Dose-dependent Increase in GH $AUC_{0\text{-}12h}$ with LUM-201 in Idiopathic Pediatric GH Deficiency from the Interim Analysis Data of the OraGrowtH212 Trial

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OraGrowtH212 TRIAL

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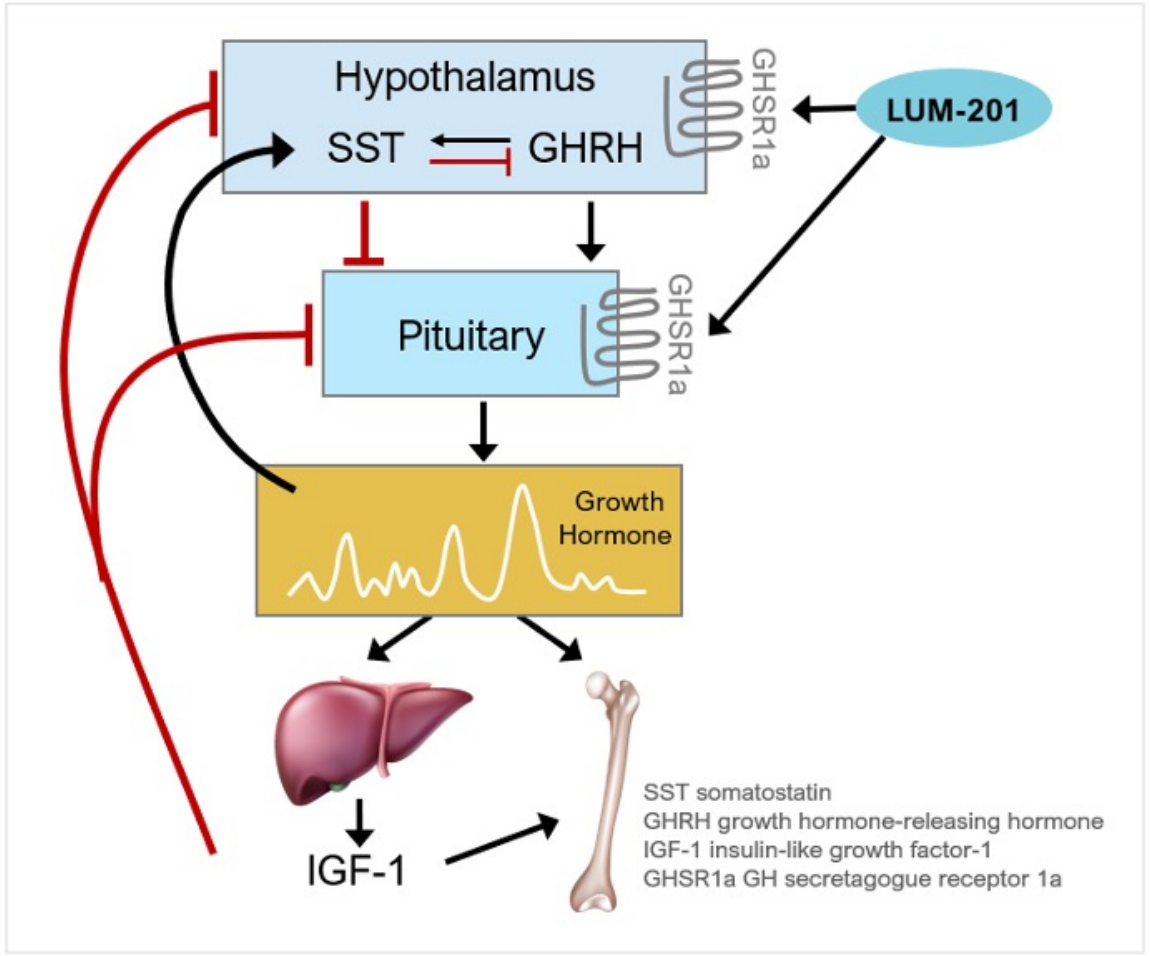
Disclosure

