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).

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OraGrowtH212 TRIAL

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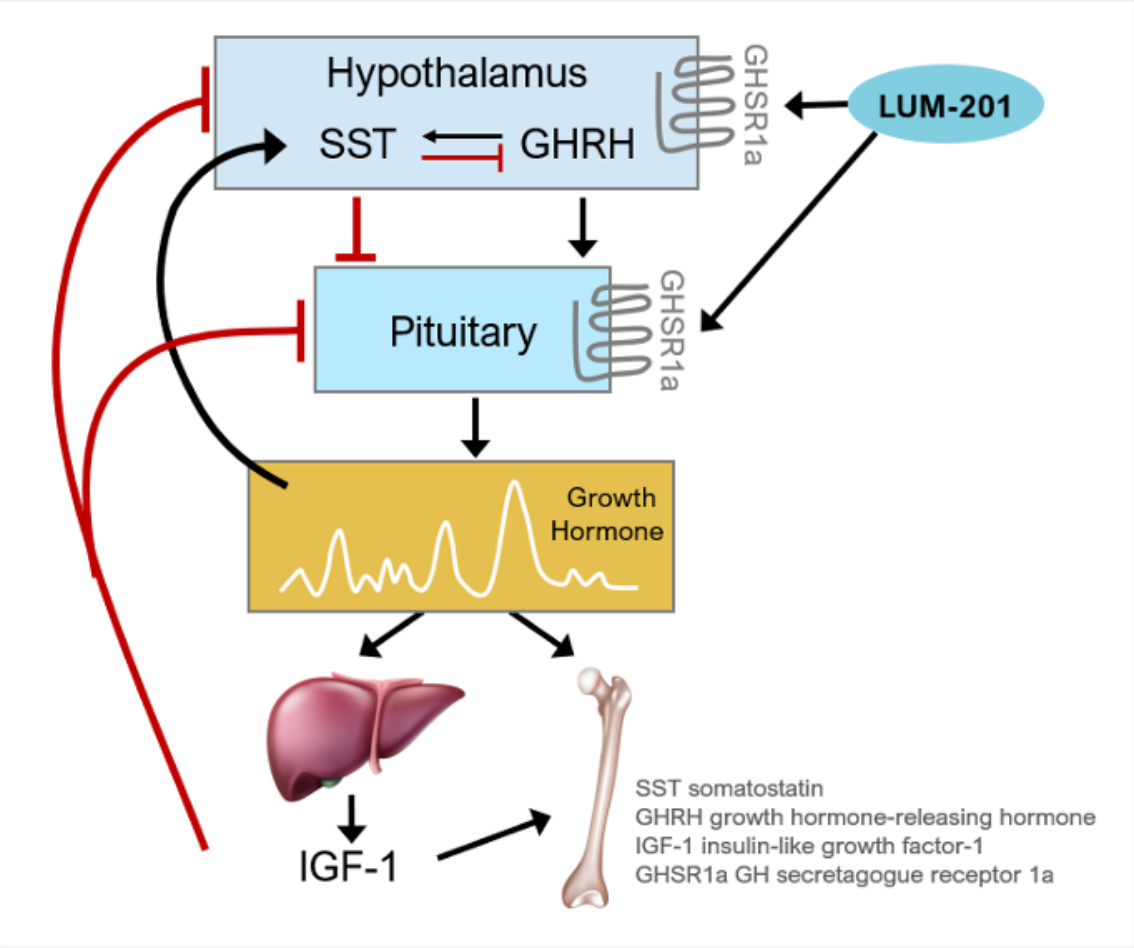
Disclosure

