Growth Response to LUM-201 in the OraGrowthH210 Trial in Idiopathic Pediatric Growth Hormone Deficiency (iPGHD): Interim Analysis Data (41 subjects) Abstract 6178

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OraGrowtH210 TRIAL

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

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Disclosures

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- Consulting fees or speaker honoraria:
  - Ascendis, OPKO, BridgeBio, Novo Nordisk, Pfizer, Ipsen, Sandoz
- Prior Research Support
  - Novo Nordisk, Ipsen, Pfizer
- Current Research Support
  - BioMarin, NICHD, Pfizer
- Site Investigator in Lumos Pharma OraGrowtH210 Trial

- 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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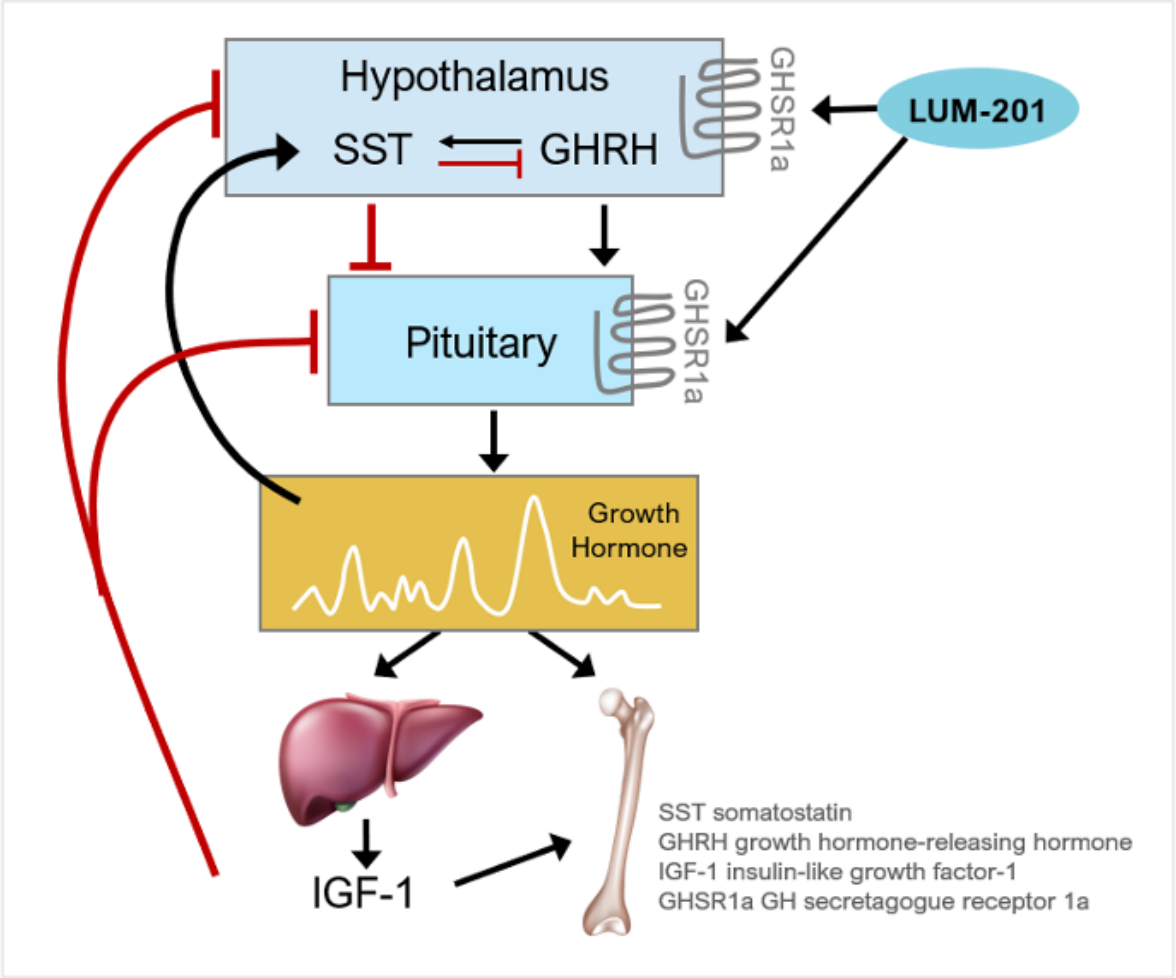
LUM-201 – Oral Growth Hormone Secretagogue

