



#### Forward Looking Statements

This presentation contains forward-looking statements of Lumos Pharma, Inc. 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. This law that, in part, gives us the opportunity to share our outlook for the future without fear of litigation if it turns out our predictions were not correct.

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 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 the plan to have an end-of-phase 2 meeting with the FDA in the first half of 2024 and the anticipated initiation of a Phase 3 program in the second half of 2024, our Phase 2 data providing a clear path to Phase 3 in PGHD, that PEMs enrich trials for patients likely to respond to LUM-201, the expected benefits to LUM-201, 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. 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 including risks related to the continued analysis of data from our LUM-201 Trials, the timing and outcome of our future interactions with regulatory authorities including our end of Phase 2 meeting with the FDA, the timing and ability of Lumos to raise additional equity capital as needed to fund our Phase 3 Trial, our ability to project future cash utilization and reserves needed for contingent future liabilities and business operations, the ability to structure and initiate our Phase 3 trial in an effective and timely manner, any statements regarding potential enrollment timelines, the ability to successfully develop our LUM-201 product candidate, the effects of pandemics, other widespread health problems or military conflicts including the Ukraine-Russia conflict and the Middle East conflict and other risks that could cause actual results to differ materially from those matters expressed in or implied by such forward-looking statements including information in the "Risk Factors" section and elsewhere in Lumos Pharma's Quarterly Report on Form 10-Q for the period ended September 30, 2023, as well as other reports filed with the SEC including our subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. All of these documents are available on our website. Before making any decisions concerning our stock, you should read and understand those documents.

We anticipate that subsequent events and developments will cause our views to change. We may choose to update these forward-looking statements at some point in the future, however, we disclaim any obligation to do so. As a result, you should not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation.

3.7.2024

### 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
- LUM-201 acts within natural endocrine pathway, differentiated from injectable therapies
- IP protection through 2042 in the US for novel formulation<sup>1</sup>



### Pipeline in a Product

- Worldwide injectable market for GHD disorders is ~\$4.7 billion\*
- Market for Pediatric GHD (PGHD), initial oral LUM-201 indication, is ~\$1.5 billion\*



### Late-stage Trials in PGHD

- Topline data from two Phase 2 OraGrowtH Trials in PGHD met all endpoints
- Growth on 1.6 mg/kg LUM-201 in line with historical benchmarks and expectations
- Ph 2 data provided preliminary validation of PEMs to identify likely LUM-201 responders\*\*



### Program Advancement

- Full 12-Month Data from OraGrowtH210 Trial to be announced in 2Q 2024
- End-of-Phase 2 meeting with FDA anticipated 2Q 2024 to review Phase 3 program
- Initiation of Phase 3 trial anticipated 4Q 2024



#### Potential for 1st oral therapeutic to disrupt injectable market for GHD

PGHD = Pediatric Growth Hormone Deficiency

<sup>&</sup>lt;sup>1</sup>Notice of Allowance from USPTO received March 14, 2024, for novel formulation patent, extending US intellectual property protection through November 2042

<sup>\*</sup>Internal Lumos GH Market Assessment, based on: EvaluatePharma consensus estimates, GlobalData, "GHD Forecast", 2021/04; Grand View Research, "hGH Market Analysis and Segment Forecast" \*\*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

### Management – Significant Clinical Development and Commercial Experience





Richard Hawkins Chairman & CEO

Developed Growth Hormone (GH) Receptor Antagonist for Acromegaly at Sensus (sold to Pfizer). Built one of the first contract recombinant protein manufacturing facilities (Covance Biotechnology). Founder of Pharmaco, a pioneer in the contract research organization sector (merged with PPD).



John McKew, PhD
President & Chief Scientific Officer

Prior VP of Research at aTyr Pharma – led team advancing protein-based therapeutics for rare diseases. Former Scientific Director, NIH - National Center for Advancing Translational Science (NCATS) and Therapeutics for Rare and Neglected Diseases (TRND).



Lori Lawley, CPA
Chief Financial Officer

Former SVP, Finance and Controller at Lumos Pharma. Previously, SVP, Finance and Member of the Office of the CEO of NewLink Genetics. Prior to that, Senior Manager in Assurance Services at Ernst and Young.



Pisit "Duke" Pitukcheewanont, MD
Chief Medical Officer

Pediatric endocrinologist and Professor, Clinical Pediatrics, Keck School of Medicine, USC. President, Human Growth Foundation. Former VP Medical Affairs and VP Global Medical Ambassador & Medical Education at Ascendis Pharma; project: long-acting TransCon GH. Former Advisory Board member at Pfizer, Ipsen, Alexion, Ultragenyx, Pharmacia, Serono, others.



Aaron Schuchart, MBA Chief Business Officer

Former Chief Business Officer of Aeglea BioTherapeutics. Former leadership roles in Business Development, Strategy, and Finance at Coherus Biosciences, Novartis Diagnostics/Grifols, and Amgen.



#### LUM-201 Program Pipeline

	Study	Pre-Clinical	Phase 1	Phase 2	Phase 3	Status
	Dose-finding trial	OraGrew TRIAL	tH210			Phase 2 Topline Data: Primary and secondary endpoints met (Nov 2023)
LUM-201 (Ibutamoren)	Long-term extension	OraGrou —— TRIAL	tH211			Long-term extension study for OraGrowtH Trials: Ongoing enrollment of patients from Phase 2 trials
in Moderate PGHD*	PK/PD trial	OraGrew TRIAL	tH212			Phase 2 Topline Data: Primary and secondary endpoints met (Nov 2023)
	Switch trial	OraGrew Trial	tH213			Switch trial evaluating LUM-201 in subjects from rhGH arm of OraGrowtH210 Trial: Ongoing
LUM-201 in NAFLD**	Phase 2 pilot trial	MGH pilot tr	ial***			Pilot trial initiated by Mass Gen Hospital (MGH) evaluating LUM-201 in NAFLD: Enrolling

**Lumos Pharma is evaluating additional indications for LUM-201 for Phase 2 studies** 

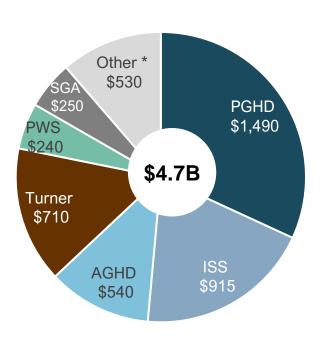
<sup>\*</sup> PGHD Pediatric Growth Hormone Deficiency \*\*NAFLD Non-Alcoholic Fatty Liver Disease

<sup>\*\*\*</sup>Trial supported by prior data evaluating rhGH in NAFLD: (ENDO 2022) JES, Volume 6, Issue Supplement\_1, November-December 2022, Page A525, and JES, June 2023.

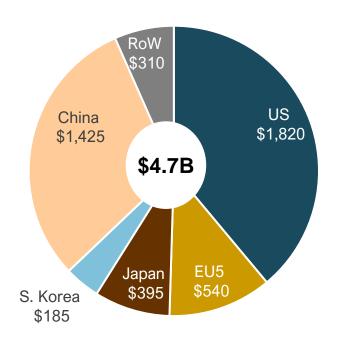


#### rhGH Market Gross Sales - by Indication and by Region

2022 rhGH Global Sales by Indication (Gross, Including China, US\$ MM)



2022 rhGH Global Sales by Region (Gross, US\$ MM)



Global rhGH Market expected to grow at 6% CAGR through 2030, reaching \$5.9B

Key Growth Drivers

- Long-acting rhGH products addressing limitations of daily rhGH treatment burden
- Growing awareness about GHrelated diseases
- Increasing healthcare access and spend in developing regions

Key Hurdles

- Very mature market
- Pricing pressures
- Inconsistent reimbursement policies

<sup>\*</sup>Includes ~\$350M in China sales, indication undisclosed, and ~\$65M in Japan sales, Other or Undetermined; also includes global sales for other short stature syndromes such as Noonan Syndrome, SHOX deficiency, cancer cachexia, etc.

Source: Internal Lumos GH Market Assessment, based on: EvaluatePharma consensus estimates, GlobalData, "GHD Forecast", 2021/04; Grand View Research, "hGH Market Analysis and Segment Forecast", updated 2022 Q1; IQVIA/MIDAS; Japan Pricing Research (Satoru GK, 2023); Regional market participant interviews; Lumos/Akrolyth Analysis

### Pediatric Growth Hormone Deficiency (PGHD) - Conversion from Injection to Oral

#### What is PGHD?

### Inadequate secretion of growth hormone during childhood

- · Majority of cases are moderate
- Slower physical growth
- Negative effect on metabolic processes
- Incidence ≈ 1:3500<sup>1</sup>

#### **Current Treatment**

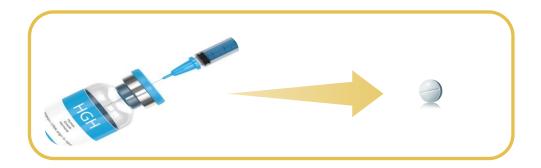
#### Injectable therapies are only options

- Daily, subcutaneous injections of recombinant human growth hormone (rhGH) represent standard of care
- Weekly rhGH injections are entering the market

#### **Unmet Need**

### Standard treatment is ~2,500 daily injections over multi-year period

- · Injections can be painful and burdensome
- Missed doses lead to suboptimal growth<sup>2,3</sup>
- Initial market research supports oral therapy vs weekly injections



#### An established market is now primed for the first oral alternative

<sup>3</sup> Cutfield 2011 PLOS ONE

<sup>&</sup>lt;sup>1</sup> GlobalData EpiCast Report for Growth Hormone Deficiency Epidemiology forecast to 2026

<sup>&</sup>lt;sup>2</sup> Rosenfeld 2008 Endocrine Practice



#### Market Research: Daily Oral Therapeutic Preferred Over Weekly Injectable

Consideration	Market Research Findings <sup>1</sup>
Unmet Need	Non-injectable (oral) therapy; Less frequent administration of injectable therapy
Preference	Vast majority of physicians & caregivers surveyed prefer daily oral tablet over weekly injectable
MOA	Favorable impression regarding LUM-201 affecting natural physiology vs bolus rhGH treatment
Treatment Decisions	Collaborative between physicians and caregivers
Payer Decisions	Price policies in place for category – small molecule COGS should provide attractive margins

#### **Interview Question:**

If a daily oral secretagogue and a weekly rhGH injectable product were both FDAapproved and available for use, which product would you prefer?



<sup>&</sup>lt;sup>1</sup> Initial Primary Research of PGHD Market conducted for Lumos by Triangle Insights. Physicians N = 20. Caregivers N = 9.