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***

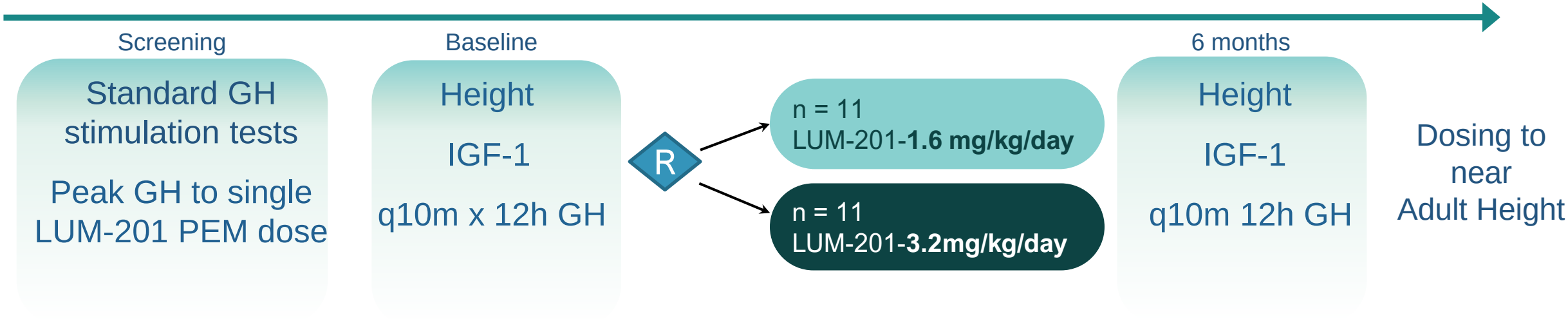
☑ Moderate Idiopathic PGHD - Axis Responsive

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
- 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

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

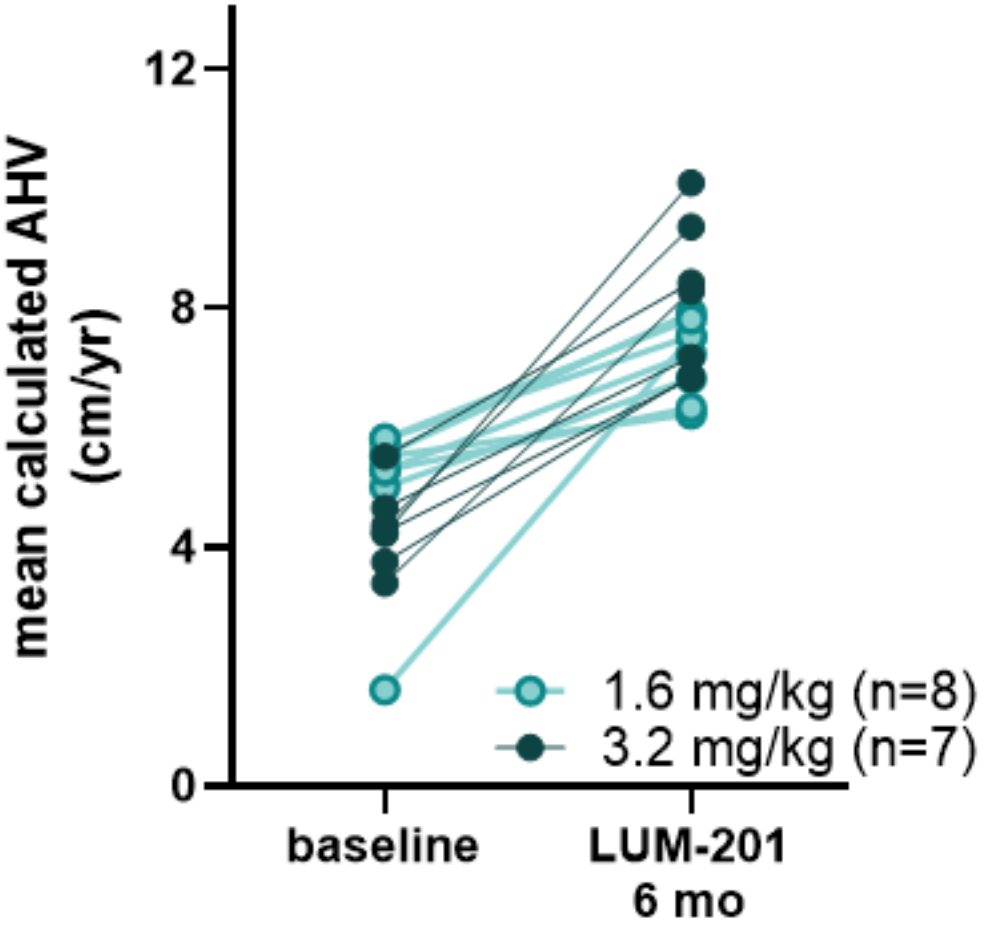
Subjects N=15	1.6 mg N=8	3.2 mg N=7
	Mean (SD)	
Age (mos)	96.9 (11.9)	**95.0** (22.7)
Height (cm)	115.2 (4.57)	113.1(9.97)
Height SDS	-2.12 (0.29)	-2.34 (0.45)
IGF-1 SDS	-1.1 (0.535)	-0.8 (0.377)
MPH (cm)	161.8 (6.98)	160.82 (5.73)
MPH SDS Δ	0.73 (0.47)	**0.81 (0.43)**
BA Delay (yrs)	1.50 (0.26)	**1.83 (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