OraGrowtH210 TRIAL

LUM-201

- Binds to GH Secretagogue (ghrelin) receptor
- Increases amplitude of endogenous GH pulses
- Acts within intact GH/IGF-1 feedback loop

- Phase 2 study ongoing- OraGrowtH210 Trial
  - 3 doses of LUM-201 vs daily rhGH
  - 24-month study
  - Pre-pubertal GH deficiency - iPGHD



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https://lumos-pharma.com/posters-publications/
ClinicalTrials.gov NCT04614337.

Single Stim Dose of LUM-201 Identifies Likely Responders

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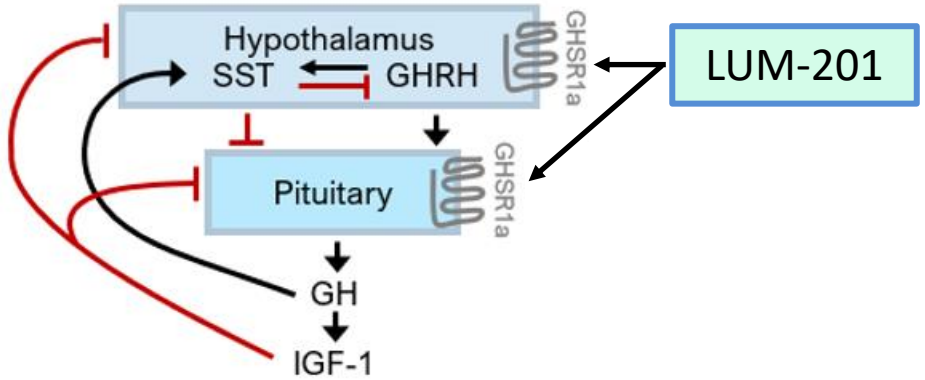
LUM-201

Stim dose

Moderate / Idiopathic PGHD
PEM-Positive

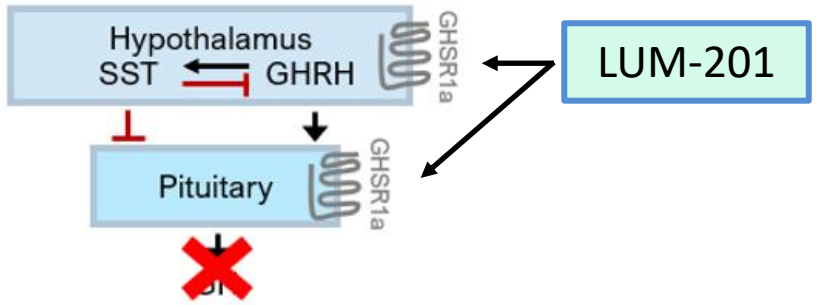
~60% of total PGHD population[1]



Responders to LUM-201[2]

Severe / Organic PGHD
PEM-Negative

~40% of total PGHD population



Non-Responders to LUM-201

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

Predictive Enrichment Marker Negative (PEM−)
- Baseline IGF-1 < 30 ng/ml
- Stim LUM-201 GH < 5 ng/ml
- Non-functional HP-GH axis

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[1] Blum 2021 JES [2] Bright 2021 JES HP-GH axis – hypothalamic pituitary growth hormone axis

Phase 2 OraGrowtH210 Trial in Moderate Idiopathic PGHD

OraGrowtH210 TRIAL

Trial Design

- N = 80 subjects
- Only PEM(+) PGHD subjects
- Inclusion: stim GH ≥ 5 ng/mL* & baseline IGF-1 > 30 ng/mL
- rhGH treatment naïve
- ~45 trial sites US & Int'l
- Trial opened Q4 2020
- Trial duration 24 months

Randomization

- n = 20 LUM-201: 0.8 mg/kg/day
- n = 20 LUM-201: 1.6 mg/kg/day
- n = 20 LUM-201: 3.2 mg/kg/day
- n = 20 Daily rhGH injection

Trial Objectives

Primary Endpoint

- Annualized Height Velocity (AHV)