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

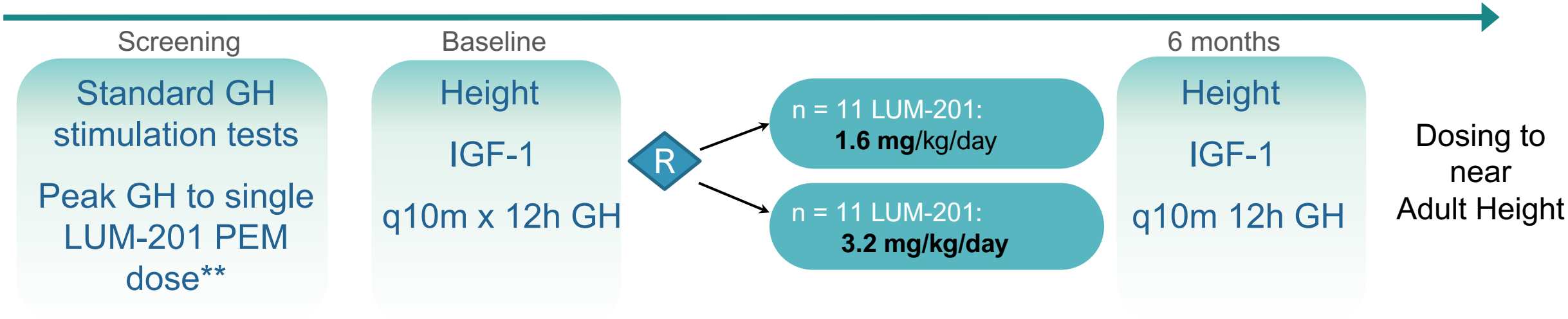


- Oral LUM-201 is a ***growth hormone (GH) secretagogue***
- Acts as a durable agonist of GH Secretagogue Receptor (GHSR1a) to stimulate GH release[1]
- LUM-201 has been observed to ***increase the amplitude of endogenous, pulsatile GH secretion over 24 hours***[2,3]
- Another differentiating feature 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***
  - ✓ Idiopathic PGHD- Axis Responsive
  - ✗ Severe PGHD- Axis NON-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

Pulsatility and PD Clinical Study Design of LUM-201 in Naive iPGHD patients

OraGrowtH212 TRIAL



Study Information:

- Open-label study: N = 22
- iPGHD patients
- rhGH-treatment naïve
- 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

Inclusion Criteria: Height < 2 SD, delayed bone age, serum IGF-1 below the mean for age, and peak GH response to a clonidine stimulation test between 3 and 10 ng

Questions

OraGrowtH212 TRIAL

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

2. Will increased GH pulses improve height velocity?

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

Baseline Demographics

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Subjects N=15	1.6 mg N=8	3.2 mg N=7
	Mean (SD)	
Age (mos)	95.6 (10.9)	**93.7** (22.7)
Height (cm)	115.2 (4.57)	113.1(9.97)
Height SDS	-2.29 (0.28)	-2.31 (0.33)
IGF-1 SDS	-1.0 (0.693)	-0.8 (0.356)
MPH (cm)	162.29 (7.36)	160.35 (5.53)
MPH SDS Δ	-1.36 (0.42)	**-1.7 (0.43)**
BA Delay (yrs)	1.50 (0.26)	**1.83 (0.88)**
BMI (SDS)	-0.014 (0.91)	**+0.22 (1.09)**
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

