrowtH212 TRIAL

First year | Second year

Severe PGHD

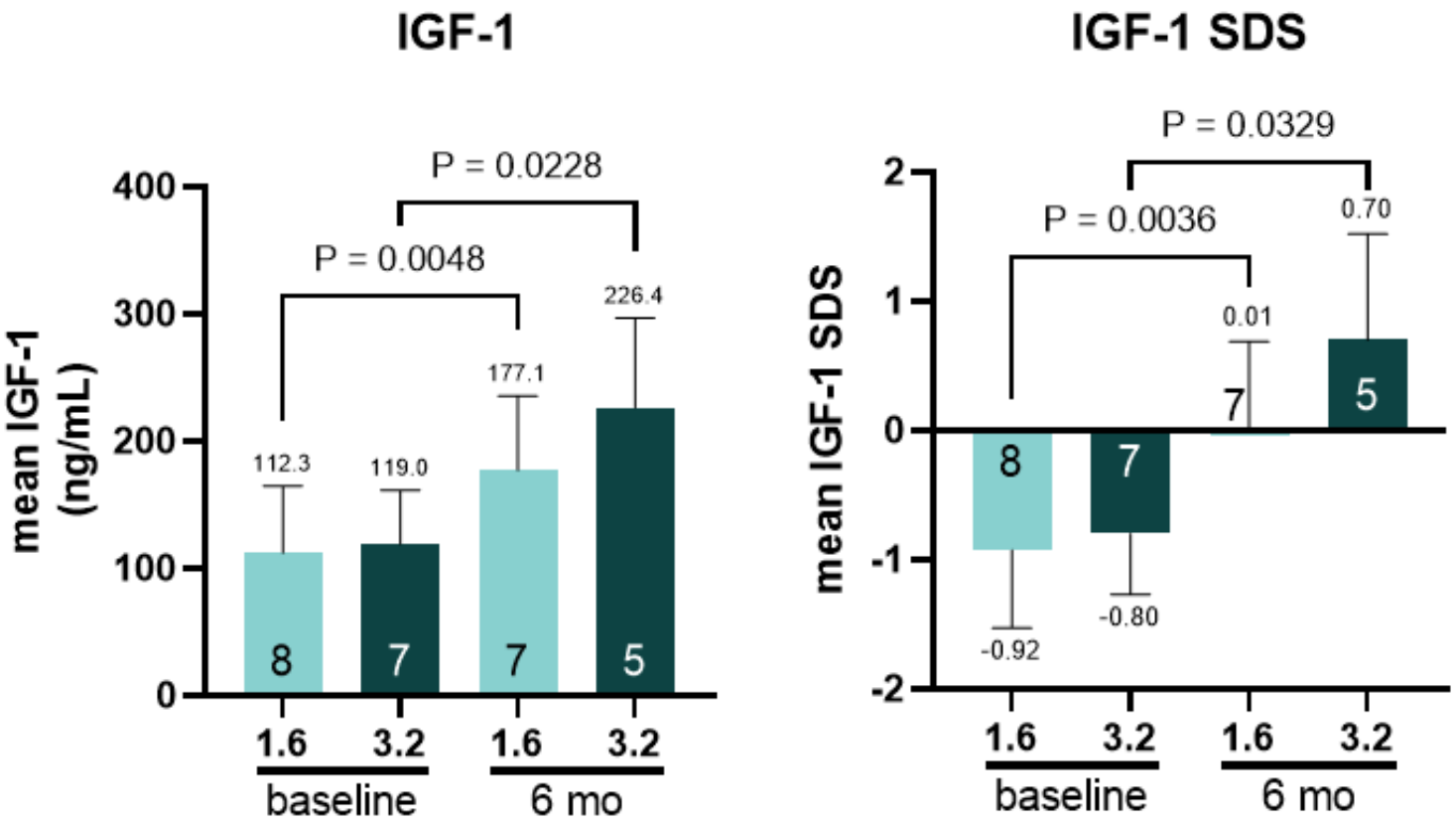
Moderate PGHD




Ranke, et.al. 2010 JCEM 95(3):1229

# IGF-1 Values: Treatment with LUM-201 Increased Serum IGF-1 Concentration and IGF-1 SDS Values

OraGrowth212 TRIAL





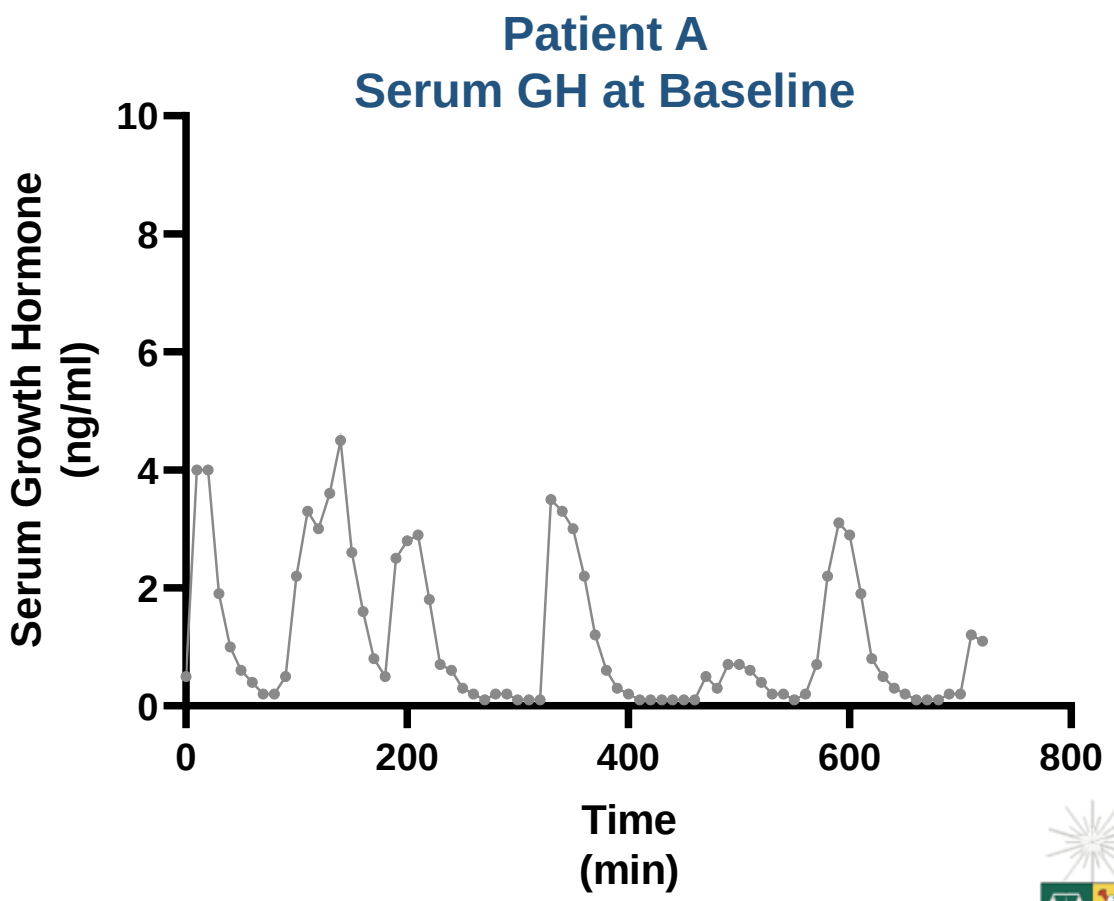


## Conclusions :

- There is a significant increase in **IGF-1 levels that remains within the normal range**
- Based on the MOA of LUM-201, these data support the physiological IGF-1 feedback

# IGF-1, GH Pulsatility, Height Velocity: Patient A **1.6 mg**/kg/day

| | | Baseline | 6 months LUM-201 1.6 mg/kg/d |
|---|---|---|---|
| | IGF-1 (ng/ml) | 179.3 | |
| Q10m 12h GH | $AUC_{0-12}$ (ng*hr/ml) | 798.8 | |
| | Height velocity (cm/yr) | 5.6 | |