Goals

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

Interim Data: 41 subjects @ 6 months on therapy – November 2022
Primary Outcome Data: 82 subjects @ 6 months on therapy – 4th Qtr. 2023

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* Peak GH response to single stimulation dose of 0.8 mg/kg dose of LUM-201

OraGrowtH210 Baseline Characteristics at Interim (n=41)

OraGrowtH210 TRIAL

	LUM-201 0.8 mg Mean (SD) N=11	LUM-201 1.6 mg Mean (SD) N=10	LUM-201 3.2 mg Mean (SD) N=10	rhGH Mean (SD) N=10
Age (months)	95.5 (28.2)	99.3 (28.3)	96.1 (21.7)	90.3 (26.7)
Height (cm)	113.8 (12.6)	114.6 (9.6)	113.8 (8.8)	111.6 (11.9)
Height SDS	-2.31 (0.32)	-2.35 (0.62)	-2.30 (0.48)	-2.29 (0.43)
Max Height SDS	-1.76	-1.66	-1.57	-1.73
IGF-1 SDS	-1.24 (0.573)	-1.17 (0.72)	-1.39 (0.61)	-1.37 (0.48)
Max IGF-1 SDS	-0.3	-0.3	-0.6	-0.7
MPH (cm)	164.47 (6.44)	166.98 (7.15)	166.20 (8.06)	168.78 (8.85)
MPH SDS Δ	1.29 (0.62)	1.76 (0.60)	1.96 (0.83)	1.76 (0.73)
BA Delay (yrs)	1.89 (1.02)	1.91 (0.53)	2.19 (0.86)	1.78 (0.96)
BMI SDS[1]	-0.29 (1.04)	-0.35 (0.79)	-0.70 (0.48)	+0.31 (1.05)

- Imbalances were observed in baseline characteristics between rhGH arm & LUM-201 arms
- Baseline characteristics predict faster 1st year growth on therapy for rhGH arm than for LUM-201 arms[2]

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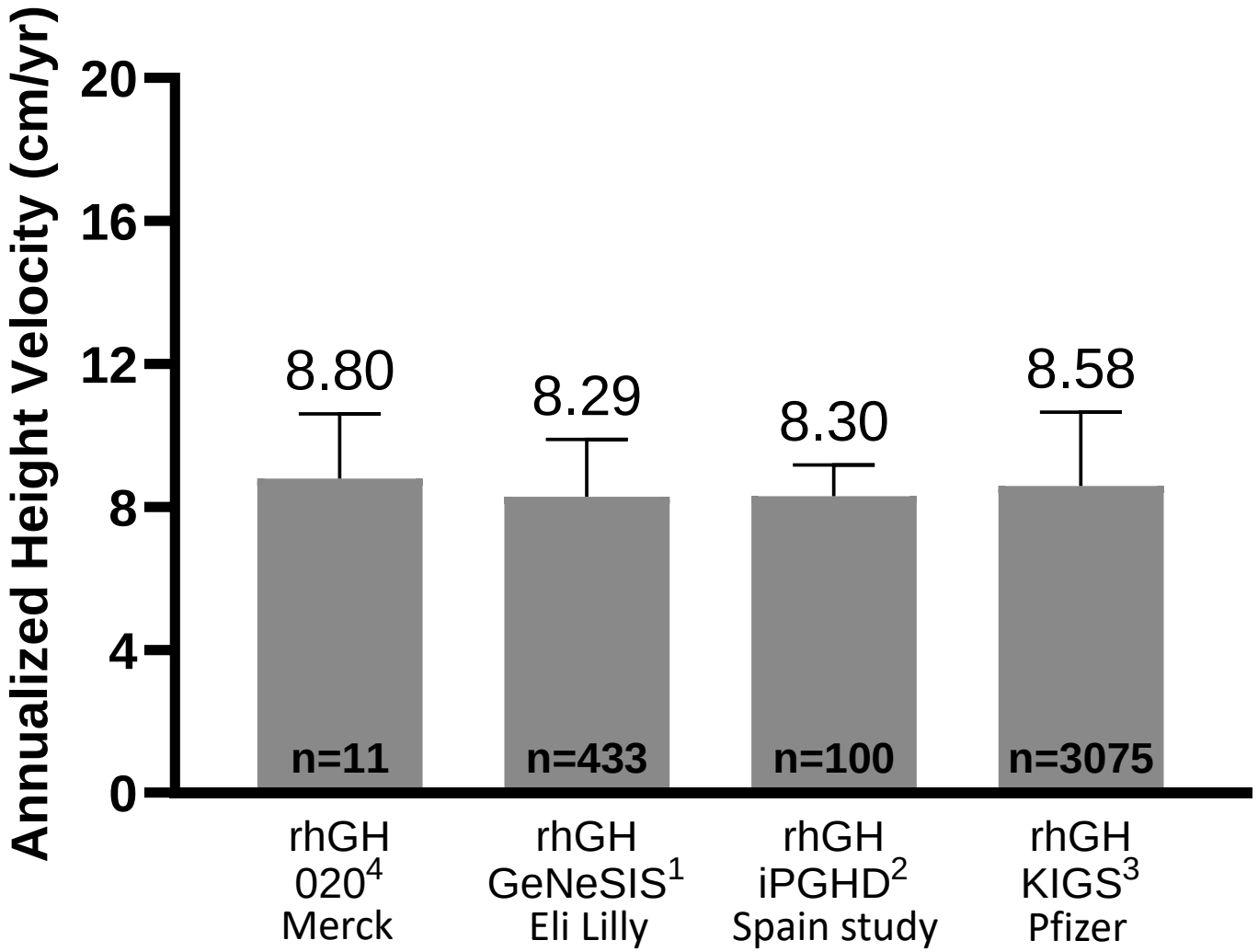
[1] Yang, et al. Nature Sci Rep 2019, 9(1); 16181 [2] Blum et al JES 2021, [3] Ranke et al JCEM 2010