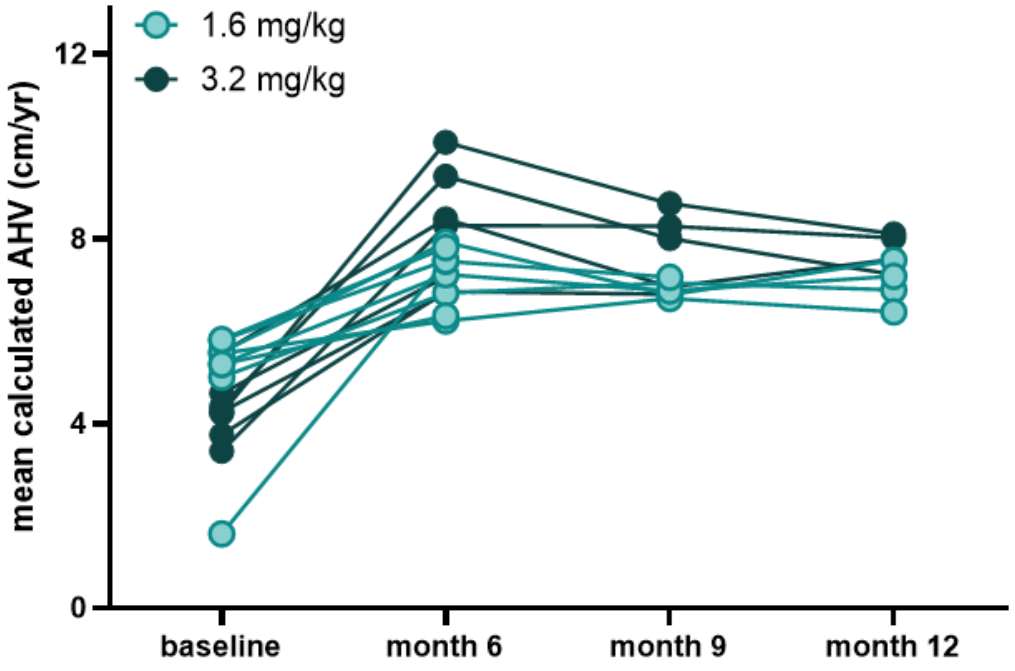
6-month observations:

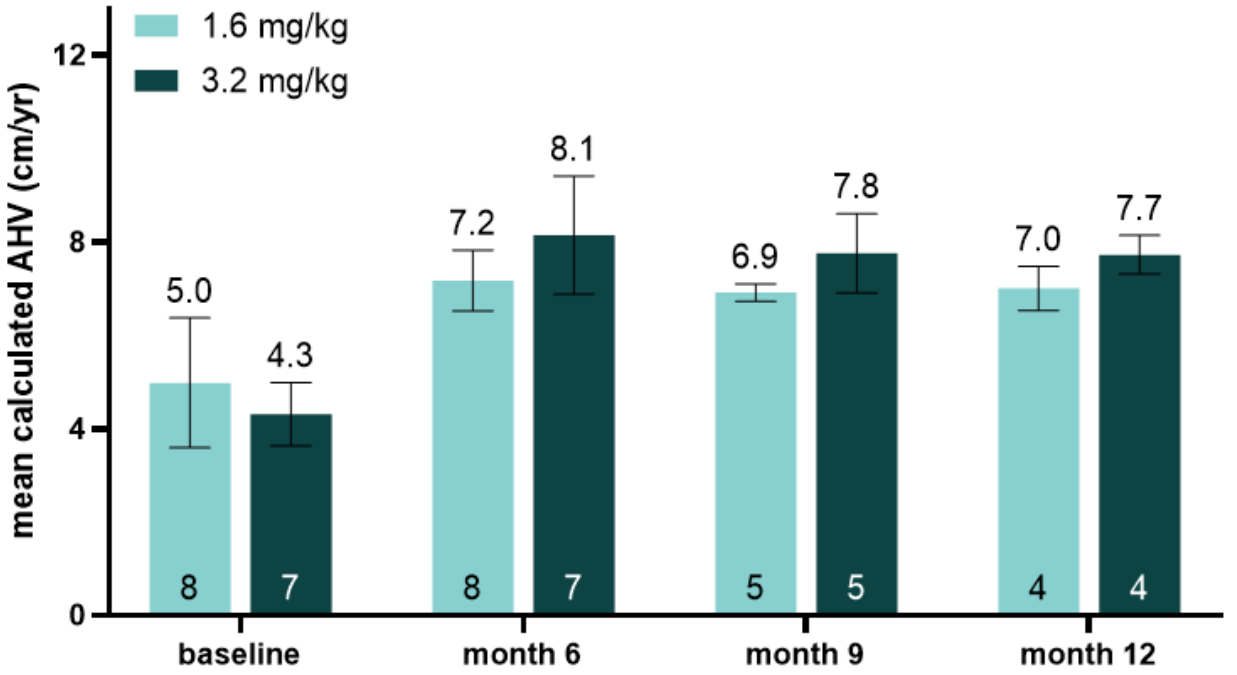
- LUM-201 raised the AHV (growth rate) from baseline after 6 months on therapy for both the 1.6 mg/kg cohort ($p = 0.0006$) and the 3.2 mg/kg cohort ($p < 0.0001$)
- No statistical difference exists between the two cohorts at each timepoint
- As expected, greater growth response was observed in patients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