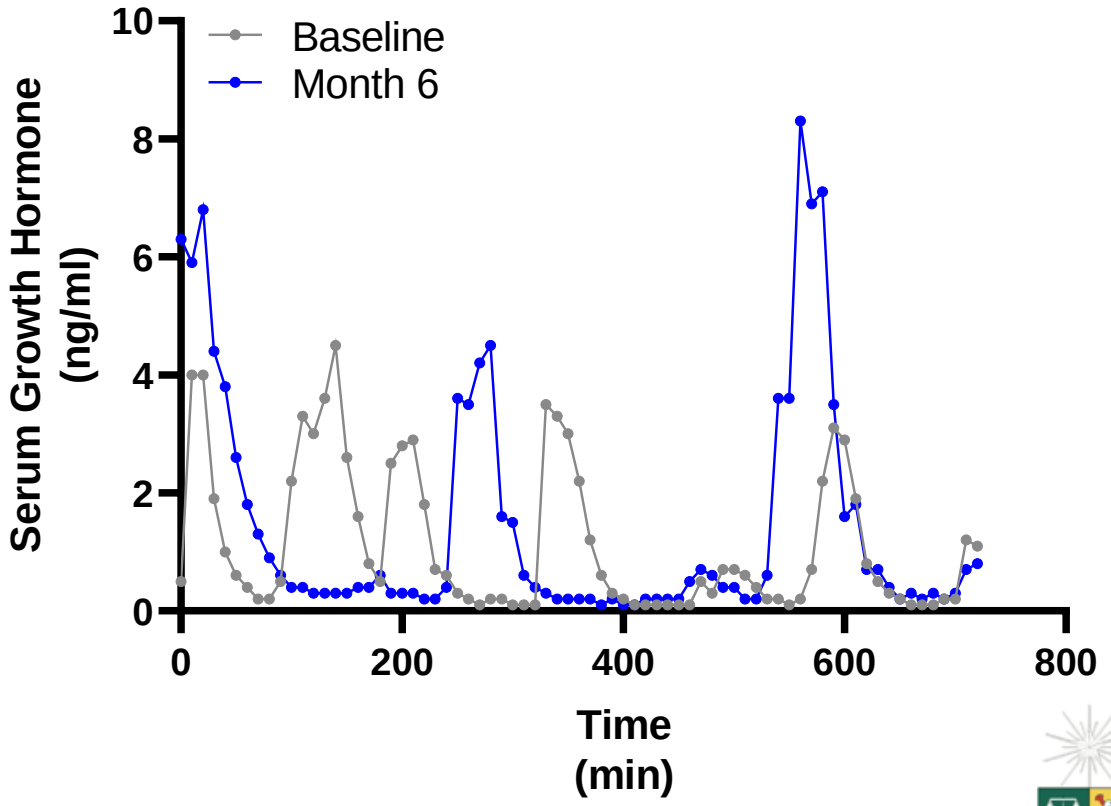
# IGF-1, GH Pulsatility, Height Velocity
# Patient A **1.6 mg**/kg/day

OraGrowth212 TRIAL

| | | Baseline | 6 months LUM-201 1.6 mg/kg/d |
|---|---|---|---|
| | IGF-1 (ng/ml) | 179.3 | 289 |
| | | % change from baseline** | 61% |
| Q10m 12h GH | $AUC_{0-12}$ (ng*hr/ml) | 798.8 | 1064.1 |
| | | % change from baseline** | 33% |
| | Height velocity (cm/yr) | 5.6 | 7.9 |