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

Historical Data for rhGH Growth Rates in Moderate PGHD

OraGrowtH210 TRIAL



Historical Datasets

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

Predictions

- Prediction for growth in OraGrowtH210 is AHV of ~8.3 cm/yr on both rhGH and LUM-201 based on this historical data

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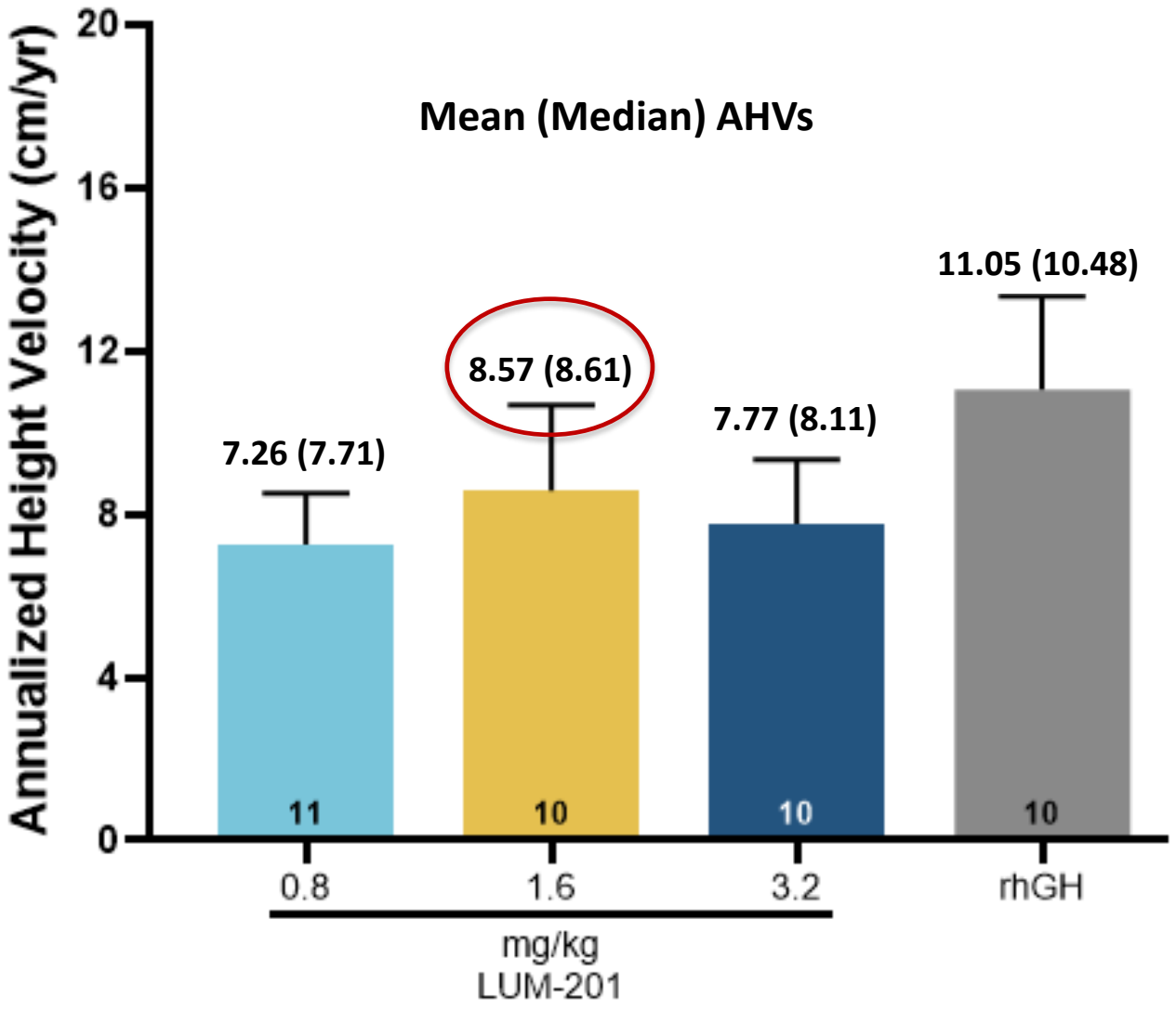
Sources: [1] Blum et al JES 2021, [2] Lechuga-Sancho et al JPEM 2009, [3] Ranke et al JCEM 2010, [4] Bright et al JES 2021.