#### Goal of All Hormone Replacement Therapy is to Normalize Hormone Levels LUM-201 Shares the Same Purpose

#### Primary aim of endocrine therapy:

- Reestablish hormonal equilibrium through hormone replacement treatments
  - A well-established practice with cortisol, thyroid hormone, and gonadal steroids

#### **Extending this principle to Growth Hormone (GH) therapy emphasizes:**

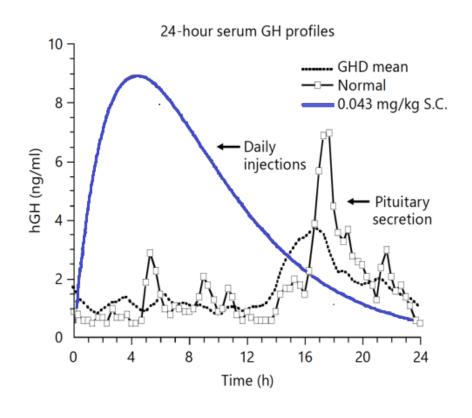
- Importance of *natural* GH secretion, IGF-I production, and restoration of typical growth patterns
- Avoidance of supraphysiological recombinant human Growth Hormone (rhGH) dosing whenever feasible
- Acceptability and convenience of oral therapies to reduce the caregiving burden, particularly in cases where extended therapy is necessary

#### Goal of All Hormone Replacement Therapy is to Normalize Hormone Levels LUM-201 Shares the Same Purpose



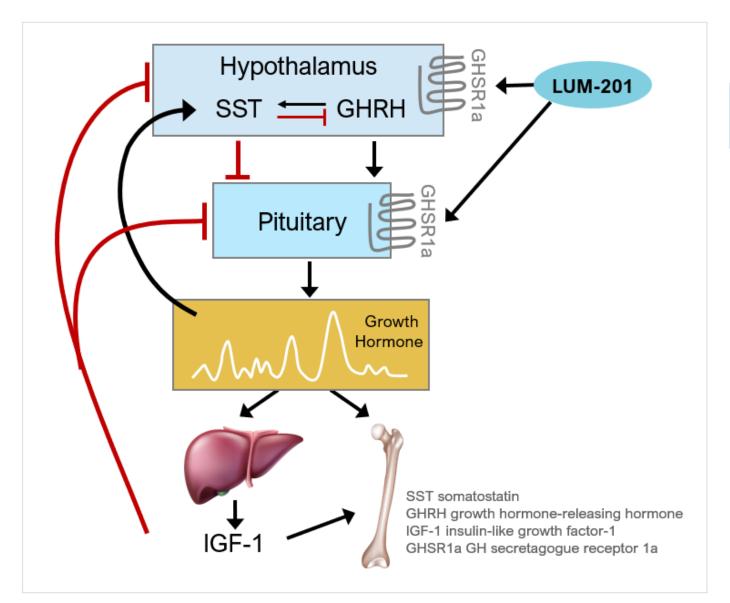
#### **Principles of LUM-201 Therapy:**

- Achieve a sustained improvement in growth velocity that leads to the normalization of final height
- Avoid unnatural trajectory observed with bolus rhGH treatment of rapid catch-up growth followed by rapid decline in annual growth rate
- Strategy supports the *physiological* increase in endogenous GH secretion during puberty, thereby facilitating a more natural progression of growth





#### LUM-201 Stimulates Natural Growth Hormone Secretion



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

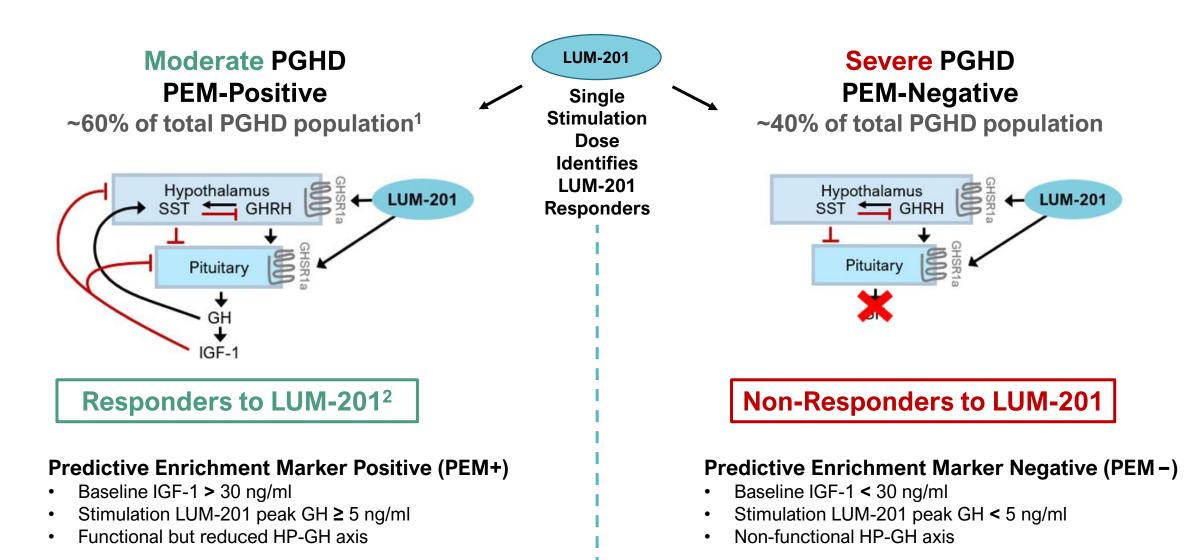
- LUM-201 is an <u>oral</u> GH secretagogue\*
- Acts on specific receptors in hypothalamus and pituitary to stimulate release of GH<sup>1</sup>
- Increases the amplitude of natural pulsatile GH secretion, <sup>2,3</sup> normalizing GH levels after 6 months on therapy<sup>4</sup>
- LUM-201 stimulated GH release regulated by natural GH/IGF-1 feedback mechanisms
- Differentiated mechanism versus exogenous injection of recombinant human growth hormone (rhGH) products

<sup>&</sup>lt;sup>1</sup> Howard 1996 Science <sup>2</sup> Nass 2008 Ann Intern Med <sup>3</sup> Chapman 1997 J Clin Endocrinol Metab <sup>4</sup> Supported by Lumos Pharma Topline Phase 2 Data \* GH secretagogue = molecule

<sup>11</sup> that stimulates the secretion of growth hormone (GH)

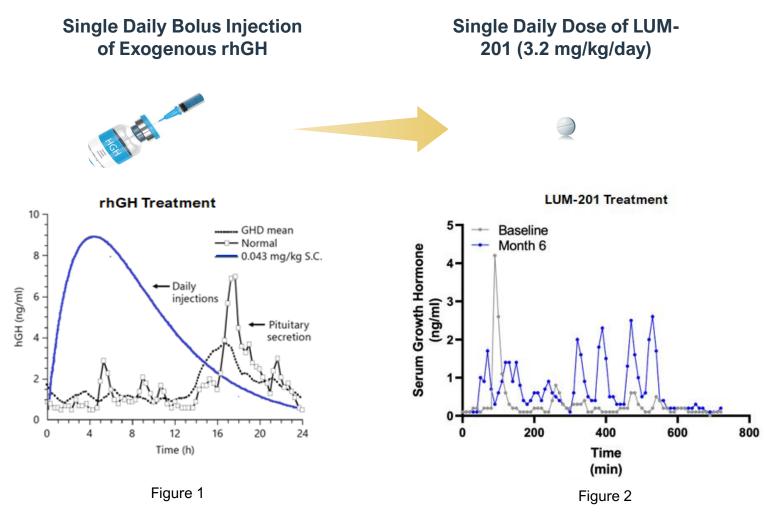
#### PEMs Enrich Trials for Patients Likely to Respond to LUM-201







#### LUM-201 Augments Endogenous Pulsatile Release of Growth Hormone



#### **LUM-201 Value Proposition**

- Daily oral therapy
- Normalizes GH and IGF-1 levels through increase in endogenous pulsatile release of Growth Hormone levels
- Consistent PD effect over 24 hours\*
- MOA avoids risk of IGF-1 excursions.
- Clean safety profile with >1,300 patients treated to date

Figure 1: Advanced Therapies in Pediatric Endocrinology and Diabetology. Endocr Dev. Basel, Karger, 2016
Figure 2: Cassorla, F, et al. IMPE, March 2023; GH concentrations sampled every 10 minutes for 12-hour period at baseline and after six months of daily oral treatment
\* Merck 020 study



### Program History and Rationale for Phase 2 Strategy

Merck previously developed LUM-201 as an anti-aging drug

- >1,200 subjects studied, primarily elderly adults
  - √ GH Levels ↑
  - √ IGF levels ↑
  - √ Consistent improvements in body composition¹
  - √ Durable effects to 24 months¹
- Post hoc analysis of PEM+ PGHD subjects demonstrated comparable growth rate to SOC at lowest dose subsequently selected for OraGrowtH210 study
- PK/PD data suggest doses above ~2.8 mg/kg hit PD plateau, likely due to IGF-1 feedback loop<sup>2</sup>

#### **OraGrowtH Phase 2 Studies**

- Prospectively validate PEM Strategy
- Dose selection to test full range of PD effect below and above PD response plateau
- Confirm clinical benefit of increasing endogenous pulsatile GH secretion
- Demonstrate clean safety profile in PGHD at higher doses

<sup>&</sup>lt;sup>1</sup> Nass 2008 Ann Intern Med

<sup>&</sup>lt;sup>2</sup> Merck Study 001 in healthy adult subjects, results based on single LUM-201 dose administered



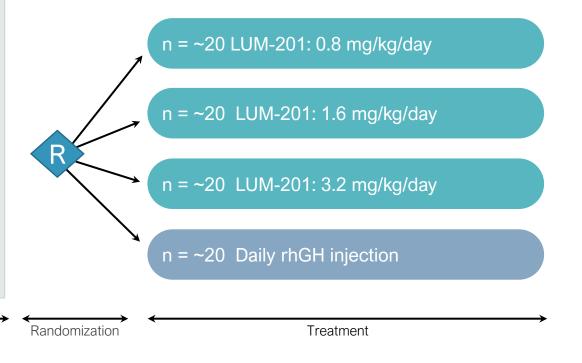


### OraGrewtH210

- n = 82
- PEM(+) PGHD subjects
- Inclusion: stim GH ≥ 5 ng/ml and baseline IGF-1 >30 ng/ml
- rhGH treatment naïve

Screening

 ~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

#### OraGrowtH210 Baseline Demographics

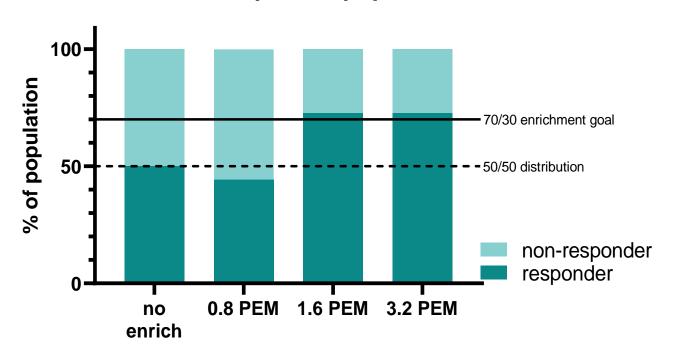


	LUM-201 0.8 mg Mean (SD) N=18	LUM-201 1.6 mg Mean (SD) N=22	LUM-201 3.2 mg Mean (SD) N=22	rhGH Mean (SD) N=19
Age (months)	101.3 (29.2)	95.2 (27.3)	94.5 (21.1)	90.7 (23.7)
Height (cm)	116.4 (12.4)	113.6 (11.0)	113.8 (9.2)	112.9 (10.7)
Height SDS	-2.32 (0.30)	-2.33 (0.54)	-2.29 (0.59)	-2.19 (0.41)
IGF-1 SDS	-1.46 (0.62)	-1.38 (0.61)	-1.39 (0.53)	-1.25 (0.49)
MPH (cm)	165.3 (7.1)	164.9 (7.4)	167.4 (7.7)	169.4 (8.7)
MPH SDS $\Delta$	-1.47 (0.67)	-1.61 (0.68)	-1.87 (0.59)	-1.94 (0.62)
BA Delay (yrs)	1.8 (0.9)	1.9 (0.8)	2.0 (0.9)	1.9 (0.9)
BMI SDS	-0.55 (1.10)	-0.18 (0.87)	-0.57 (0.99)	+0.16 (0.88)