Durable Response After 12 Months of LUM-201 Administration

OraGrowtH212 TRIAL

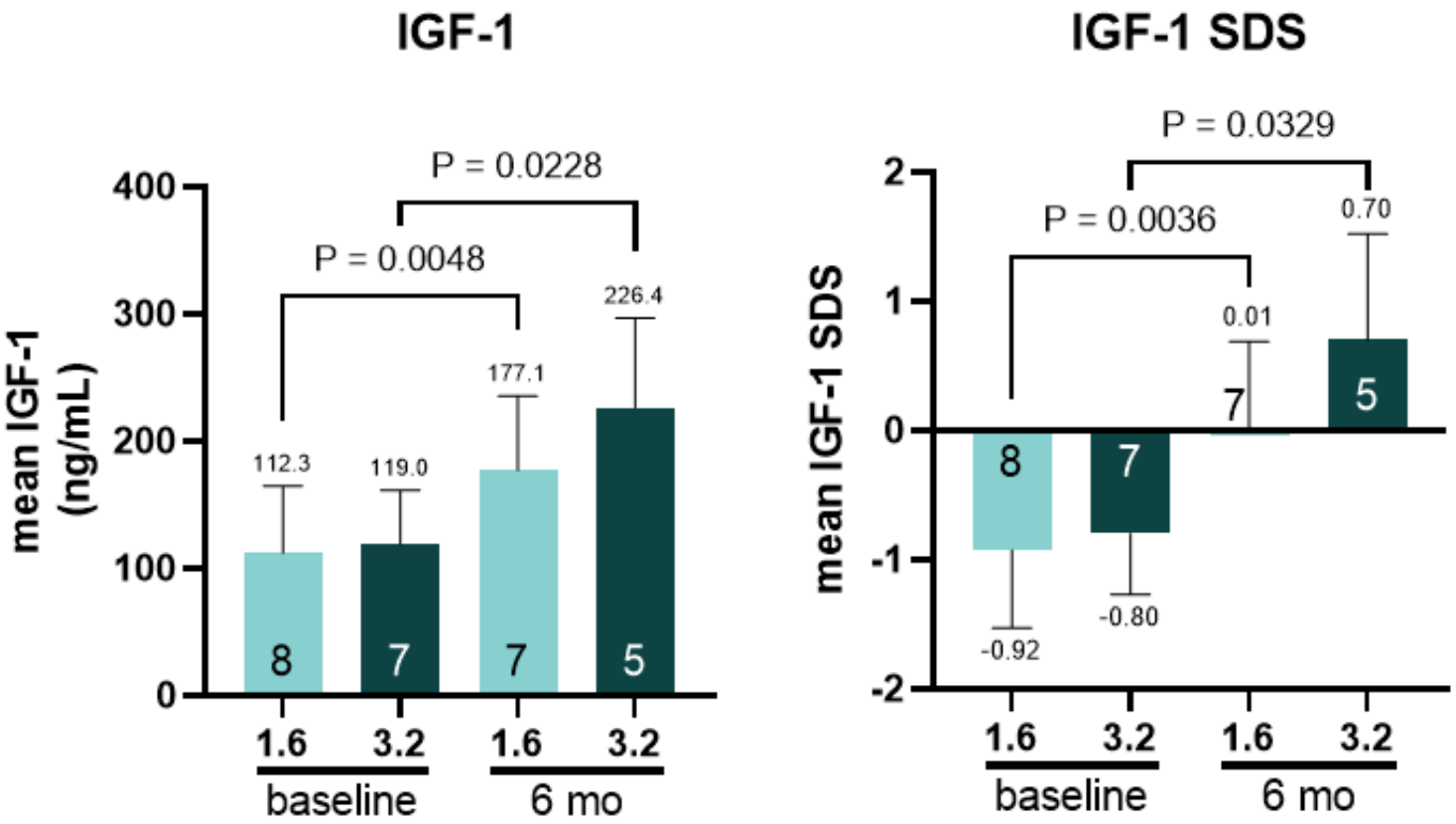
Mean AHV's in OraGrowtH212 Trial