OraGrowthH210 Interim Analysis: AHV at 6 Months (41 Subjects)



Interim Results

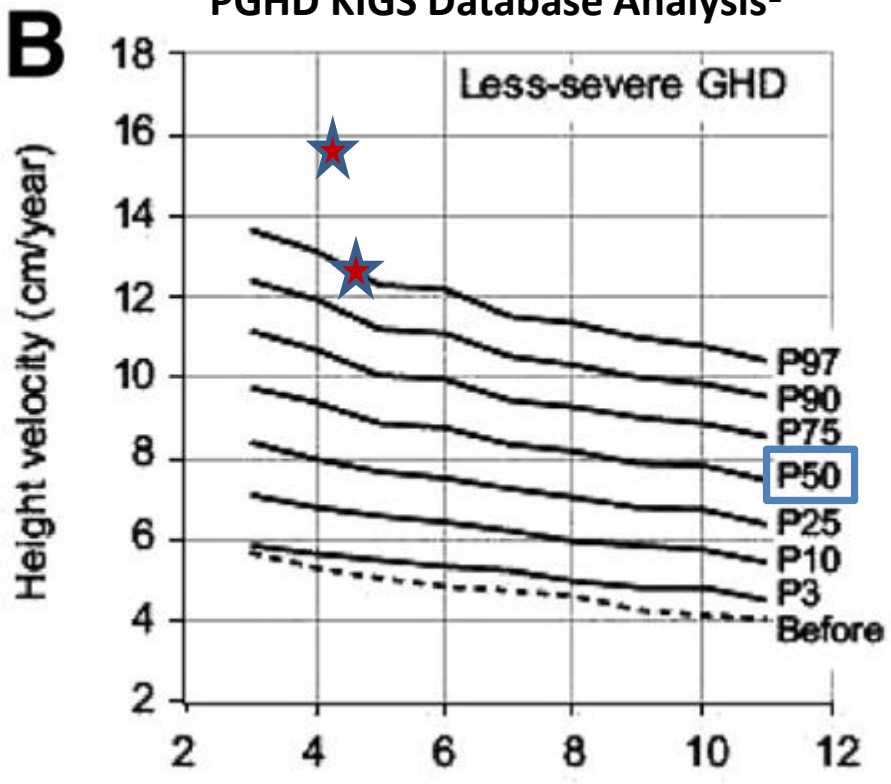
- 1.6 mg/kg/day LUM-201 cohort growth of 8.6 cm/year was in line with the expected rate of 8.3 cm/year based on historical data
- rhGH cohort grew at a much faster rate than expected or previously reported in moderate idiopathic PGHD population
- Cohort baseline differences predict faster first-year growth in the rhGH arm[1,2]
- Median AHV values offer more authentic comparison by minimizing impact of outliers