# OraGrowtH210 Met Primary Statistical Objective: PEM enriched the responder population



## Application of PEM enriched responder population



#### **Highlights**

- PEM test ensured patients enrolled in the study were capable of secreting GH in response to a single-dose of LUM-201
- 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 prespecified target growth in 1.6 and 3.2 mg/kg/day cohorts

# OraGrowtH210 Secondary Statistical Objective: PEM Test Yielded Highly Reproducible Results

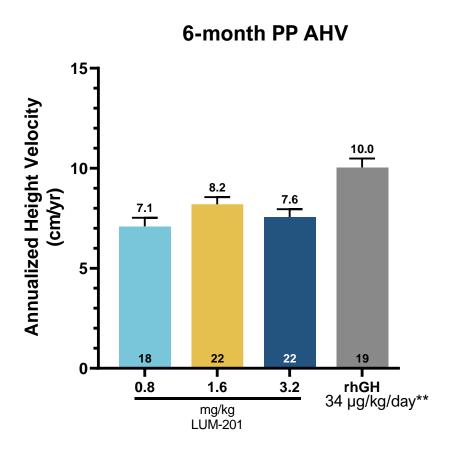


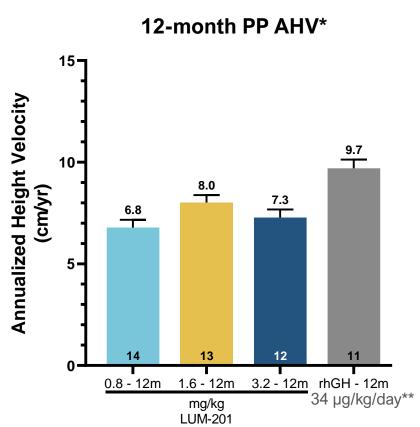
PEM Test Reproducibility	
Subjects with Positive Agreement on PEM Tests	76/76
Reproducibility Rate	100%
95% Confidence Interval	(95.3%, 100%)

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

# OraGrowtH210 Met Primary Objective: 6 and 12-Month AHV Data Support 1.6 mg/kg as Optimal Dose for Phase 3







#### **Highlights**

- 1.6 mg/kg best performing LUM-201 cohort
  - Growth of 8.0 cm comparable to historical 12-month AHV for moderate population
- 1.7 cm difference between 1.6mg/kg and rhGH cohorts at 12 months
  - Differences less than 1.8 2.0 cm have been the historical Phase 3 non-inferiority margin for rhGH approvals

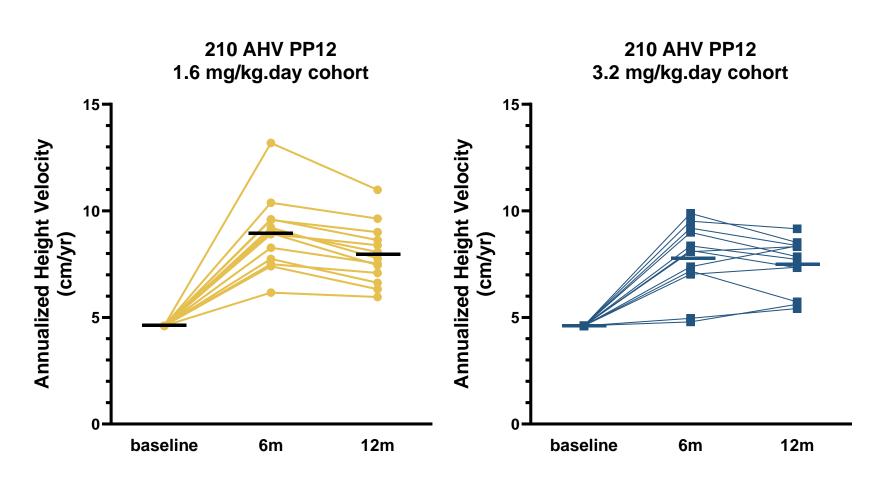
Bars represent Least Squares Mean (LSM), Error bars represent the Standard Error of LSM

<sup>\*</sup> AHV ANCOVA Model Terms: treatment, Age at dose 1, Sex, Baseline HT SDS, Baseline BMI SDS, Baseline IGF-1 SDS, LUM-201 PEM, Baseline BA Delay, HT SDS-MPH SDS

<sup>\*\*</sup> Equates to 0.24 mg/kg/wk (approved rhGH dose range: 0.17-0.24 mg/kg/wk for Norditropin)

# AHV After 6 and 12 Months of LUM-201 Treatment At 100% Enrollment; Per Protocol 12-month Population



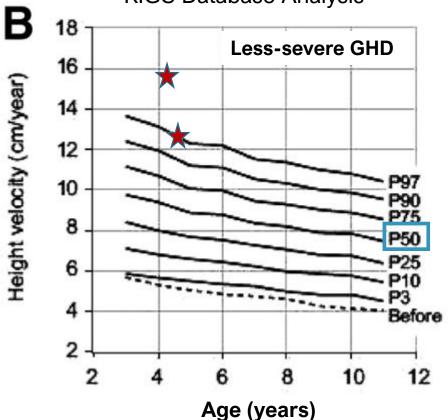


#### **6-Month Observations**

- LUM-201 raised the AHV (growth rate) from baseline after 6 months on therapy for both the 1.6 mg/kg cohort and the 3.2 mg/kg cohort
- AHVs durable to 12 months on treatment for both doses
- No statistical difference exists between the two cohorts at each timepoint

#### IUMOS Growth Outliers in the rhGH Cohort: 2 of 3 Subjects under Age 5 Randomized to rhGH

First-year Growth on rhGH for Moderate PGHD KIGS Database Analysis<sup>1</sup>





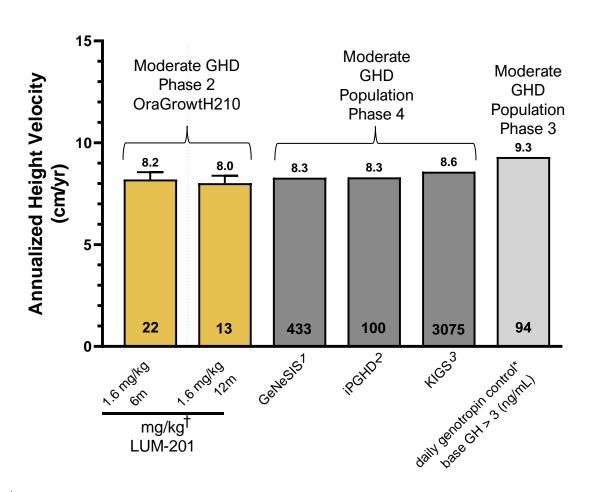
OraGrowtH210 youngest subjects in rhGH cohort at 6-months AHV grew well beyond expectations

#### Analysis of Pfizer's KIGS database of moderate PGHD¹:

- P lines = Percentiles of expected growth on rhGH for moderate PGHD based on age started on therapy
- "Before" line marks height velocity before GH therapy

#### LUM-201 Growth Comparable to Multiple 12-Month Historical Datasets





#### **Highlights**

- AHVs range from 8.3-9.3 cm/yr in datasets of moderate PGHD patients treated with daily rhGH
- LUM-201 AHVs in line with historical rhGH growth rates in comparable patient populations

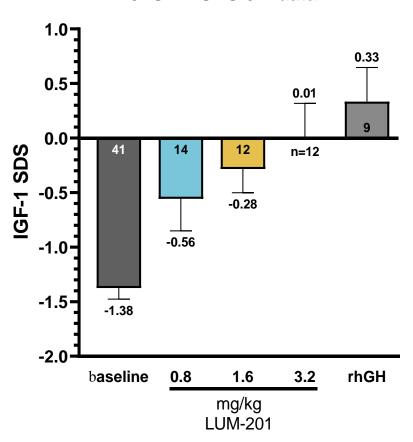
<sup>&</sup>lt;sup>†</sup>ANCOVA Model Terms: treatment, Age at dose 1, Sex, Baseline HT SDS, Baseline BMI SDS, Baseline IGF-1 SDS, LUM-201 PEM, Baseline BA Delay, HT SDS-MPH SDS Bars represent Least Squares Mean (LSM), <sup>†</sup> Error bars represent the Standard Error of LSM Sources: <sup>1</sup> Blum et al JES 2021, <sup>2</sup> Lechuga-Sancho et al JPEM 2009, <sup>3</sup> Ranke et al JCEM 2010

<sup>\*</sup>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.

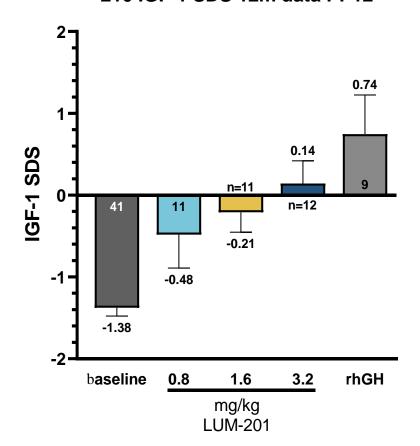
# OraGrowtH210 Phase 2: IGF-1 Standard Deviation Score (SDS) LUM-201 Normalized IGF-1 SDS with Durable Effect out to 12 months







#### 210 IGF-1 SDS 12m data PP12



#### **Highlights**

- LUM-201 normalized IGF-1 within 6 months
- Durable effect out to 12 months

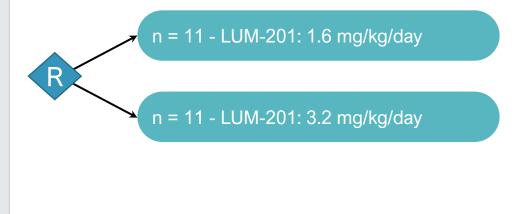
#### OraGrowtH212 Trial: PK/PD Trial in Naïve Moderate PGHD



### OroGrowtH212

- n = 22
- Open-label study
- Moderate PGHD patients
- 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

OraGrowtH212 was a single-site trial with a more homogenous patient population than larger international OraGrowtH210 Trial

Treatment

Screening

Randomization

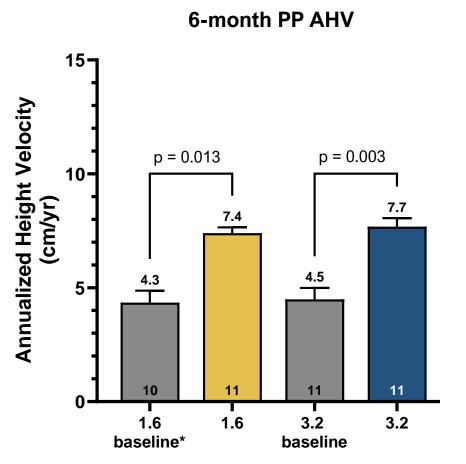
#### OraGrowtH212 Trial Baseline Demographics