**Percent change from baseline calculated as: (6mo value – baseline value) / (baseline value)

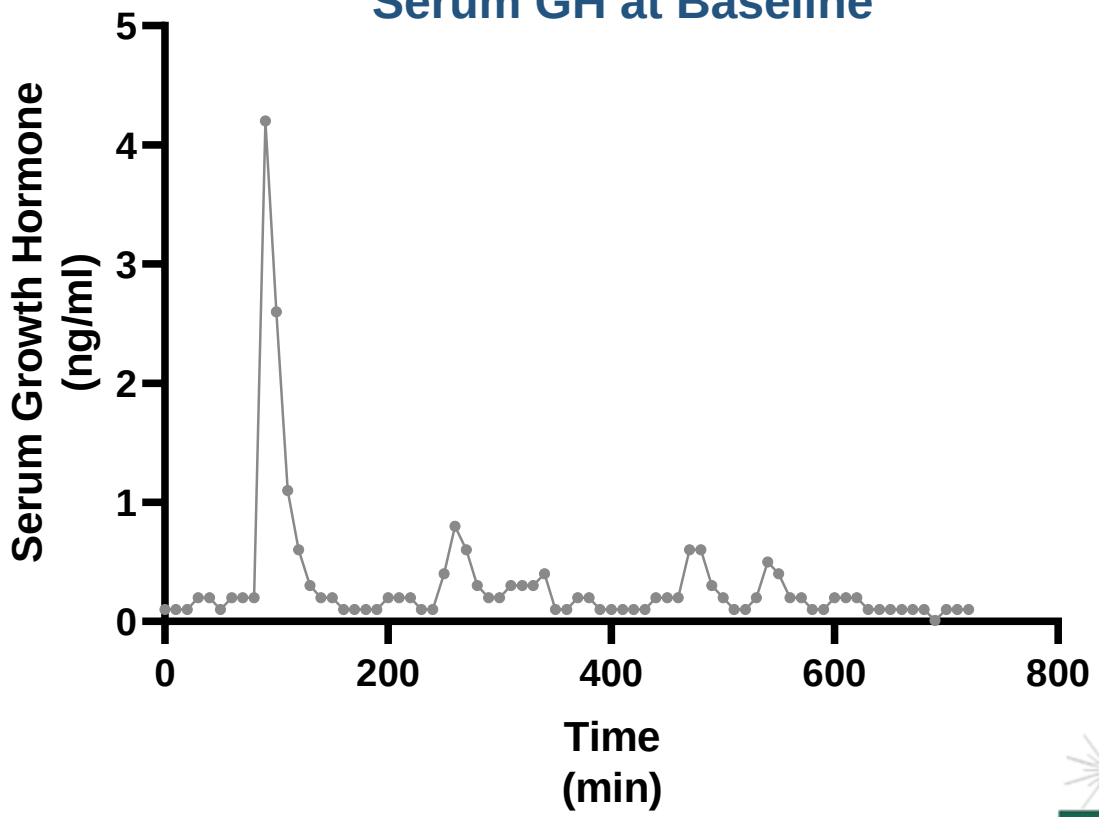
**Patient A**
**Serum GH at Baseline & at 6 months on LUM-201**



# IGF-1, GH Pulsatility, Height Velocity: Patient B **3.2 mg**/kg/day

OraGrowtH212 TRIAL

| | | Baseline | 6 months LUM-201 3.2 mg/kg/d |
|---|---|---|---|
| | IGF-1 (ng/ml) | 48 | |
| Q10m 12h GH | $AUC_{0-12}$ (ng*hr/ml) | 252.9 | |
| | Height velocity (cm/yr) | 4.4 | |



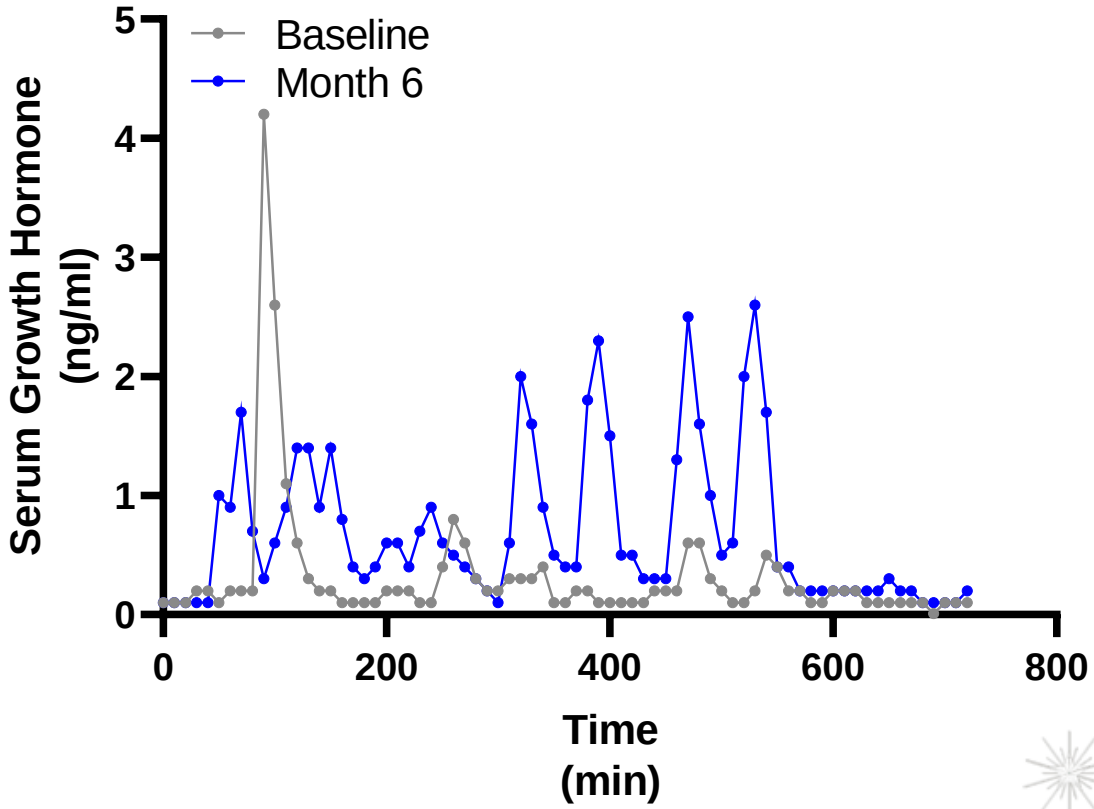
# IGF-1, GH Pulsatility, Height Velocity: Patient B **3.2 mg**/kg/day