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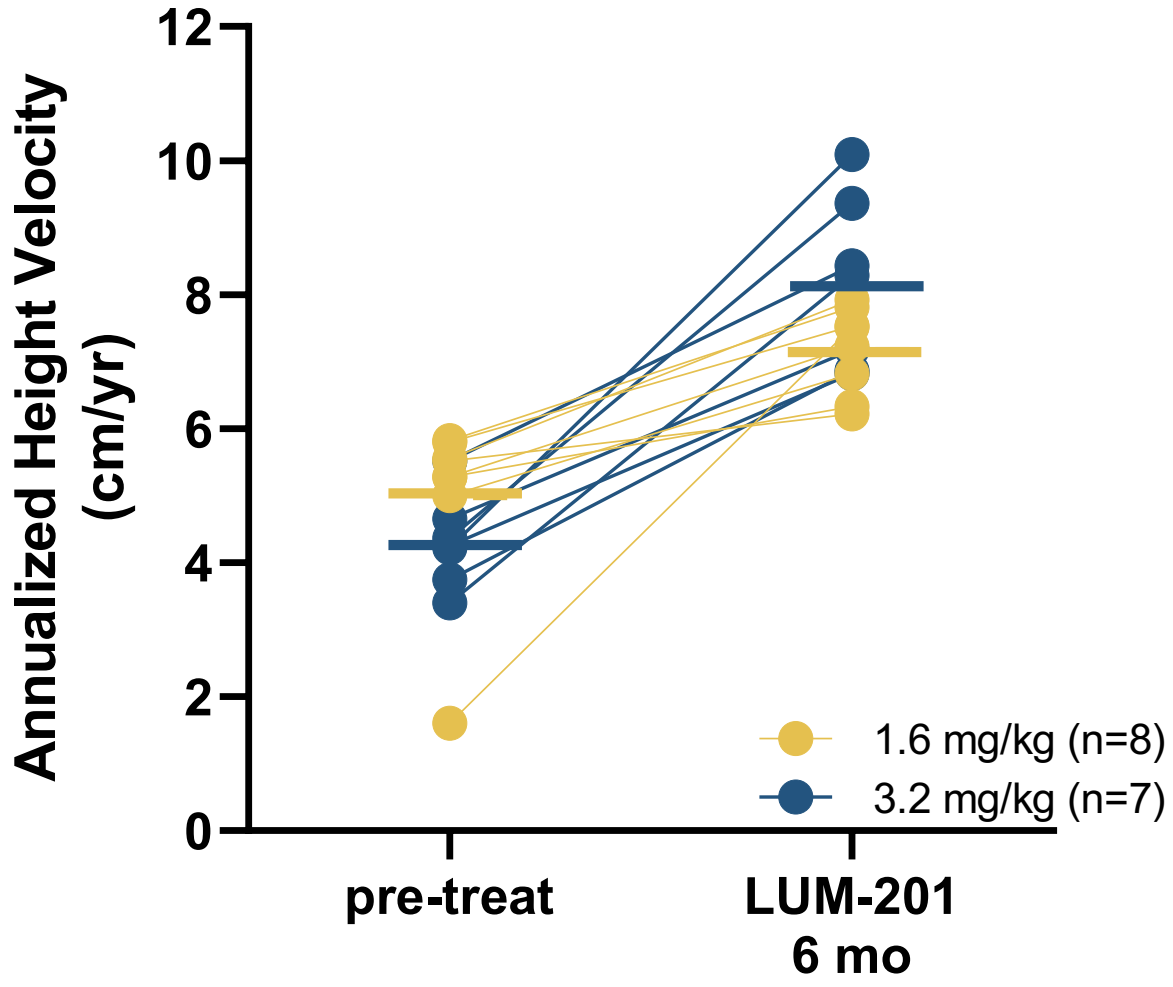
AHV Before and After 6 months of LUM-201 Treatment

OraGrowtH212 TRIAL



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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

Interim 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 Related 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%)

Conclusion:

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

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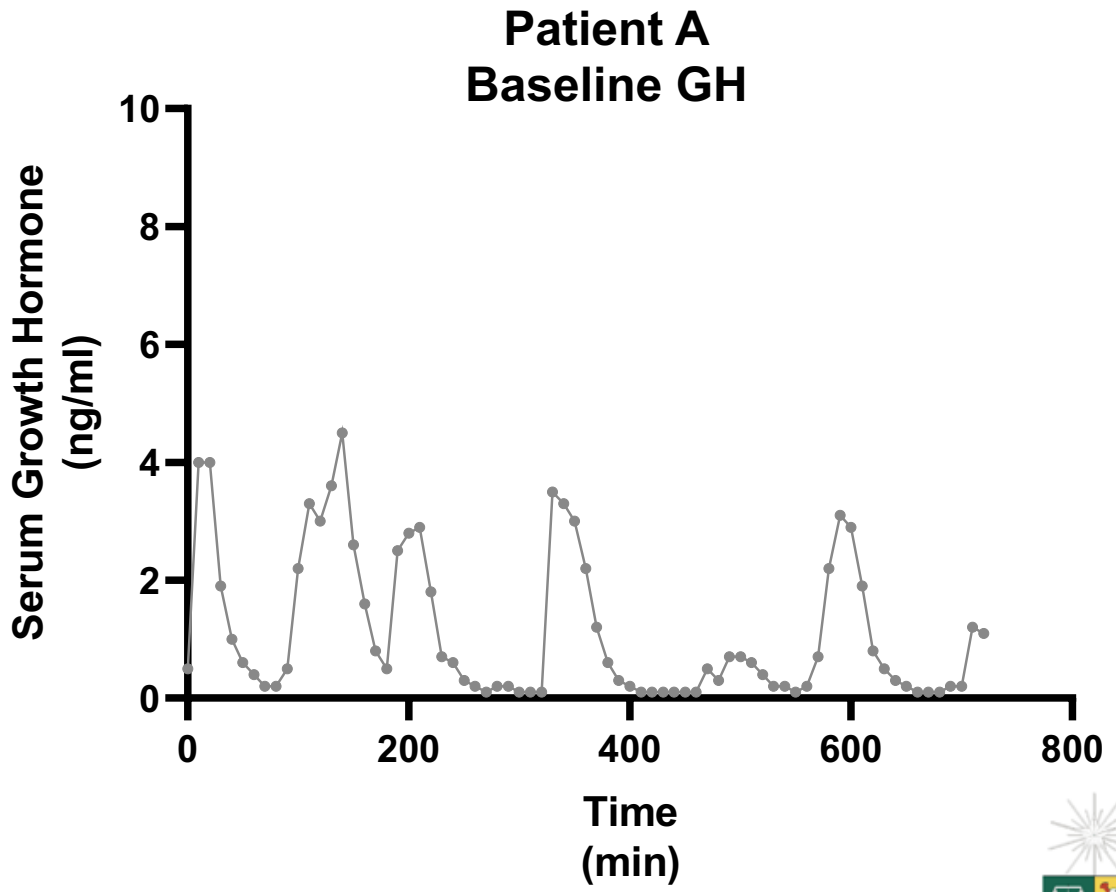
IGF-1, GH Pulsatility, Height Velocity: **Baseline** – Patient A **1.6 mg**/kg/day