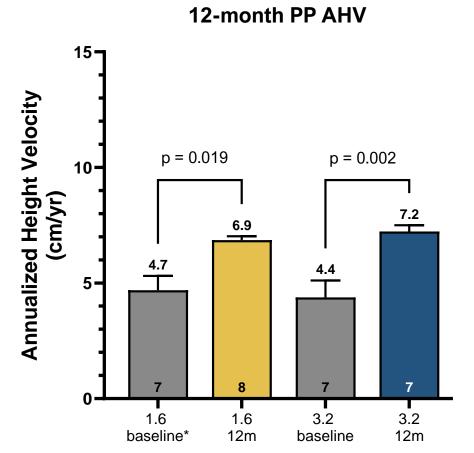


	LUM-201 1.6 mg Mean (SD) N=11	LUM-201 3.2 mg Mean (SD) N=11
Age (months)	99.7 (15.2)	100.9 (21.1)
Height (cm)	116.5 (5.5)	116.6 (9.5)
Height SDS	-2.15 (0.28)	-2.26 (0.38)
IGF-1 SDS	-1.01 (0.64)	-0.85 (0.50)
MPH (cm)	162.6 (7.0)	160.3 (8.7)
MPH SDS $\Delta$	-0.85 (0.53)	-0.73 (0.51)
BA Delay (yrs)	1.7 (0.86)	1.8 (0.96)
BMI SDS	-0.07 (0.85)	0.28 (0.97)

# OraGrowtH212: Significant Increase in Growth from Baseline AHV at 6 and 12 Months Per Protocol (PP)







#### **Highlights**

- Considerable increase in growth from baseline
- Durable effect to 12 months
- Minimal drop off in AHV between 6 and 12 months
- No material difference between 2 dose cohorts at 6 or 12 months

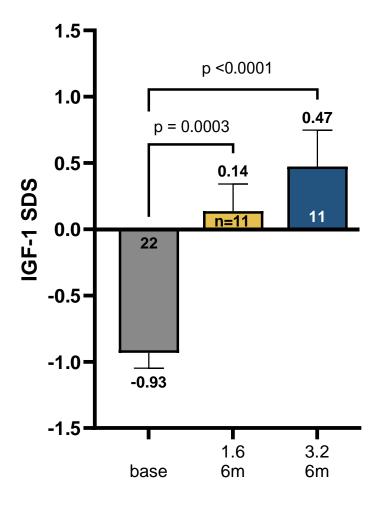
- AHV = Annualized Height Velocity
- Bars represent sample mean
- Error bars represent SEM

AHV ANCOVA Model Terms: treatment, Age at dose 1, Sex, Baseline HT SDS, Baseline BMI SDS, Baseline IGF-1 SDS, LUM-201 PEM, Baseline BA Delay, HT SDS-MPH SDS Bars represent Least Squares Mean (LSM),

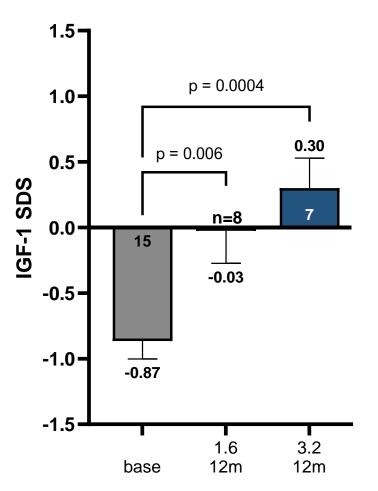
#### OraGrowtH212 Phase 2: IGF-1 SDS LUM-201 Normalized IGF-1 Level with Durable Effect out to 12 months







#### IGF-1 SDS - 12m cohort



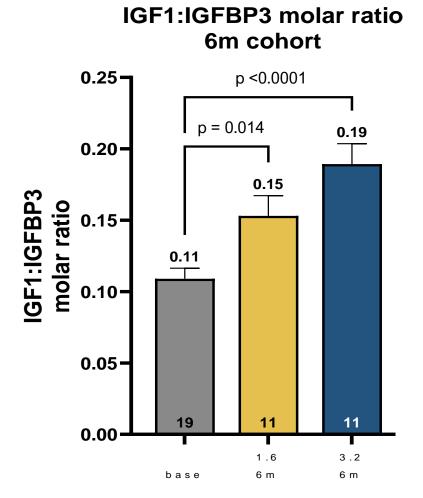
#### **Highlights**

- LUM-201 normalized IGF-1 within 6 months
- Durable effect on IGF-1 out to 12 months
- No Subjects > 2 SDS between
   0 and 12 months

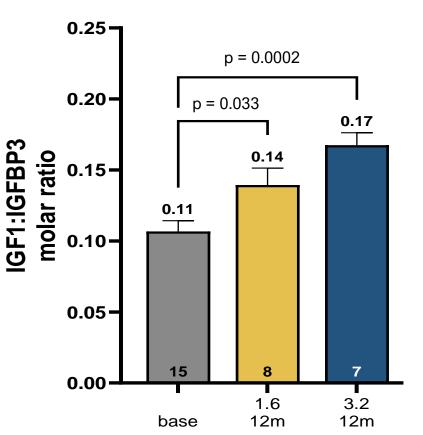
- Bars represent sample mean
- Error bars represent Standard Error of the Mean (SEM)
- Data represent number of patients for whom data was available at each timepoint; not all patients had reached 12 months on treatment at time of data pull.

# OraGrowtH212: LUM-201 Increased IGF1:IGFBP3 Ratios with Durable Effect out to 12 months





### IGF1:IGFBP3 molar ratio 12m cohort



#### **Highlights**

- This ratio is a valuable indicator of GH action
- LUM-201 increased
   IGF1:IGFBP3 ratios within
   6 months of treatment
- Durable effect on IGF1:IGFBP3 ratios out to 12 months of treatment

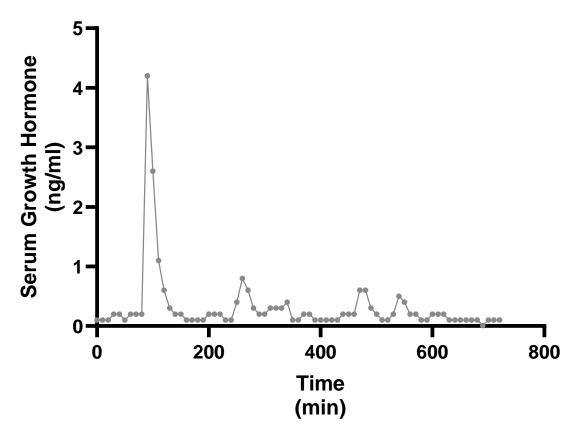
- Bars represent sample mean
- Error bars represent SEM
- Data represent number of patients for whom data was available at each timepoint; not all patients had reached 12 months on treatment at time of data pull.



#### Pulsatility and Annualized Height Velocity Data: Month 6 for Patient A (3.2 mg/kg/day)

	Baseline	6 months LUM-201 3.2 mg/kg/d
IGF-1 (ng/ml)	48	
Q10m AUC <sub>0-12</sub> 12h GH (ng*hr/ml)	252.9	
Height velocity (cm/yr)	4.4	

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

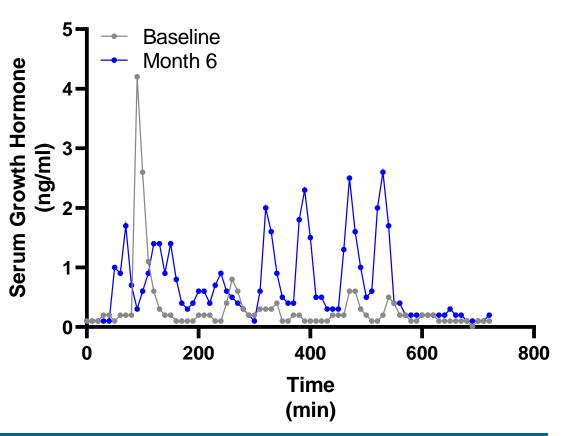


#### Pulsatility and Annualized Height Velocity Data: Month 6 for Patient A (3.2 mg/kg/day)



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

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



LUM-201 raises AHV from baseline by augmenting pulsatile secretion of GH and increasing IGF-1



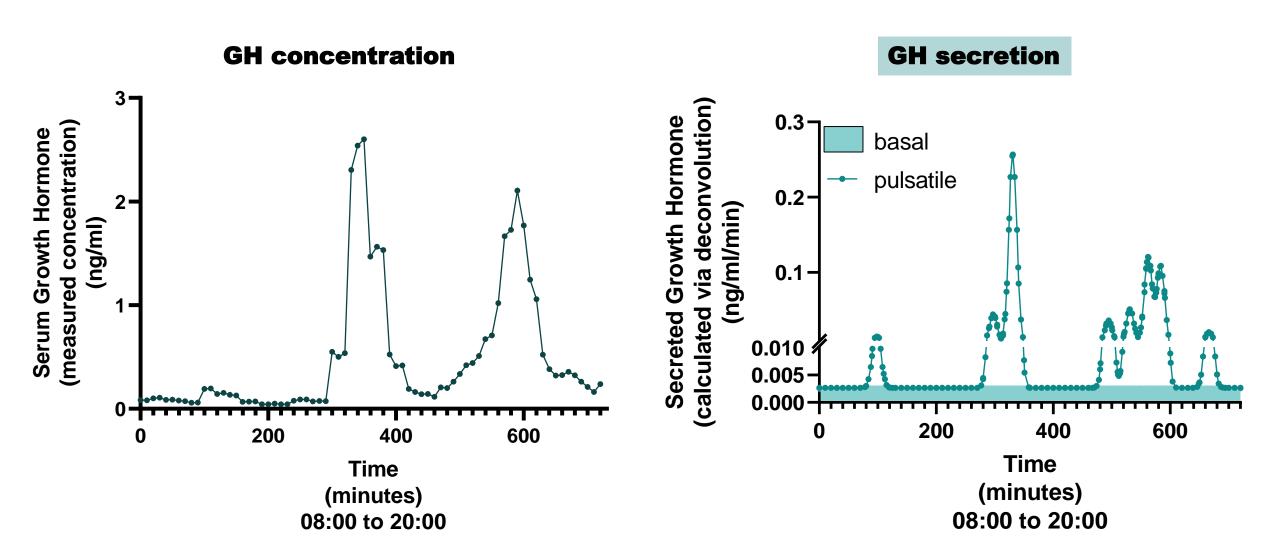
### Principles of Deconvolution Analysis<sup>1</sup>

- 1. Peaks of GH concentration are identified and analyzed by combining these features:
  - a) a rapid increase representing secretion described by a Gaussian curve
  - b) a slow decay representing **elimination** based on the half-life of GH in the circulation
- 2. This generates episodes of GH secretion expressed as ng/ml/min
- 3. The distribution volume of GH in plasma is used to define secretion over 12 hours per ml of blood, which is then converted into secretion from the pituitary as µg/kg body weight/12 hours

1.ML Johnson et al, "Signal-Response Modeling of Partial Hormone Feedback Networks", Journal of Diabetes Science and Technology 2009



# Deconvolution Analysis of Serum GH Pulsatility Provides a measure of pituitary secretion of GH





# LUM-201 Treatment Modulated the Amplitude of GH Secretory Peaks, with Minimal Influence on Number of Secretory Episodes