OraGrowtH212 TRIAL

| | | Baseline | 6 months LUM-201 3.2 mg/kg/d |
|---|---|---|---|
| | IGF-1 (ng/ml) | 48 | 111 |
| | | % change from baseline** | 131% |
| Q10m 12h GH | $AUC_{0-12}$ (ng*hr/ml) | 252.9 | 481.8 |
| | | % change from baseline** | 91% |
| | Height velocity (cm/yr) | 4.4 | 9.4 |

**Percent change from baseline calculated as: (6mo value – baseline value) / (baseline value)

**Patient B**
**Serum GH at Baseline & at 6 months on LUM-201**



# Interim Analysis Safety Profile

OraGrowth212 TRIAL

## Safety Profile:

- No treatment-related Serious Adverse Events (SAEs) or Severe AEs
- No meaningful safety signals observed in either laboratory values, adverse event data, or in electrocardiogram values.

## Most Common AEs (% of subjects) noted are:

- Transient increased appetite (76.5%)
- Pain in extremity (17.6%)
- Arthralgia (11.8%)
- Abdominal pain (5.9%)
- Influenza (5.9%)

## Safety Conclusion:

- At time of interim analysis, LUM-201 was well tolerated and showed no significant safety signals

# Questions

1. Does LUM-201 dose-dependently augment endogenous GH pulses in patients with idiopathic Pediatric Growth Hormone Deficiency (iPGHD)?

2. Will increased amplitude of GH pulsatility, driving increased IGF-1, improve height velocity?

3. Is the effect on AHV durable out to 12 months?

# Conclusions

- Based on Interim Analysis data, OraGrowtH212 data demonstrates that growth acceleration is durable through 12 months in our study population, pre-pubertal, treatment naïve PGHD patients.
- No statistical difference exists between the cohorts at any time point.
- Due to some baseline imbalance, the optimal dose cannot be determined from this data set.
- We plan to continue the OraGrowtH212 Trial until near adult height.
- The observed growth is in line with rhGH historical growth of 8.3-8.6 cm (KIGS [1], GeNeSiS [2]) in this moderate idiopathic PGHD population.