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	



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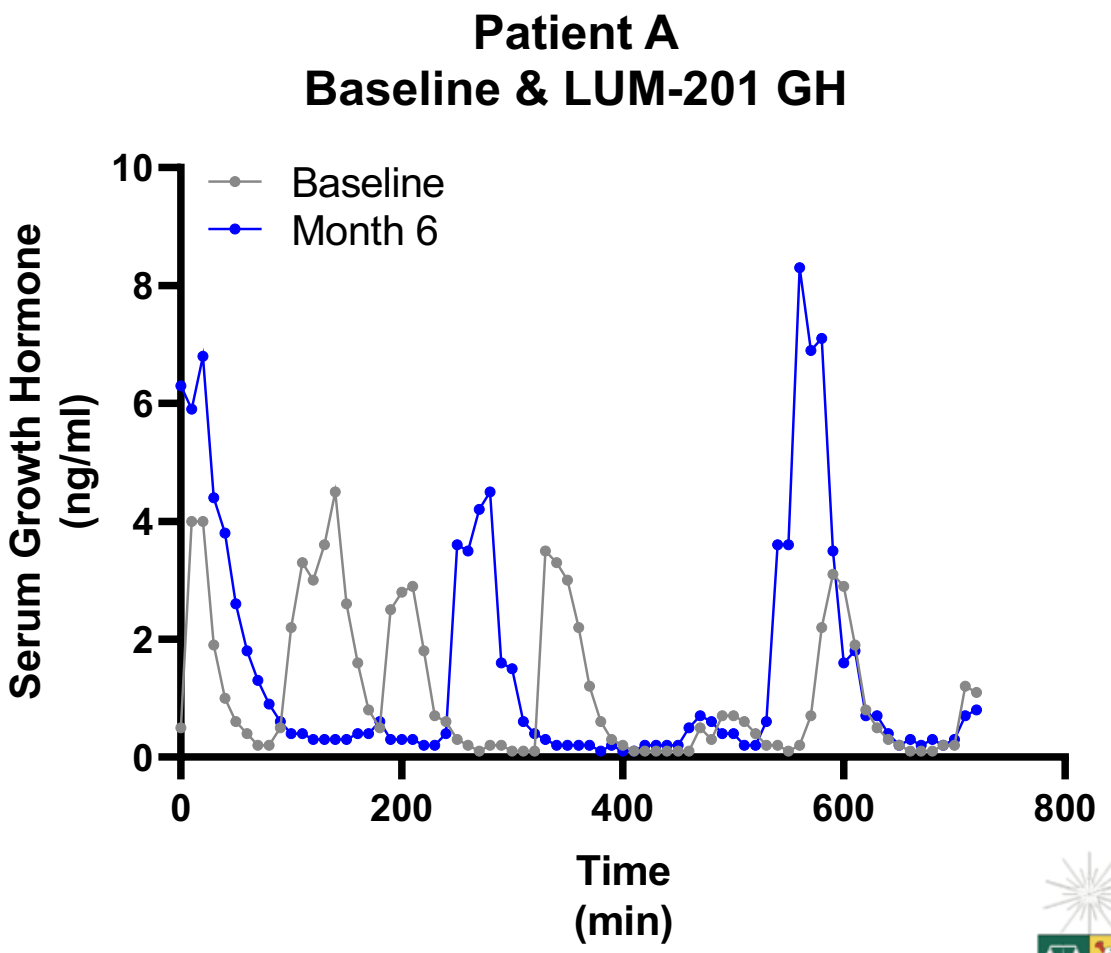
Pulsatility and AHV data: **Month 6**
Patient A **1.6 mg**/kg/day

		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)



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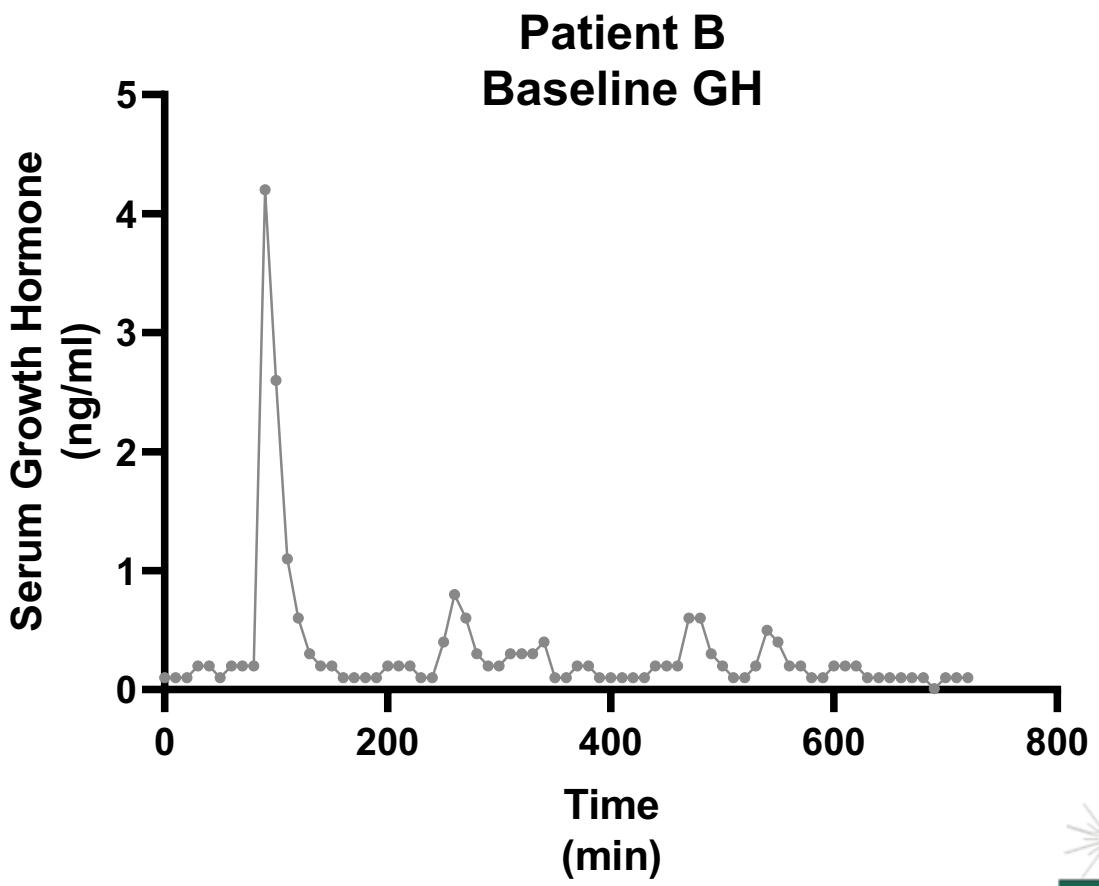
IGF-1, GH Pulsatility, Height Velocity: **Baseline** - Patient B **3.2 mg**/kg/day