1 Blum et al JES 2021, 2 Ranke et al JCEM 2010

Growth Outliers in the rhGH Cohort:

Two of Three Subjects Under Age 5 Randomized to rhGH

First-year Growth on rhGH for Pfizer's Moderate PGHD KIGS Database Analysis[1]



OraGrowtH210 youngest subjects in rhGH cohort at 6-months AHV

P lines = Percentiles
"Before" line marks height velocity before GH therapy

[1] Ranke, et al 2010 JCEM

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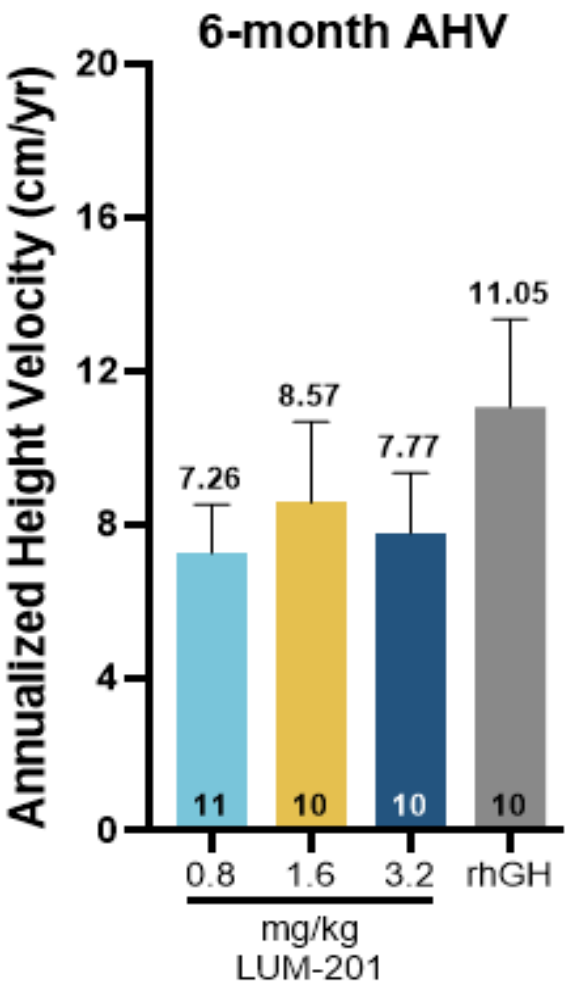
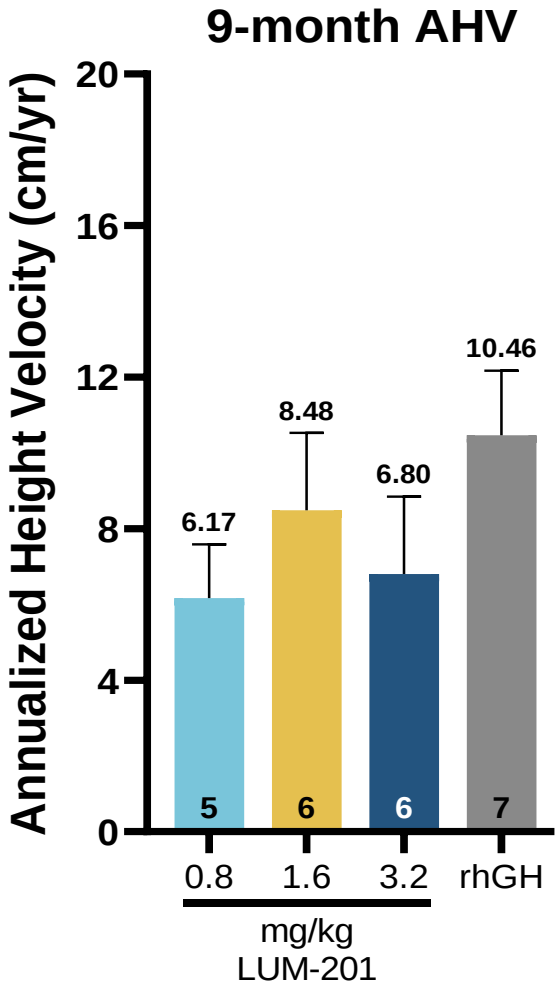
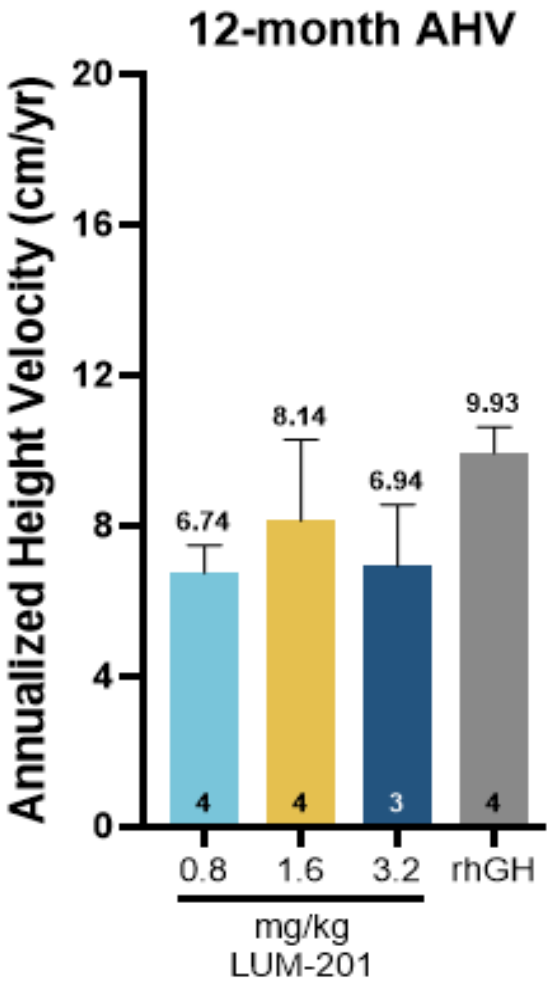
Interim OraGrowtH210 Data: LUM-201 Demonstrates Durable Response to 12 Months