Sources: [1] Blum et al JES 2021, [2] Ranke et al JCEM 2010

# University of Chile, Santiago

## Institute of Maternal and Child Research Pediatric Team

# 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.

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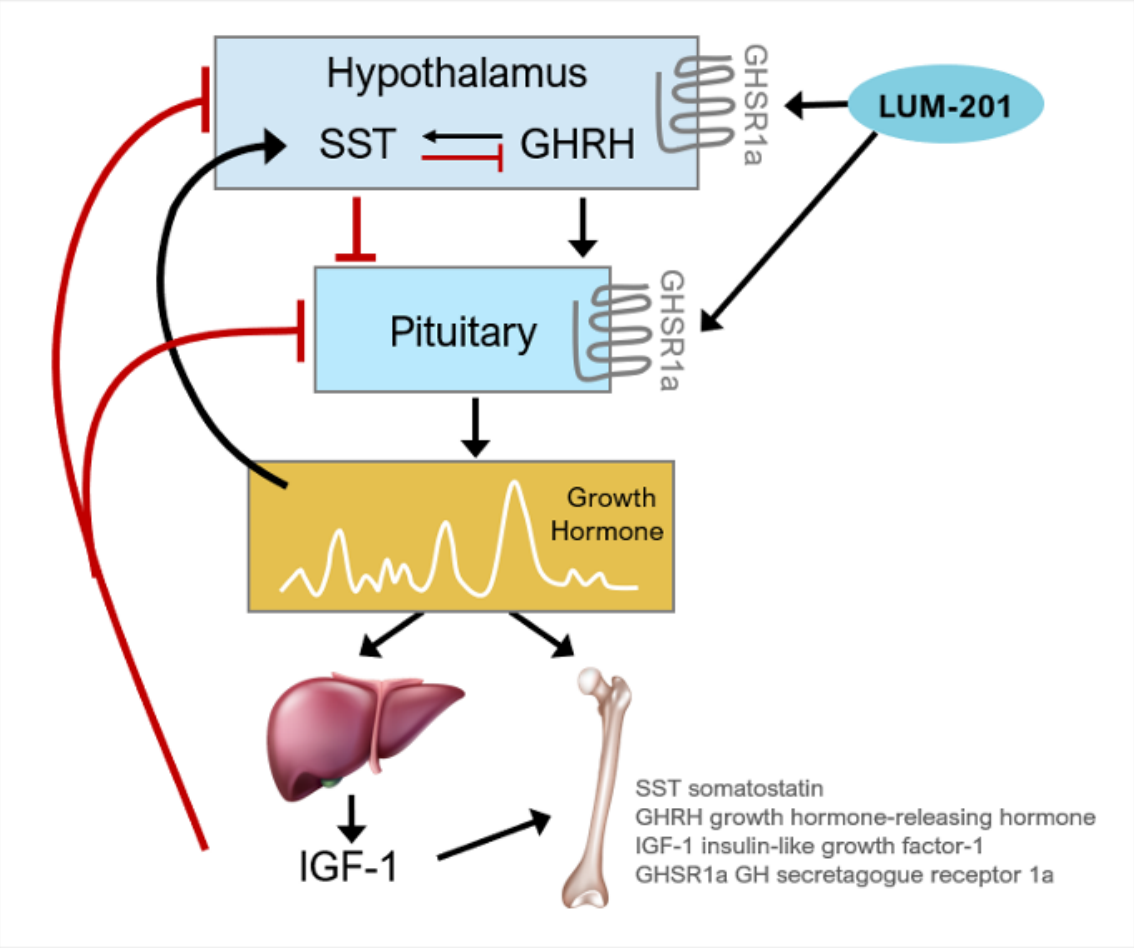
# Objective of the Presentation

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 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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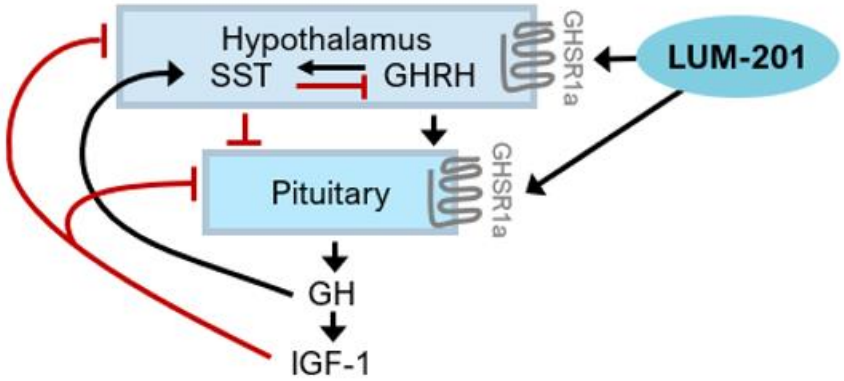
# Single Stim Dose of LUM-201 Identifies PEM+ Responders