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	



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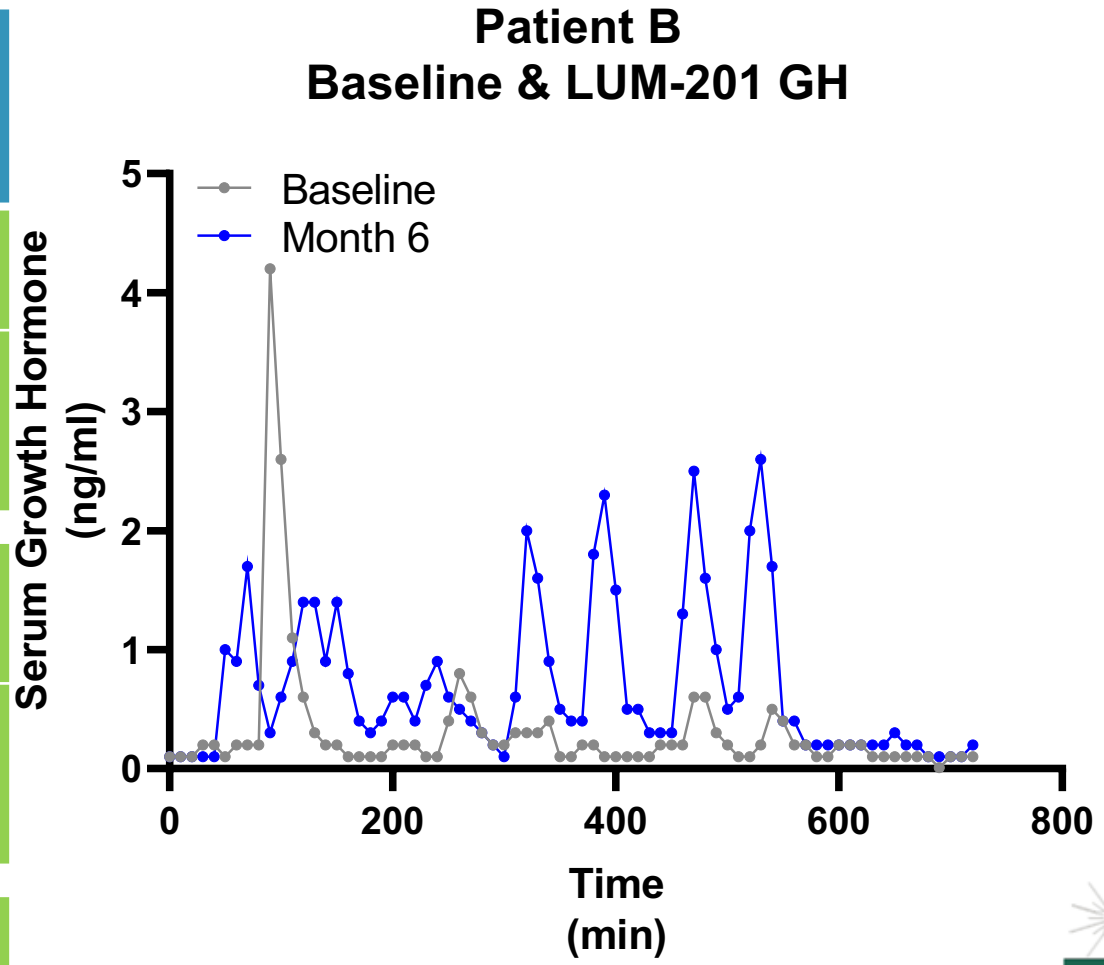
Pulsatility and AHV data: **Month 6**
Patient B **3.2 mg**/kg/day