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

OraGrowth212 TRIAL



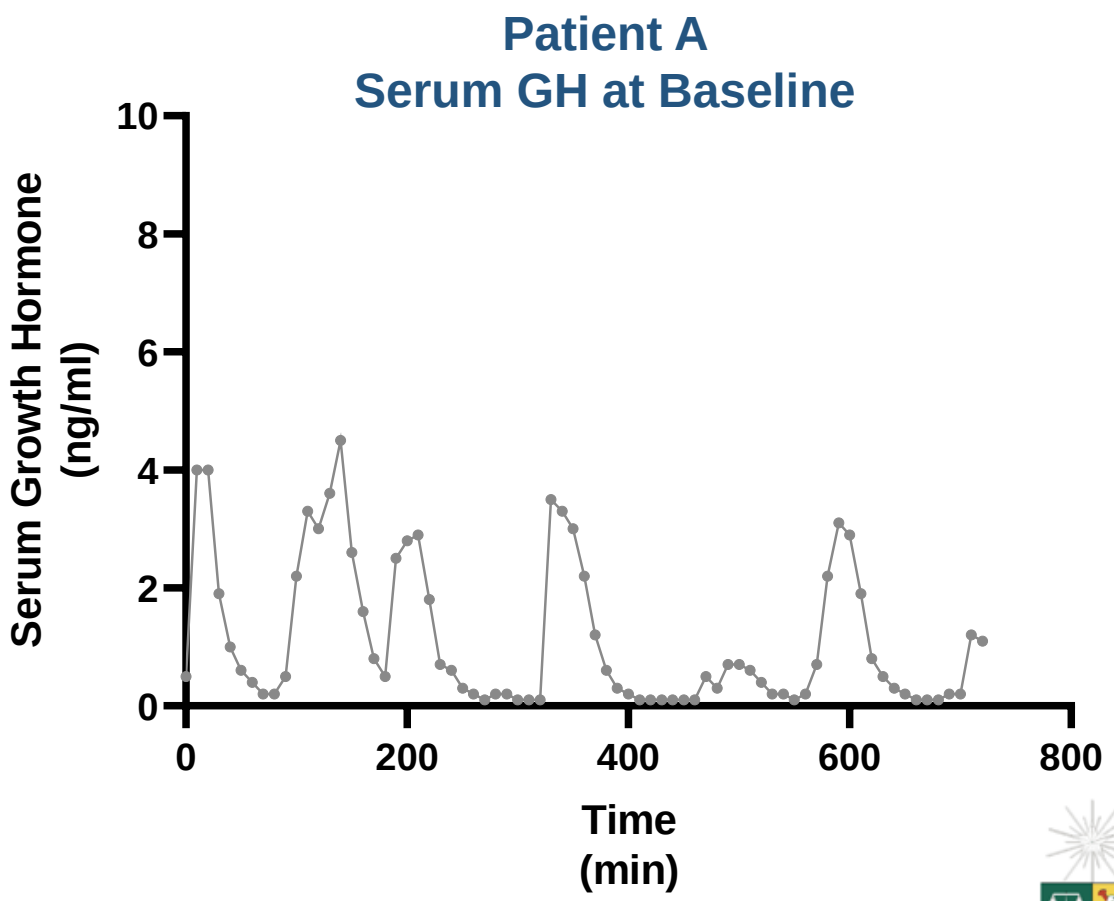
Conclusions :