1.6 mg/kg/day*	Baseline	6m LUM-201	
Secretory episodes per 12hr	6.1 (2.6)	6.1 (1.4)	
Pulsatile release (ng/mL.12hr)	25.5 (14.1)	40.8 (17. 5)	
3.2 mg/kg/day*	Baseline	6m LUM-201	
Secretory episodes per 12hr	6.9 (2.7)	6.6 (2.2)	
Pulsatile release (ng/mL.12hr)	24.0 (22.8)	55.1 (39.5)	
Combined cohorts*	Baseline	6m LUM-201	
Secretory episodes per 12hr	6.5 (2.6)	6.4 (1.8)	
Pulsatile release (ng/mL.12hr)	24.8 (18.5)	48.0 (30.7)	

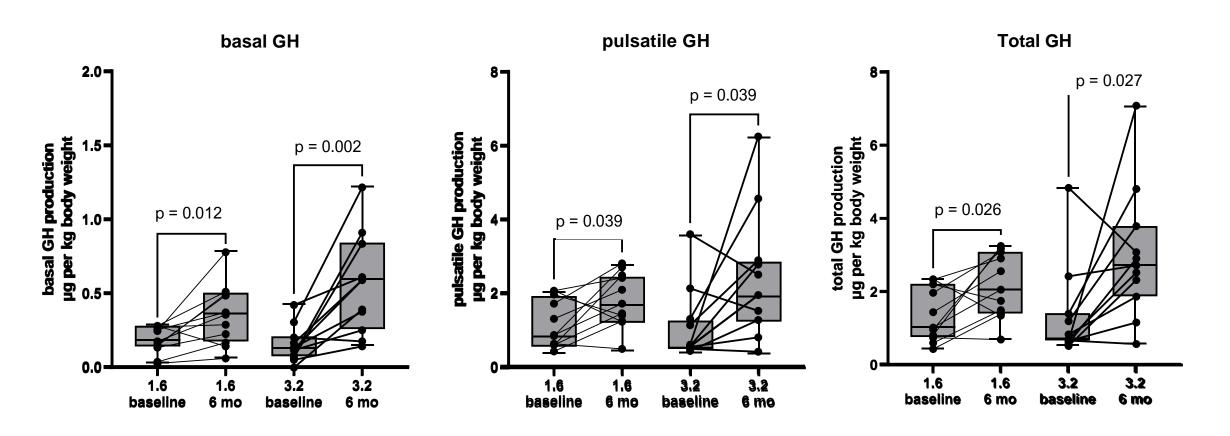
Summary data represent mean <u>+</u> standard deviation

Secretory episodes = number of secretion events in 12hr sampling during daytime

<sup>\*</sup>n = 11 per cohort; combined cohort data is n = 22



# Growth Hormone secretion at 0 vs 6 months of oral LUM-201 All variables from deconvolution based on 72 samples in 12 hours



LUM-201 1.6mg/kg and 3.2 mg/kg dose cohorts showed similar increases in GH secretion profiles

NOTE: box and whisker data plots represent median (bars), 75% (boxes), and individual subject data (whiskers)





Time period	Normal healthy (IC-GH <sup>‡</sup> )	Untreated GHD (IC-GH <sup>‡</sup> )	LUM-201 (baseline GH)*	LUM-201 (treat 6M GH)*
	Zadik <sup>†</sup>		N =	22
12h (day) μg/kg.12hr	3.3 <u>+</u> 1.3	1.1 <u>+</u> 0.5	1.3 <u>+</u> 1.0	2.6 <u>+</u> 1.4
24h μg/kg/24hr	5.0 <u>+</u> 1.3	1.4 <u>+</u> 0.5	1.7 <u>+</u> 1.3**	3.3 <u>+</u> 1.8 to 4.0 <u>+</u> 2.1**
Ratio 24:12(day)	1.52	1.27	1.27	1.27-1.52

# LUM-201 stimulated an increase in pulsatile secretion of GH approximating normal physiologic levels

<sup>&</sup>lt;sup>‡</sup>IC-GH: integrated concentration of Growth Hormone; data represent mean <u>+</u> standard deviation

<sup>\*</sup>GH concentrations from the combined 1.6 and 3.2 mg/kg/day cohorts

<sup>\*\*24</sup>hr GH concentrations for LUM-201 were calculated based on 12hr data

<sup>&</sup>lt;sup>†</sup>Zadik et al Horm Res 1992

<sup>&</sup>lt;sup>††</sup> Adapted from data in Albertsson-Wikland et al JCEM 1994; 24h exposures listed reflect absorbance/bioavailability of ~60% of the administered dose





Time period	Normal healthy (IC-GH <sup>‡</sup> )	Untreated GHD (IC-GH <sup>‡</sup> )	LUM-201 (baseline GH)*	LUM-201 (treat 6M GH)*	Comparator arm rhGH 34 µg/kg/day
	Zadik <sup>†</sup>		N = 22		Albertsson- Wikland <sup>††</sup>
12h (day) μg/kg.12hr	3.3 <u>+</u> 1.3	1.1 <u>+</u> 0.5	1.3 <u>+</u> 1.0	2.6 <u>+</u> 1.4	-
24h μg/kg/24hr	5.0 <u>+</u> 1.3	1.4 <u>+</u> 0.5	1.7 <u>+</u> 1.3**	3.3 <u>+</u> 1.8 to 4.0 <u>+</u> 2.1**	~20
Ratio 24:12(day)	1.52	1.27	1.27	1.27-1.52	-

Increasing 24-hour pulsatile secretion, LUM-201 achieved similar growth to exogenous injectable rhGH, with only 20% of GH concentration levels

<sup>&</sup>lt;sup>‡</sup>IC-GH: integrated concentration of Growth Hormone; data represent mean <u>+</u> standard deviation

<sup>\*</sup>GH concentrations from the combined 1.6 and 3.2 mg/kg/day cohorts

<sup>\*\*24</sup>hr GH concentrations for LUM-201 were calculated based on 12hr data

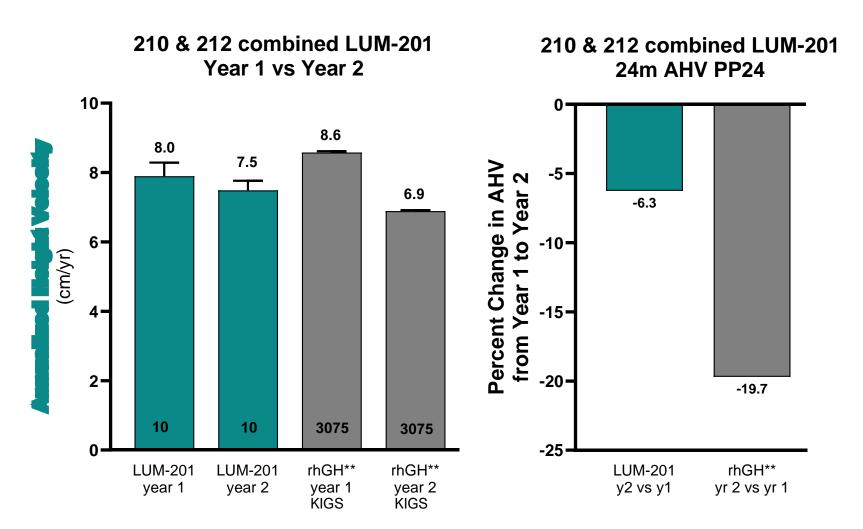
<sup>&</sup>lt;sup>†</sup>Zadik et al Horm Res 1992

<sup>††</sup> Adapted from data in Albertsson-Wikland et al JCEM 1994; 24h exposures listed reflect absorbance/bioavailability of ~60% of the administered dose



# OraGrowtH210 and OraGrowtH212 Trials Combined Data

# LUM-201 Data Suggests Greater Durability of Response than rhGH to 24 Months IUMOS OraGrowtH210 & OraGrowtH212 Combined (1.6 and 3.2 mg/kg LUM-201)



#### **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

AHV values from the OraGrowth studies are based on ANCOVA model (details provided on previous slides)

<sup>\*</sup> At 24 months, data include a subset of subjects from OraGrowtH210 trial who met protocol criteria to continue past 12 months.

<sup>\*\*</sup> Ranke et.al. 2010 – rhGH treated cohort of moderate 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.



### Safety Data from Combined Trials

	PEM	0.8 mg/kg	1.6 mg/kg	3.2 mg/kg	rhGH
	N =129	N =18	N =33	N=33	N =20
Number of AEs	38	59	155	150	54
Subjects with AE (%)	24 (18.6%)	14 (77.8%)	31 (93.9%)	30 (90.9%)	16 (80.0%)
Treatment Related AEs *	7	2	16	19	6
Subjects with Treatment Related AEs (%)	4 (3.1%)	1 (5.6%)	13 (39.4%)	13 (39.4%)	5 (25.0%)
Subjects with SAEs (%)	0 (0%)	2# (11.1%)	1 (3.0%)	0 (0%)	1 <sup>##</sup> (5.0%)
Subject with Treatment Related SAEs (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0.0%)

#### **Topline 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)

#One subject had SAE between PEM dose and randomized dose

## Subject had SAE between PEM dose and randomized dose



### Summary of Topline Phase 2 Data and Upcoming Milestones

#### OraGrowtH210 and OraGrowtH212 Phase 2 Clinical Trials

- Met all primary and secondary endpoints
- PEM test was reproducible and predicted response to LUM-201
- LUM-201 restored GH secretion through increased amplitude of pulsatility and normalized IGF-1
- o LUM-201 promoted growth similar to injectable rhGH with only 20% of GH concentration levels
- AHV of 1.6 mg/kg LUM-201 arm vs rhGH arm was within historical Phase 3 non-inferiority margins\*
- Preliminary 24-month data demonstrated sustained growth on LUM-201
- Favorable safety profile to date

#### **Upcoming Milestones**

- Full 12-month data from OraGrowtH210 Trial to be announced in 2Q 2024
- End-of-Phase 2 meeting with FDA in 2Q 2024
- Initiate Phase 3 program in 4Q 2024



### LUM-201: Exclusivity and Barriers with Orphan Designation and IP

# Novel Formulation Patent

- Patent allowance granted March 14, 2024, by USPTO for novel LUM-201 formulation
- Formulation consists of capsule with mini-tablets of LUM-201 drug product inside
- Patent grant extends intellectual property protection through 2042

# Orphan Drug Designation

- Orphan Drug Designation (ODD) granted in US & EU for GHD in 2017
- LUM-201 eligible for 12 years of exclusivity in EU and 7.5 years of exclusivity in US\*

# Intellectual Property

- Prior patent granted for "Detecting & Treating GHD"
- Use of LUM-201 in PGHD and other GHD indications based on PEM strategy
- Patents for LUM-201 in GHD with protection through 2036
- Patents granted in US, Australia, EU, Israel, Japan, S. Korea, Hong Kong and Ukraine
- Additional applications pending in multiple jurisdictions
- Applications for LUM-201 in NAFLD being prosecuted in multiple jurisdictions

### Lumos Pharma Financial Information as of December 31, 2023 Values in USD



Cash, Equivalents & Short-term Investments	\$36.1M
Debt	\$0
Shares Outstanding	8.1M
Cash Runway	Through 3Q 2024
Fiscal Year End	December 31



Cash, cash equivalents, & short-term investments to support operations through 3Q 2024, inclusive of activities related to advancing the PGHD program into Phase 3

# Investment Thesis Lead asset targeting children with growth disorders



# Attractive Market Opportunity

- Daily oral expected to be well received in GH markets
- Market research supports rapid conversation to oral and potential expansion opportunities\*