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)



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Change from baseline in mean GH concentration and GH $AUC_{0\text{-}12h}$ after 6-months LUM-201 daily dosing

OraGrowtH212 TRIAL

Dose of LUM-201		1.6 mg/kg (n = 8)		3.2 mg/kg (n=7)	
		baseline	6 mo	baseline	6 mo
mean GH conc (ng/ml)	Median	**1.04**	1.22	**0.47**	1.36
	95% CI	0.51-1.59	0.81-1.93	0.25-1.17	0.49-3.02
GH $AUC_{0\text{-}12h}$	Median	**758.6**	894.0	**343.8**	992.3
	95% CI	376.4-1161	587.1-1411	182.0-854.9	357.3-2207

Conclusions

- Increases in GH $AUC_{0\text{-}12}$ are driven primarily by increased amplitude of GH pulses to generate increases in height velocity
- Number of GH pulses is unchanged from baseline to 6 months of treatment
- The 3.2 mg/kg cohort started with lower GH secretion at baseline than the 1.6 mg/kg cohort

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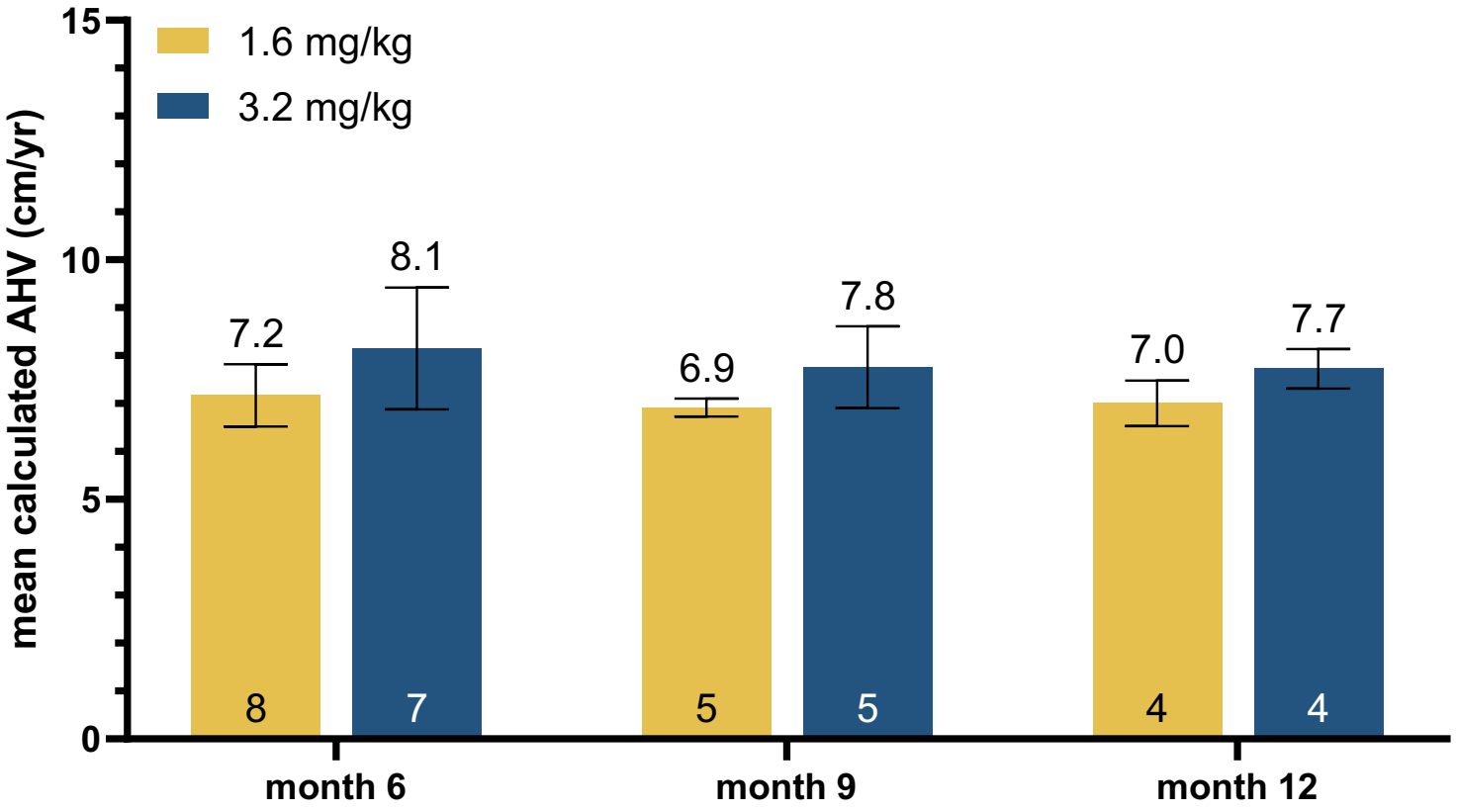
Durable response after 12 months of LUM-201 administration