- 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

OraGrowtH212 TRIAL

		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	



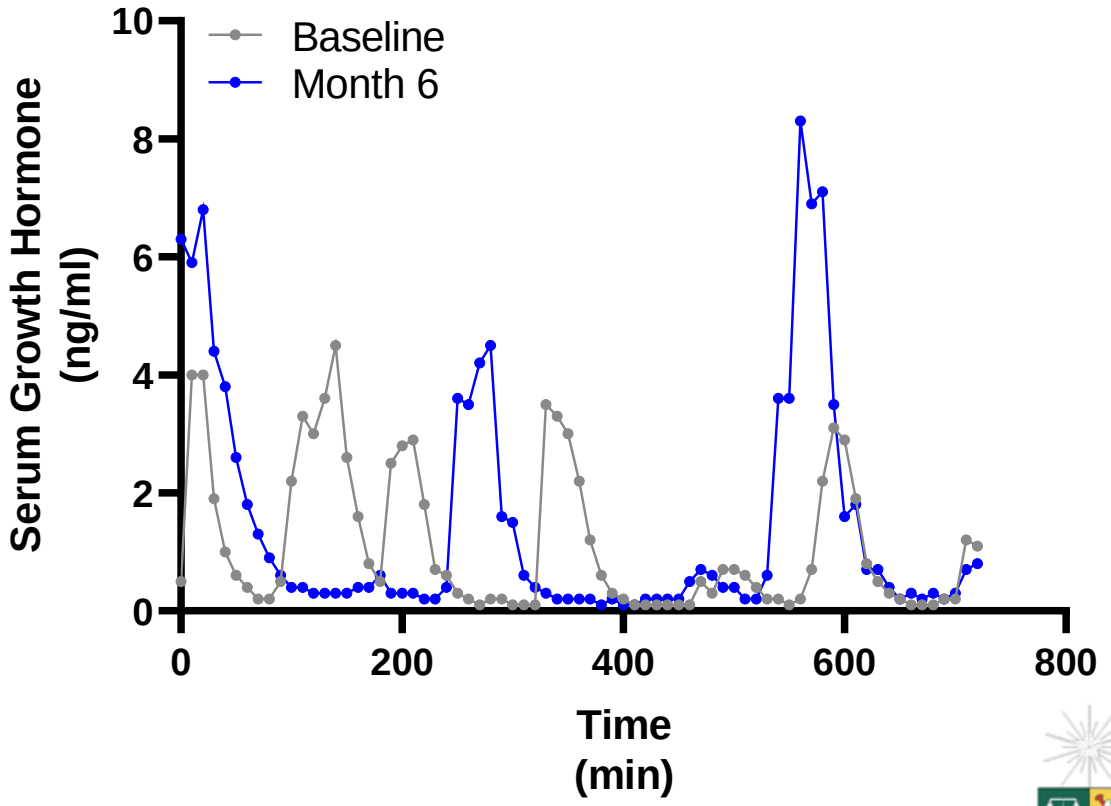
IGF-1, GH Pulsatility, Height Velocity
Patient A **1.6 mg**/kg/day

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)