# Novel Asset with Unique MOA

- Novel MOA takes advantage of natural physiology
- Orphan Drug Designation in US/EU and issued patents in major markets
- IP protection through 2042 in the US for novel formulation



### Clear Proof of Concept

- PEM strategy de-risks patient selection, identifying likely LUM-201 responders\*\*
- Phase 2 trials met all primary and secondary endpoints
- Consistent PK/PD and attractive safety profile to date in > 1,300 subjects studied



#### **Focused Execution**

- Full 12-month data from OraGrowtH210 Trial to be announced in 2Q 2024
- End-of-Phase 2 meeting with FDA in 2Q 2024 to review Phase 3 program
- Initiation of Phase 3 trial anticipated 4Q 2024



Potential for 1st oral therapeutic to disrupt injectable market for GHD

<sup>\*</sup> Initial Primary Research of PGHD Market conducted for Lumos by Triangle Insights

<sup>\*\*</sup> 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

# Additional Analyses of Phase 2 Data

#### Safety Profile at Interim Analysis for OraGrowtH210 Trial Data cut October 2023



	0.8 mg/kg	1.6 mg/kg	3.2 mg/kg	ALL LUM-201	rhGH 34 mcg/kg
N =	18	22	22	<u>62</u>	20
Number of AEs	59	79	74	212	54
Subjects with AE (%)	14 (77.8%)	20 (90.9%)	19 (86.4%)	53 (85.5%)	16 (80.0%)
Treatment Related AEs (N)	2	2	4	8	6
Subjects with Treatment Related AEs (%)	1 (5.6%)	2 (9.1%)	3 (13.6%)	6 (9.7%)	5 (25.0%)
Subjects with SAEs (%)	2# (11.1%)	1 (4.5%)	0 (0.0%)	2 (3.2%)	1## (5.0%)
Subjects with Treatment Related SAEs (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

<sup>#</sup> One subject had SAE between PEM dose and randomized dose ## Subject had SAE between PEM dose and randomized dose

AE = Adverse Event

### Related OraGrowtH210 Adverse Events



Preferred Term, N (%)	0.8 N=18	1.6 N=22	3.2 N=22	ALL N=62	rhGH N=20	Comments		
Contusion					1 (5.0)	Grade	1, Recove	ered by next visit
Injection Site Bruising					2 (10.0)	Grade 1, Recovered by next visit		
Increased Appetite (All Grade 1)	1 (5.6)	1 (4.5)	1 (4.5)	3 (4.8)	2 (10.0)	Duration:	0.8 mg 1.6 mg 3.2 mg rhGH	Ongoing 1 & 7 months Ongoing 9, 13 & 15 months
Arthralgia		1 (4.5)	1 (4.5)	2 (3.2)		Both Grad	le 1, Dura	tion was a few days
Growing Pains	1 (5.6)			1 (1.6)		Grade 1		
Pain in Extremity			2 (9.1)	2 (3.2)	1 (5.0)	All Grade 1, Intermittent or short duration		

#### Serious Adverse Events OraGrowtH210 Trial



Serious Adverse Event	System Organ Class	Gr	Study Treatment	Relatedness	Serious Criteria
Product Administration Error	Injury, Poisoning and Procedural Complications	1	NA (occurred prior to receiving any study drug)	<u>Unrelated</u>	Hosp
Dehydration	Metabolism and Nutrition Disorders		*PEM (single 0.8 mg/kg)	<u>Unrelated</u>	Hosp
Glycosuria	Renal and Urinary Disorders	1	**PEM (single 0.8 mg/kg)	<u>Unrelated</u>	Hosp
Cartilage Development Disorder	Musculoskeletal and Connective Tissue Disorders	3	0.8 mg/kg/day	<u>Unrelated</u>	Hosp
Pain in Extremity	Musculoskeletal and Connective Tissue Disorders	2	1.6 mg/kg/day	<u>Unrelated</u>	Hosp

There have been no SAEs in the OraGrowtH212 Trial to date

<sup>\*</sup> This subject was later randomized to the 0.8mg/kg study arm

<sup>\*\*</sup> This subject was later randomized to the rhGH arm



### Related OraGrowtH212 AEs

Preferred Term, N (%)	1.6 N=11	3.2 N=11	ALL N=22	Comments		
			0.9) 21 (95.5)		9 ongoing	
Increased Appetite	11 (100.0)	10 (90.9)		21 (95.5)	19 Grade 1	10 resolved (duration 1-23, avg 9.7 months)
				2	Grade 2, both ongoing	
Arthralgia	1 (9.1)	2 (18.2)	3 (13.6)	All Grade 1, Duration: < 2 weeks		
Pain in Extremity	2 (18.2)	3 (27.3)	5 (22.7)	All Grade 1, All with duration: < 2 weeks, except one with ongoing intermittent leg pain		

### Specific OraGrowtH210 AEs – No meaningful signal



Safety data	available for	r 82 subjects	at interim	analysis,	October	2023

	0.8 N=18	1.6 N=22	3.2 N=22	ALL N=62	rhGH N=20
Arthralgia	2 (11.1%)	3 (13.6%)	2 (9.1%)	7 (11.3%)	2 (10.0%)
Myalgia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (15.0%)
Headache	5 (27.8%)	7 (31.8%)	5 (22.7%)	17 (27.4%)	3 (15.0%)
Lethargy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abd. pain	1 (5.6%)	3 (13.6%)	5 (22.7%)	9 (14.5%)	1 (5.0%)
Emesis	0 (0.0%)	1 (4.5%)	3 (13.6%)	4 (6.5%)	3 (15.0%)
Inc. appetite	1 (5.6%)	1 (4.5%)	1 (4.5%)	3 (4.8%)	2 (10.0%)
Hypoglycemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Orophary. pain	2 (11.1%)	2 (9.1%)	0 (0.0%)	4 (6.5%)	1 (5.0%)

# Laboratory Shifts: No meaningful signal 82 subjects



	0.8 mg/kg N=18	1.6 mg/kg N=22	3.2 mg/kg N=22	ALL N=62	rhGH N=20
ALT NI to high	2/17 (11.8%)	5/22 (22.7%)	4/22 (18.2%)	11/61 (18%)	7/20 (35%)
AST NI to high	3/14 (21.4%)	4/21 (19%)	5/22 (22.7%)	12/57 (21.1%)	6/20 (30%)
Bicarb NI to high	0/18 (0%)	0/22 (0.0%)	1/22 (4.5%)	1/62 (1.6%)	0/20 (0%)
Bicarb NI to low	8/18 (44.4%)	6/22 (27.3%)	8/22 (36.4%)	22/62 (35.5%)	5/20 (25%)
Bilirubin NI to high*	4/18 (22.2%)	4/22 (18.2%)	4/22 (18.2%)	12/62 (19.4%)	2/20 (10%)
Calcium NI to low	1/18 (5.6%)	2/21 (9.5%)	4/22 (18.2%)	7/61 (11.5%)	2/20 (10%)
Calcium NI to high	0/18 (0%)	2/22 (9.1%)	0/22 (0.0%)	2/61 (3.3%)	0/20 (0%)
Creatinine NI to low	2/18 (11.1%)	3/22 (13.6%)	2/22 (9.1%)	7/62 (11.3%)	2/20 (10%)
GGT NI to high	2/17 (11.8%)	6/22 (27.3%)	8/22 (36.4%)	16/61 (26.2%)	1/20 (5%)

For the shift to study visit, the denominator is the number of subjects with a non-missing value for the given parameter at baseline and the visit. Baseline is defined as the latest results obtained prior to the first dose of study drug.

<sup>\*</sup> Bilirubin Q2 laboratory normal range high values are lower than most laboratories

### **Laboratory Shifts**



	0.8 mg/kg N=18	1.6 mg/kg N=22	3.2 mg/kg N=22	ALL N=62	rhGH N=20
Urea nitro NI to low	4/18 (22.2%)	4/21 (19%)	7/22 (31.8%)	15/61 (24.6%)	7/20 (35%)
Urea nitro NI to high	1/18 (5.6%)	0/22 (0%)	1/22 (4.5%)	2/62 (3.2%)	0/20 (0%)
Basophils NI to high	7/17 (41.2%)	12/22 (54.5%)	10/21 (47.6%)	29/60 (48.3%)	4/20 (20%)
Eosinophils NI to high	2/17 (11.8%)	4/22 (18.2%)	3/21 (14.3%)	9/60 (15%)	5/20 (25%)
Hematocrit NI to low	2/18 (11.1%)	0/22 (0.0%)	2/22 (9.1%)	4/61 (6.6%)	0/20 (0%)
Hematocrit NI to high	1/17 (5.9%)	1/22 (4.5%)	2/22 (9.1%)	4/61(6.6%)	0/20 (0%)
Hemoglob. NI to low	4/18 (22.2%)	2/22 (9.1%)	5/22 (22.7%)	11/62 (17.7%)	0/20 (0%)
Lymphoc. NI to low	3/17 (17.6%)	0/21 (0.0%)	1/21 (4.8%)	4/59 (6.8 %)	1/20 (5%)
Lymphoc. NI to high	0/17 (0.0%)	0/22 (0.0%)	2/21 (9.5%)	2/60 (3.3%)	0/20 (0%)

### **Laboratory Shifts**



	0.8 mg/kg N=18	1.6 mg/kg N=22	3.2 mg/kg N=22	ALL N=62	rhGH N=20
Globulin NI to low	6/18 (33.3%)	4/22 (18.2%)	4/22 (18.2%)	14/62 (22.6%)	5/20 (25%)
Glucose NI to high	0/18 (0%)	5/22 (22.7%)	6/22 (27.3%)	11/61 (18%)	0/20 (0%)
Glucose NI to low	0/18 (0%)	0/22 (0.0%)	1/22 (4.5%)	1/62 (1.6%)	0/20 (0%)
Insulin NI to low	2/17 (11.8%)	2/20 (10%)	1/21 (4.8%)	5/58 (8.6%)	0/20 (0%)
Phosphate NI to low	0/18 (0%)	0/22 (0.0%)	1/22 (4.5%)	1/61 (1.6%)	1/20 (5%)
Phosphate NI to high	6/17 (35.3%)	4/22 (18.2%)	7/22 (31.8%)	17/61 (27.9%)	7/20 (35%)
Protein NI to high	0/18 (0%)	1/22 (4.5%)	5/22 (22.7%)	6/62 (9.7%)	1/20 (5%)
Protein NI to low	0/18 (0%)	2/22 (9.1%)	2/22 (9.1%)	4/62 (6.5%)	3/20 (15%)
Potassium NI to high	4/16 (25%)	9/22 (40.9%)	7/22 (31.8%)	20/60 (33.3%)	1/20 (5%)