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

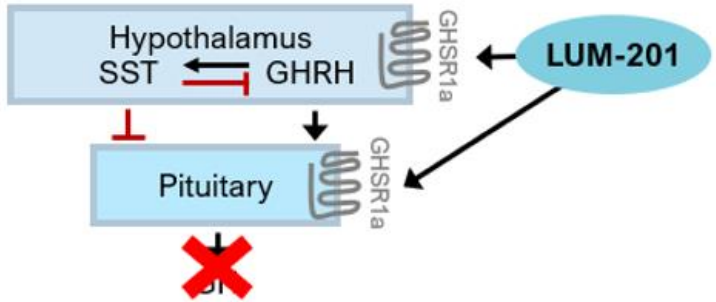



**Responders to LUM-201**

**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**

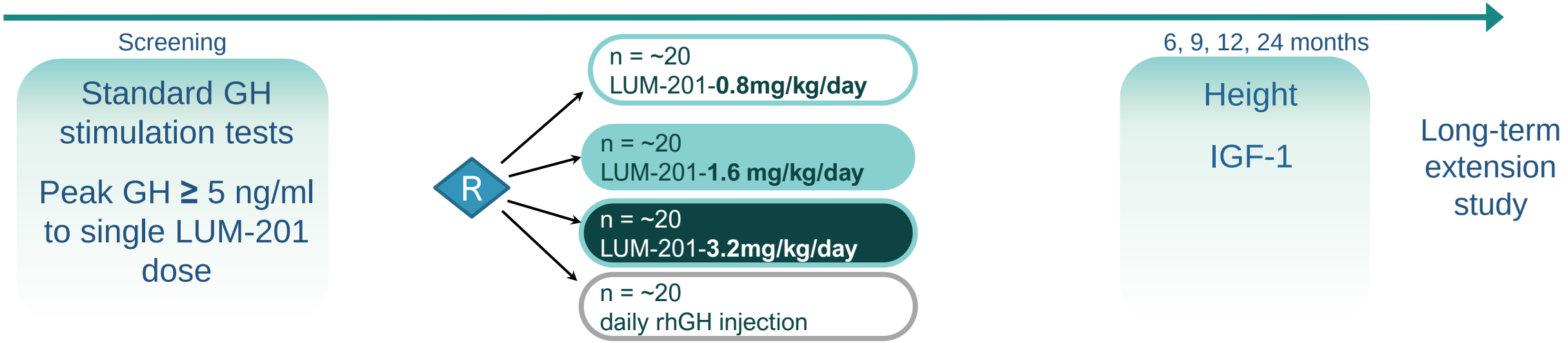
**Severe / Organic PGHD**
**PEM Negative**
**~40% of total PGHD population**