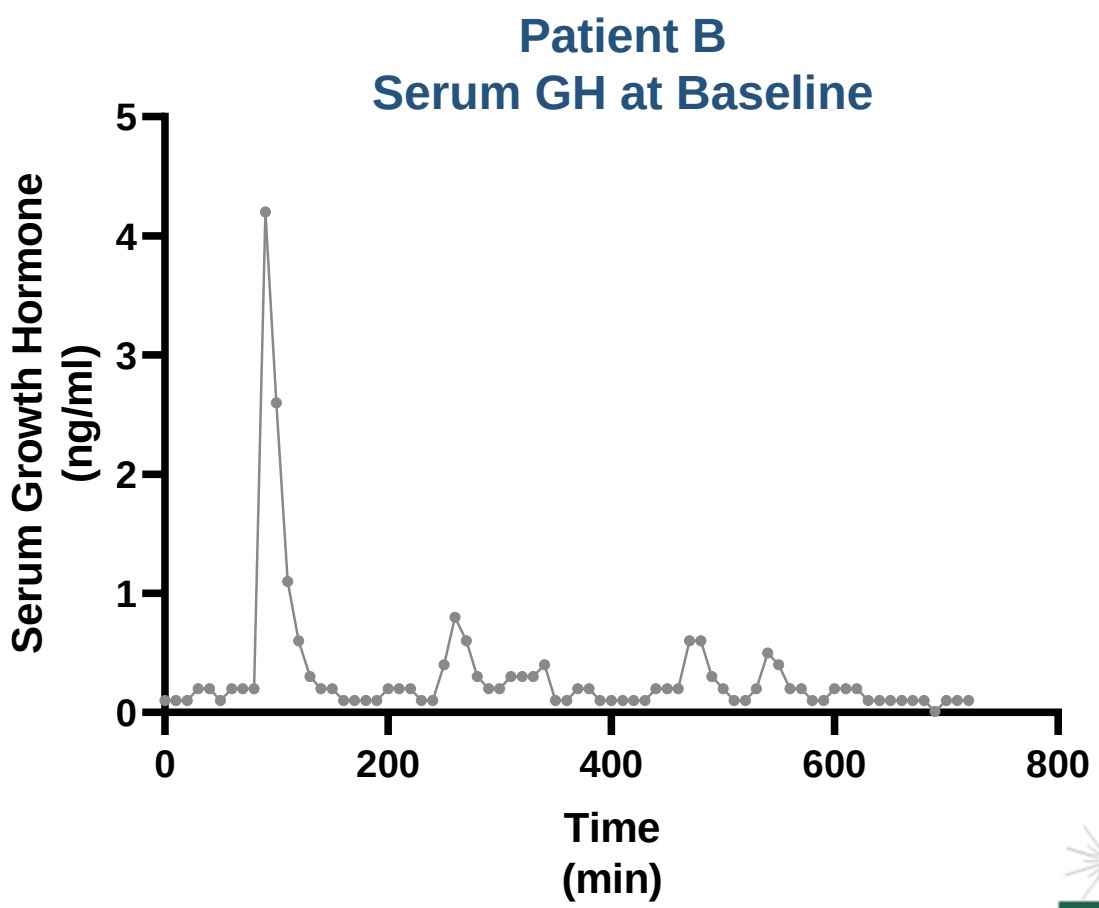
Patient A
Serum GH at Baseline & at 6 months on LUM-201



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	



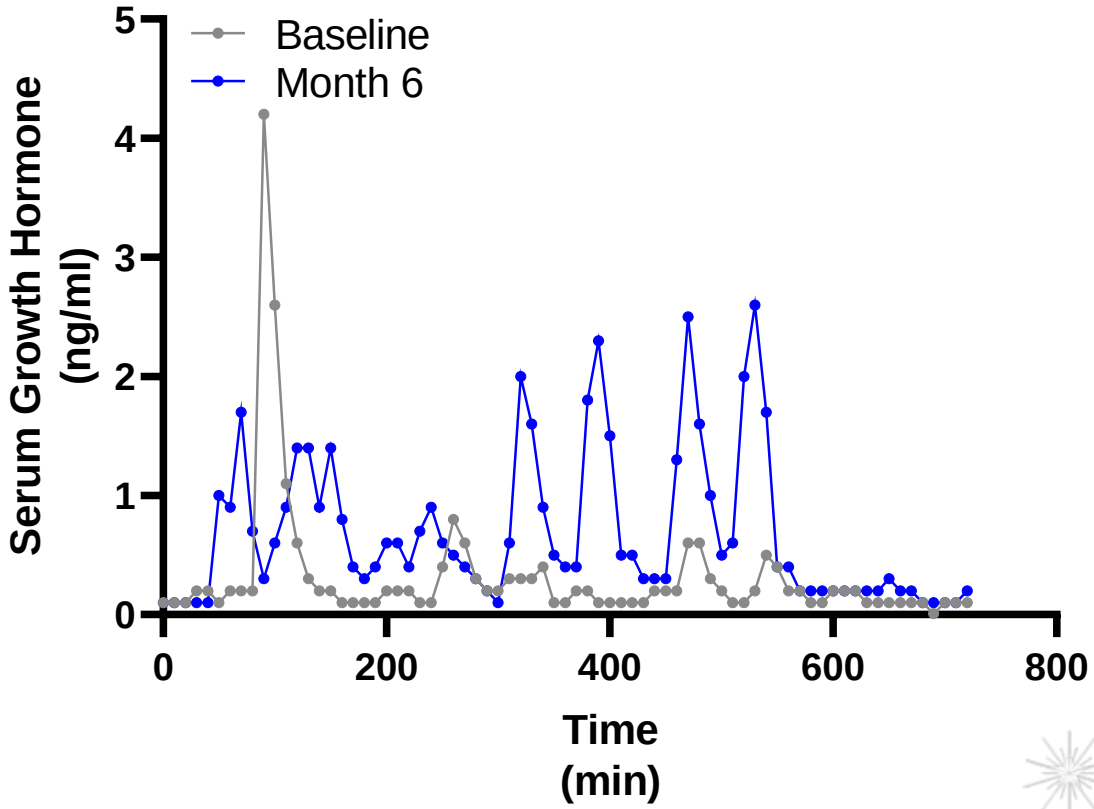
IGF-1, GH Pulsatility, Height Velocity: Patient B **3.2 mg**/kg/day