### **Laboratory Shifts**



	0.8 mg/kg N=18	1.6 mg/kg N=22	3.2 mg/kg N=22	ALL N=62	rhGH N=20
Ery. crp. Hb NI to low	2/17 (11.8%)	2/22 (9.1%)	3/22 (13.6%)	7/61 (11.5%)	2/20 (10%)
Ery. crp. vol NI to low	1/18 (5.6%)	3/21 (14.3%)	3/22 (13.6%)	7/61 (11.5%)	1/20 (5%)
Ery. crp vol NI to high	0/17 (0.0%)	0/22 (0.0%)	0/22 (0.0%)	0/61 (0%)	0/20 (0%)
Monocytes NI to low	3/17 (17.6%)	3/21 (14.3%)	1/21(4.8%)	7/59(11.9%)	1/20(5%)
Monocytes NI to high	3/17 (17.6%)	3/22 (13.6%)	4/21 (19%)	10/60(16.7%)	0/20 (0%)
Neutroph. NI to high	0/18 (0%)	2/22 (9.1%)	2/21 (9.5%)	4/60 (6.7%)	1/20 (5%)
Neutroph. NI to low	3/17 (17.6%)	4/21 (19%)	6/21 (28.6%)	13/59 (22%)	3/20 (15%)
Platelets NI to low	0/18 (0.0%)	0/22 (0%)	1/22 (4.5%)	1/62 (1.6%)	0/20 (0%)
Platelets NI to high	6/17 (35.3%)	5/22 (22.7%)	6/22 (27.3%)	17/61 (27.9%)	0/20 (0%)

### Laboratory Shifts: No meaningful signal



	0.8 mg/kg N=18	1.6 mg/kg N=22	3.2 mg/kg N=22	ALL N=62	rhGH N=20
Eryth. NI to high	1/17 (5.9%)	2/22 (9.1%)	2/22 (9.1%)	5/61 (8.2%)	1/20 (5%)
Eryth. NI to low	1/18 (5.6%)	0/22 (0.0%)	0/22 (0.0%)	1/62 (1.6%)	0/20 (0%)
Leukocyt. NI to high	1/17 (5.9%)	2/22 (9.1 %)	2/22 (9.1%)	5/61 (8.2%)	1/20 (5%)
Leukocyt. NI to low	4/17 (23.5%)	4/21 (19%)	2/22 (9.1%)	10/60 (16.7%)	2/20 (10%)

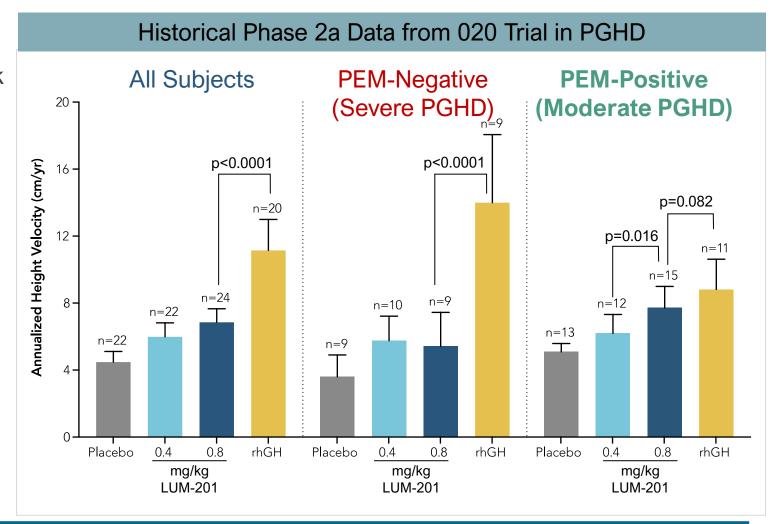
# **Supplementary Materials**



### Study 020 Post-Hoc Analysis: PEM-Positive Patients Responsive to LUM-201

#### **PEM = Predictive Enrichment Marker**

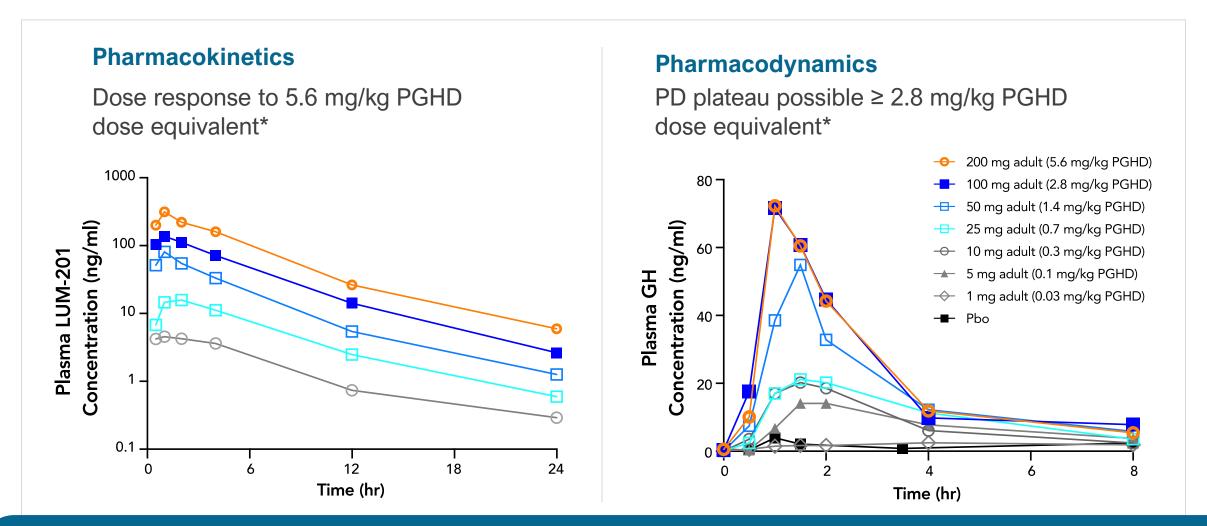
- Multiple LUM-201 trials conducted by Merck
  - o In ~1000 adults − for sarcopenia, other
    - GH/IGF-1 raised from baseline by LUM-201
  - In ~200 children for PGHD
- Naïve PGHD, Study 020
  - N=68; three arms
  - Placebo patients switched to rhGH at 6 mos.
  - Annualized growth shown for each arm
- PEM-positive subset\*:
  - LUM-201 0.8 mg/kg not statistically different from rhGH
  - Dose response: 0.8 mg/kg statistically superior to 0.4 mg/kg



Expect prospective inclusion of only PEM(+) patients and higher doses to improve response to LUM-201



### PK/PD: Evidence of a PK and PD Dose Response in Healthy Volunteers

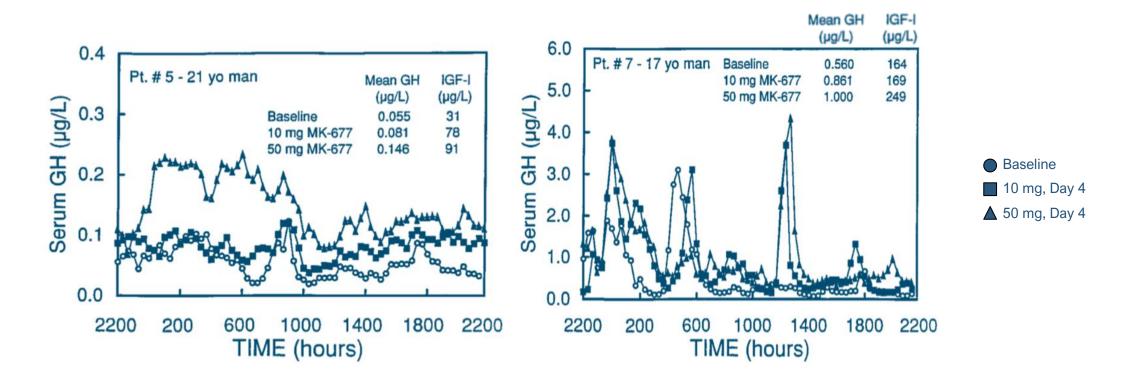


Higher LUM-201 doses produce higher plasma concentrations of LUM-201 & GH up to PD plateau PD curve shows potential for LUM-201 doses in OraGrowtH210 Trial to produce greater GH response

# Historical Data Show LUM-201 Augmented Growth Hormone (GH) Pulsatility and Increased Circulating IGF-1



- Adults with GH deficiency
- Individual subjects
- Representative 24-hour GH profiles on Day 4 of treatment

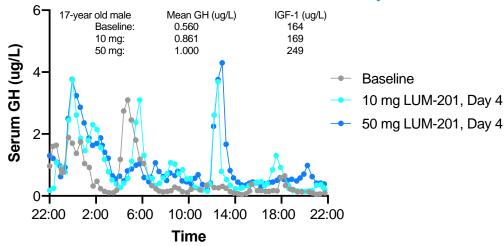


# Historical Data Demonstrate Differentiated MOA of LUM-201 vs rhGH LUM-201 Augments Growth Hormone (GH) Pulsatility in GHD Adults

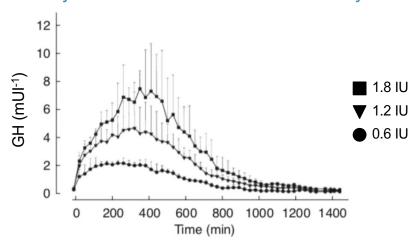


- Adults with GH deficiency
- LUM-201 augments endogenous GH pulses
- rhGH is administered as single, daily bolus doses

24h GH profile following oral LUM-201 administration in an adult with GH deficiency<sup>1</sup>



24h PK profile following subcutaneous rhGH injection in adults with GH deficiency<sup>2</sup>



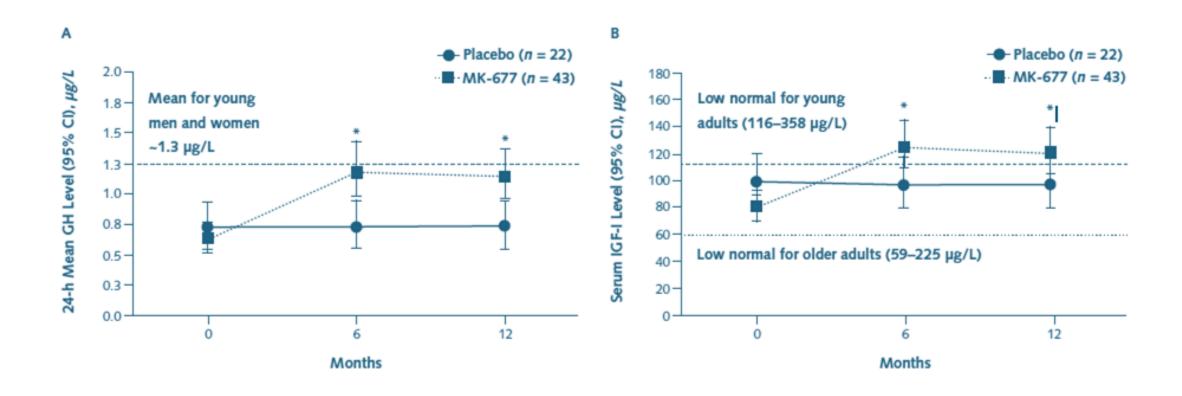
Potential to achieve non-inferior growth from smaller GH AUC via LUM-201 pulsatile delivery vs rhGH bolus administration

<sup>&</sup>lt;sup>1</sup> Adapted, Chapman 1997 J Clin Endocrinol

<sup>&</sup>lt;sup>2</sup> Janssen 1999 Br J Clin Pharmacol (Genotropin)