OraGrowtH210 TRIAL







Conclusions

- Growth rates for LUM-201 are consistent from 6 to 12 months
- A Phase 3 non-inferiority trial is expected to be a 12-month study in a significantly larger population

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Safety Profile at Interim Analysis for OraGrowtH210 Trial

OraGrowtH210 TRIAL

	0.8 mg/kg	1.6 mg/kg	3.2 mg/kg	ALL LUM-201	rhGH 34 mcg/kg
N =	**14**	**15**	**14**	**43**	**15**
Number of AEs	31	45	38	114	21
Subjects with AE (%)	8 (57.1%)	13 (86.7%)	9 (64.3%)	30 (69.8%)	9 (60.0%)
Treatment Related AEs (N)	2	1	3	6 Increased appetite (2) Pain in extremity (2) Arthralgia (1) Growing Pains (1)	3 Increased appetite (2) Injection site bruising (1)
Subjects with Treatment Related AEs (%)	1 (7.1%)	1 (6.7%)	2 (14.3%)	4 (9.3%)	2 (13.3%)
Subjects with SAEs (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Data Available

- No treatment-related Serious Adverse Events (SAEs)
- No drop-outs due to SAE's
- No meaningful safety signals observed in either laboratory values, adverse event data, or in EKG values.

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Summary of Interim OraGrowtH210 Data

OraGrowtH210 TRIAL

- In a selected patient population (idiopathic PGHD) using the LUM-201 PEM (Prediction Enrichment Marker), LUM-201 demonstrates an increase in height velocity with three doses of this oral growth hormone secretagogue.

- Oral LUM-201 1.6 mg/kg/day cohort grew 8.6 cm/year, in line with the expected historical rate of ~ 8.3 - 8.6 cm/year from prior data of moderate iPGHD rhGH treated patients.

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

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