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

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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 idiopathic 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 pre-pubertal 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

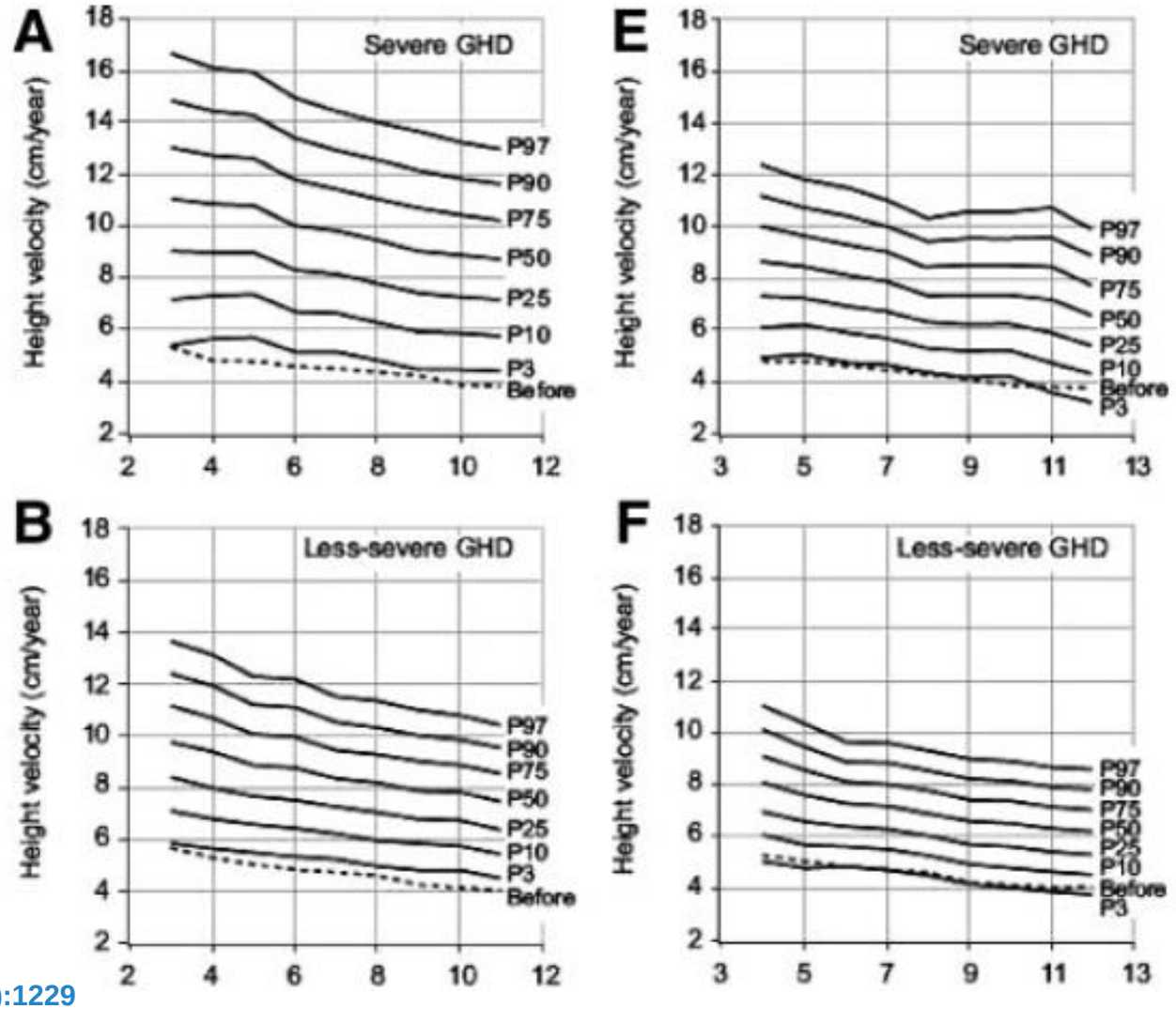
Height Velocity During Daily rhGH Therapy

OraGrowtH212 TRIAL

First year | Second year

Severe PGHD

Moderate PGHD



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