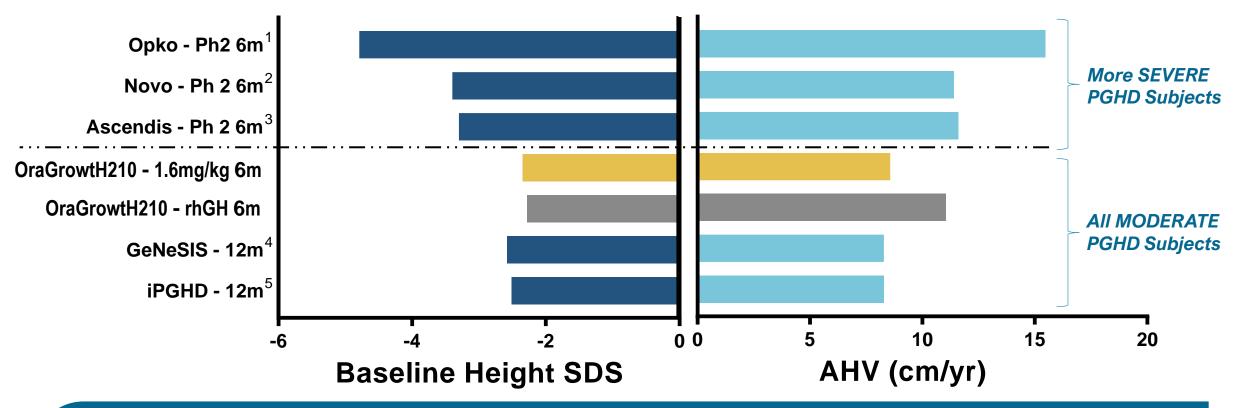
#### Historical Data Show LUM-201 Effects Were Durable in Healthy Elderly



LUM-201 mediated increases in serum GH and IGF-1 are sustained over 1 year of treatment

# Interim OraGrowtH210 Data (November 2022): rhGH Cohort Grew More than Historical Norms in Moderate PGHD Patient Population





Unprecedented rhGH growth response in OraGrowtH 210 in moderate PGHD at ~50% enrollment likely due to outlier & small sample size

Expect larger N from fully enrolled OraGrowtH210 Trial to reduce impact of growth outliers

SDS = Standard Deviation Score

<sup>1)</sup> Rosenfeld, ENDO 2014 presentation interim analysis, full analysis Zelinska et al JCEM 2017 2) Sävendahl et al JCEM, 2020 3) Chatelain et al JCEM, 2017

<sup>4)</sup> Blum et al JES 2021 5) Lechuga-Sancho et al JPEM 2009

### Key Baseline Characteristics that Predict Better AHV With rhGH Treatment of PGHD Patients

Historical data from multiple peer-reviewed scientific publications demonstrate the following metrics as key predictors of first-year growth

- Baseline Age
  - Age is the top predictor of growth on treatment
  - Younger PGHD subjects grow faster<sup>1</sup>
- Baseline Height
  - Shorter stature at baseline predicts greater 1<sup>st</sup> year growth<sup>2</sup>
- Baseline IGF-1 SDS
  - Lower baseline IGF-1 SDS predicts faster growth<sup>3</sup>
- Baseline Mid-parental height & Delta MPH SDS
  - Greater mid-parental height and subject Height SDS farther below MPH SDS predicts greater 1<sup>st</sup> year growth<sup>4</sup>
- Baseline weight (BMI)
  - Greater baseline weight (higher BMI) predicts faster growth<sup>5</sup>

<sup>&</sup>lt;sup>1</sup> Ranke, et al. Growth Horm & IGF Res (2009) 19:1–11; Lee, et al. Internat J Pediat Endocrin (2011):6; Yang, et al. Nature Sci Rep (2019) 9(1):16181; Blum et al JES (2021); Ranke et al JCEM (2010); Blethen, et al. JCEM (1993 Mar);76(3):574-9; Cho, et al. J Korean Med Sci. (2020 May) 35(19):e151

<sup>&</sup>lt;sup>2</sup> Ranke, et al. Growth Horm & IGF Rese (2009) 19:1–11; Lee, et al. Intern J Pediat Endocrin (2011):6; Cho, et al. J Korean Med Sci. (2020 May) 35(19):e151; Ranke et al. JCEM (2005) 90(4);1966-1971

<sup>&</sup>lt;sup>3</sup> Ranke, et al. Growth Horm & IGF Res (2009) 19:1–11; Lee, et al. Internat J Pediat Endocrin (2011):6

<sup>&</sup>lt;sup>4</sup> Ranke, et al. Growth Horm & IGF Res (2009) 19:1–11; ; Lee, et al. Intern J Pediat Endocrin (2011):6; Cho, et al. J Korean Med Sci. 2020 May 18;35(19):e151

<sup>&</sup>lt;sup>5</sup> Ranke, et al. Growth Horm & IGF Res (2009) 19:1–11; Lee, et al. Intern J Pediat Endocrin 2011:6; Cho, et al. J Korean Med Sci. 2020 May 18;35(19):e151; Blethen, et al. JCEM (1993 Mar);76(3):574-9; Ranke, et al. JCEM (2005) 90(4);1966-1971; Yang, et al. Nature Sci Rep 2019, 9(1); 16181



#### Ranke Model is the Gold Standard in Growth Prediction for GHD

•	Parameter Rank 1st	[-1.37 X (In max GH stim)]	A measure of how GHD subject is by stim test value
•	Parameter Rank 2nd	(-0.32 X Age)	Age at treatment start is a very important predictor
•	Parameter Rank 6th	(0.32 X BWt SDS)	Birth weight SDS
•	Parameter Rank 5th	(-0.5457)	Dose of rhGH (constant for this trial)
•	Parameter Rank 3rd	(-0.4 X HtSDS-MPH SDS)	Measure of how far away from their target height
•	Parameter Rank 4th	(0.29 X Wt SDS)	Body weight at start of treatment

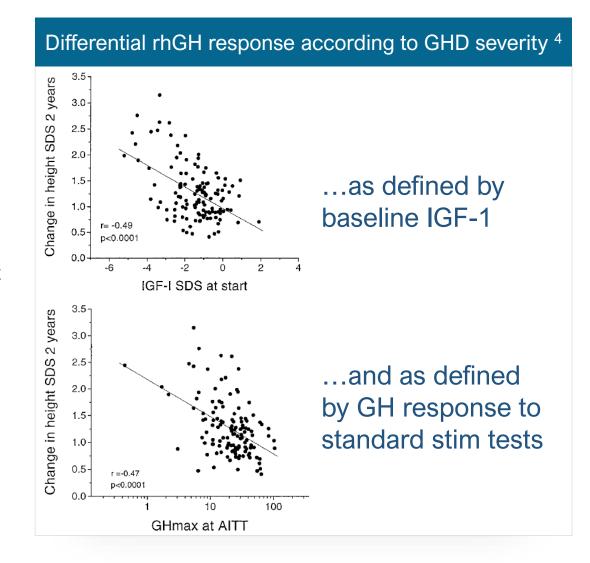
- The model was developed based on mining the KIGS data set of rhGH PGHD treatment data
  - Phase 4 database for Genotropin N= 593 when model developed
  - Developed models to predict 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> year growth

Growth for both rhGH and LUM-201 1.6 mg/kg cohorts was predicted using Ranke models



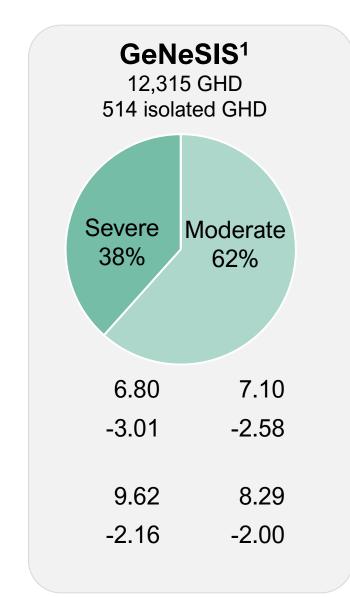
### Growth Hormone Deficiency Patients Have a Range of Secretion Insufficiency

- Well established in the literature:
  - A wide range of severity in GHD¹
  - Variability in responses to GH therapy
  - Severely GH deficient patients exhibit greater growth response to rhGH compared to moderately deficient patients<sup>1</sup>
- Several prediction models attempt to explain variability and optimize GH treatment<sup>2</sup>
  - Multiple factors may contribute
  - GH response to standard stimulation tests is most important predictor of first year growth response to rhGH in PGHD in one analysis<sup>3</sup>
  - Inclusion of baseline IGF-1 strengthened model<sup>4</sup>
- Recent publications
  - Baseline IGF-1 and GH response to standard stimulations tests are independent predictors of growth when patients are treated with rhGH<sup>5</sup>
  - Moderate GHD represents ~60% of total PGHD population<sup>5</sup>





### PEM Segmentation Aligns With Patients' Differentiated Baseline Characteristics



#### **Conclusions**

Analysis of 20-yr multinational database for Eli Lilly's rhGH:

Illustrates PGHD population can be segmented by severity

- Segmentation achieved using PEMs (markers) IGF-1 and peak GH to stimulation tests
- Moderate and Severe PGHD have distinct characteristics

Lumos PEMs applied to GeNeSIS show Moderates ~60% of PGHD

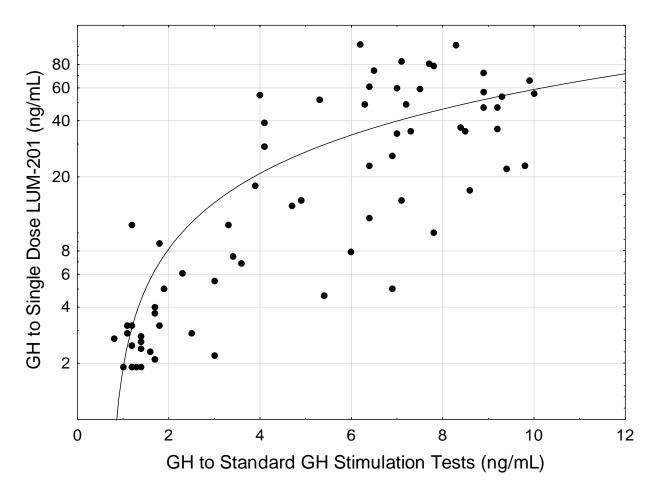
- Likely LUM-201 responders
- Moderate<sup>2</sup>: LUM-201 PEMs baseline IGF > 30 ng/ml and stim GH ≥ 5 ng/ml

Baseline Chronological age (y)
Height SDS

rhGH Height velocity (cm/y)
Height SDS



### More GH Released from LUM-201 Stim than from Standard Stim Test Agents



68 children with growth hormone deficiency

All had 2 standard GH stimulation tests

 Standard test agents: arginine, clonidine, l-dopa, glucagon, insulin

All had a single dose of LUM-201 stim test

Data presented at the 2021 Annual Meeting of The Endocrine Society and published online in the journal, Hormone Research in Paediatrics, March 2022

# Study of Oral LUM-201 in Non-Alcoholic Fatty Liver Disease (NAFLD) Mass General Investigator-Initiated Phase 2 Pilot Trial



#### MGH Initiated Phase 2 Pilot Trial#

- n = 10
- Adult NAFLD subjects with relative GH/IGF-1 deficiency
- Open-label
- Single-site pilot study
- 6-month dosing

#### Currently enrolling subjects

Study Duration – 6 months

n = 10 – LUM-201 at dose level of 25 mg/day

#### **Objectives**

#### **Primary Objective:**

 Determine changes in intrahepatic lipid content, inflammation, and potentially fibrosis resulting from LUM-201 induced GH augmentation compared to historical placebo-treated controls

Massachusetts General Hospital (MGH) initiated pilot study of oral LUM-201 in NAFLD: Enrollment ongoing