1 Blum 2021 JES

# 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)

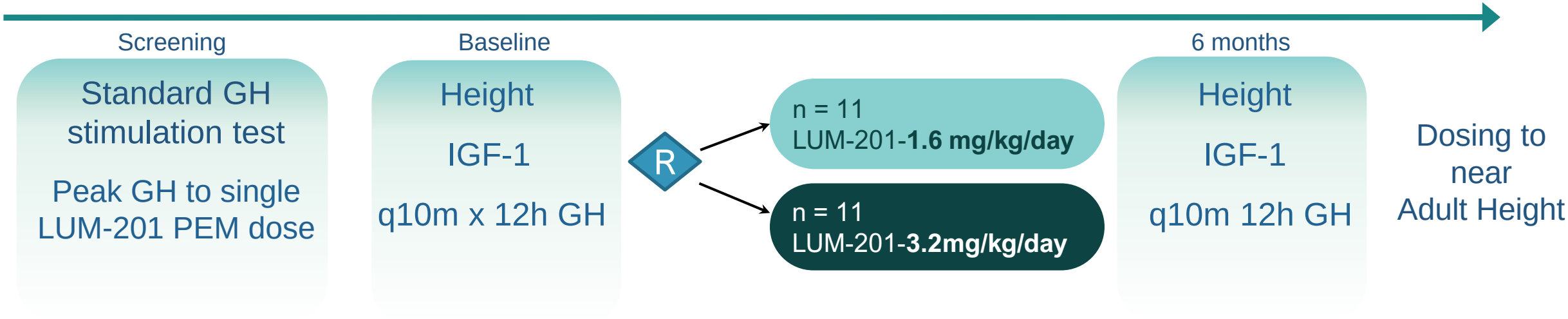
**Goals:**

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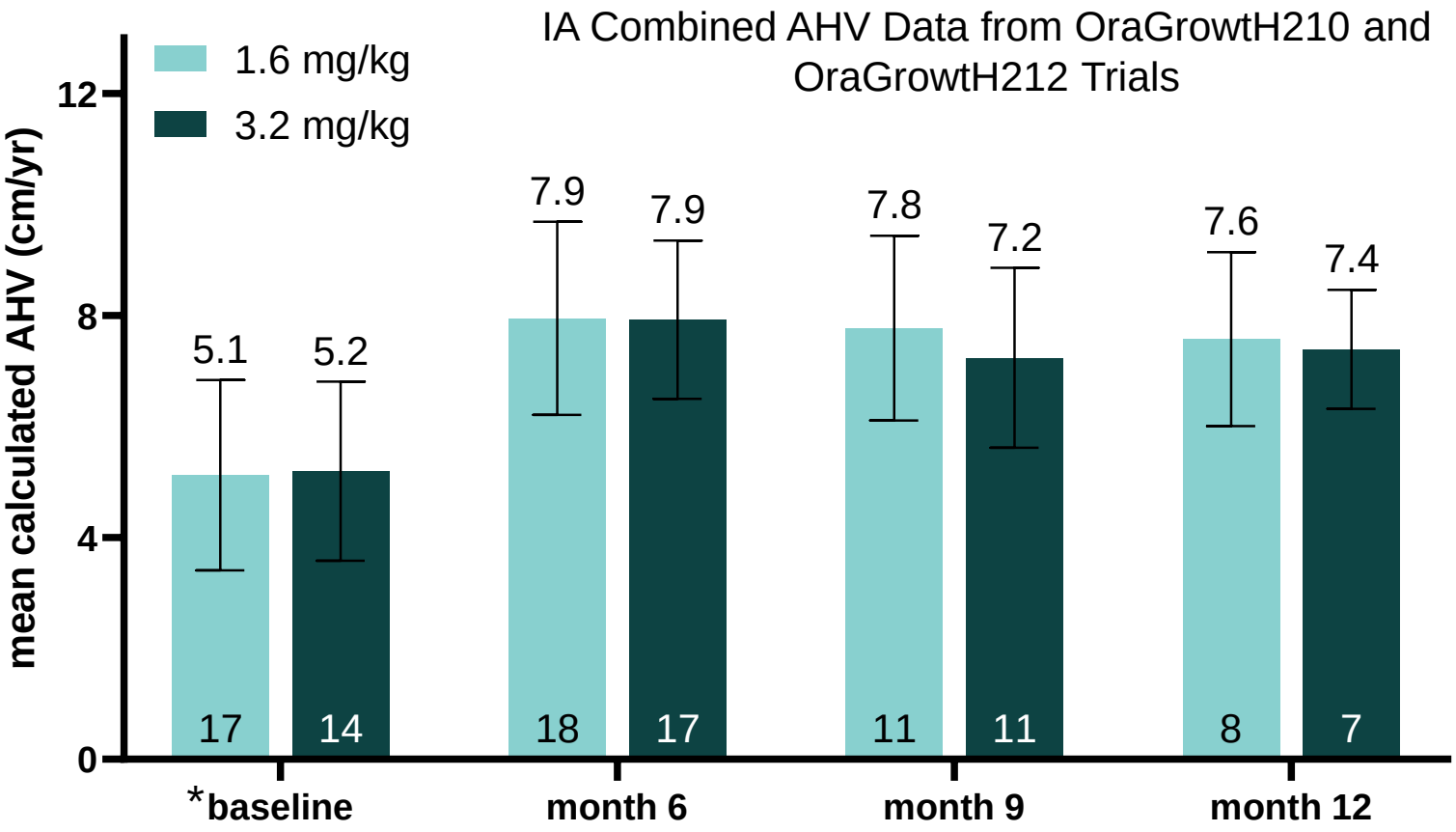
# Annualized Height Velocity of 2 Doses Show Durable Response from 6-12 Months




## 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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# Questions & Answers