OraGrowtH212 TRIAL

Mean AHV's in OraGrowtH212 Trial



Conclusions:

- Based on Interim data, OraGrowtH212 data demonstrates that growth acceleration is durable through 12 months
- 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 (KIGS, GeNeSiS)[1], in this moderate iPGHD population

Data presented at IMPE March 2023

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

Questions

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

2. Will increased GH pulse amplitude improve height velocity?

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

For information on OraGrowtH210 Trial with a reference to rhGH historical growth data, please see IMPE poster #83 Dr Alison Lunsford.

University of Chile, Santiago

Institute of Maternal and Child Research Pediatric Team

OraGrowtH212 TRIAL

Backup Slides

Change from baseline in GH $AUC_{0\text{-}12h}$ and Pulsatile GH Secretion after 6-months LUM-201 daily dosing

OraGrowtH212 TRIAL

Dose of LUM-201		1.6 mg/kg (n = 8)		3.2 mg/kg (n=7)	
		baseline	6 mo	baseline	6 mo
mean GH conc ng/ml	Median	**1.04**	1.22	**0.47**	1.36
	95% CI	0.51-1.59	0.81-1.93	0.25-1.17	0.49-3.02
GH $AUC_{0\text{-}12h}$	Median	**758.6**	894.0	**343.8**	992.3
	95% CI	376.4-1161	587.1-1411	182.0-854.9	357.3-2207
pulsatile GH (ng/ml/12hr)	Median	35.7	32.4	11.0	46.5
	95% CI	18.8-46.5	21.8-57.9	3.57-43.0	14.3-83.4
interpulse GH (ng/ml/12hr)	Median	5.1	5.5	2.7^{++}	8.5^{++}
	95% CI	2.1-7.0	3.0-12.0	1.5-4.2	3.8-17.0
total GH (ng/ml/12hr)	Median	40.7	39.0	12.9	56.9
	95% CI	21.9-52.5	26.0-68.6	5.8-46.3	24.3-94.2

Conclusions

- Increases in GH $AUC_{0\text{-}12}$ are driven primarily by increased pulsatile GH secretion to generate substantive increases in AHV
- Number of GH pulses is unchanged from baseline to 6m
- The 3.2 mg/kg cohort started with lower GH secretion at baseline than the 1.6 mg/kg cohort.
- This GH monitoring occurred over 12 hours (8AM to 8PM). GH secretion follows a 24-hour pattern with large peaks occurring during the night.

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$^{++}$The baseline vs. 6m interpulse GH in the 3.2mg/kg cohort was statistically significant. All other comparisons between cohort and timepoint were not statistically significant.

supplemental