

OraGrowth

TRIALS

oral therapy to increase natural GH secretion

The Amount and The Pattern Of Pulsatile GH Secretion Induced By The Oral Growth Hormone Secretagogue LUM-201 Is Related To Growth And IGF-1 Responses In Moderate Pediatric Growth Hormone Deficiency (PGHD)

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ESPE European Society for
Paediatric Endocrinology

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Disclosure

Dr. Peter Clayton is a paid consultant for Lumos Pharma, Inc.

LUM-201 is an investigational compound and is not approved for use by the FDA or any other regulatory agency.

Abstract Authors and Affiliation

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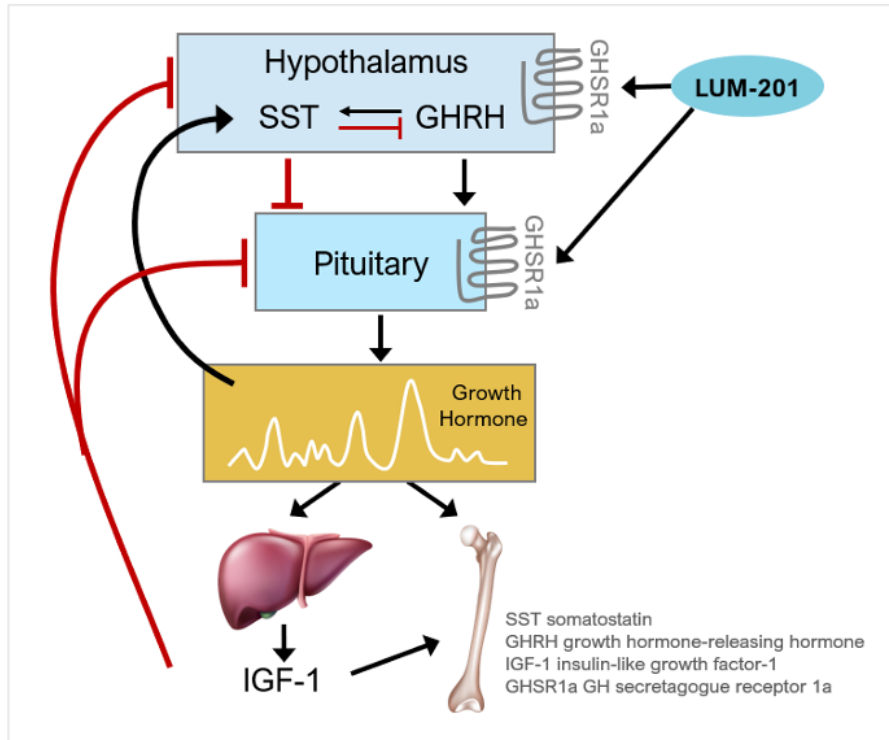
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LUM-201 Stimulates Endogenous GH Secretion

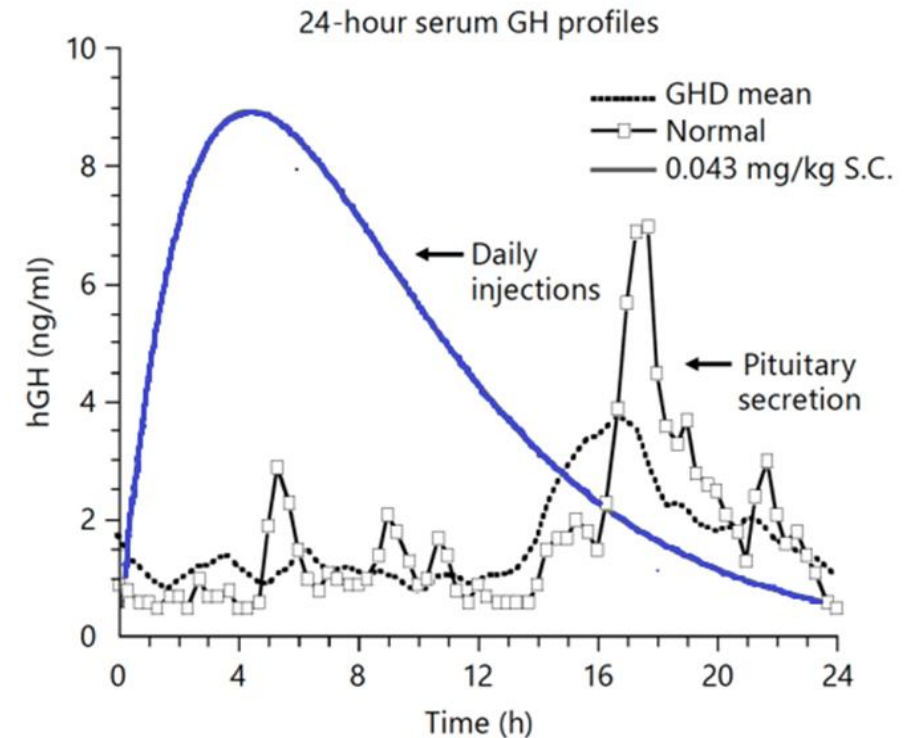


LUM-201 is an oral **growth hormone (GH) secretagogue**

Targeted to those with moderate GH deficiency, and identified by a Predictive Enrichment Marker (PEM) test:

PEM Positive Responders ¹

- Baseline IGF-1 > 30 ng/ml
- Stimulation LUM-201 0.8mg/kg peak GH ≥ 5 ng/ml
- Functional but reduced HP-GH axis



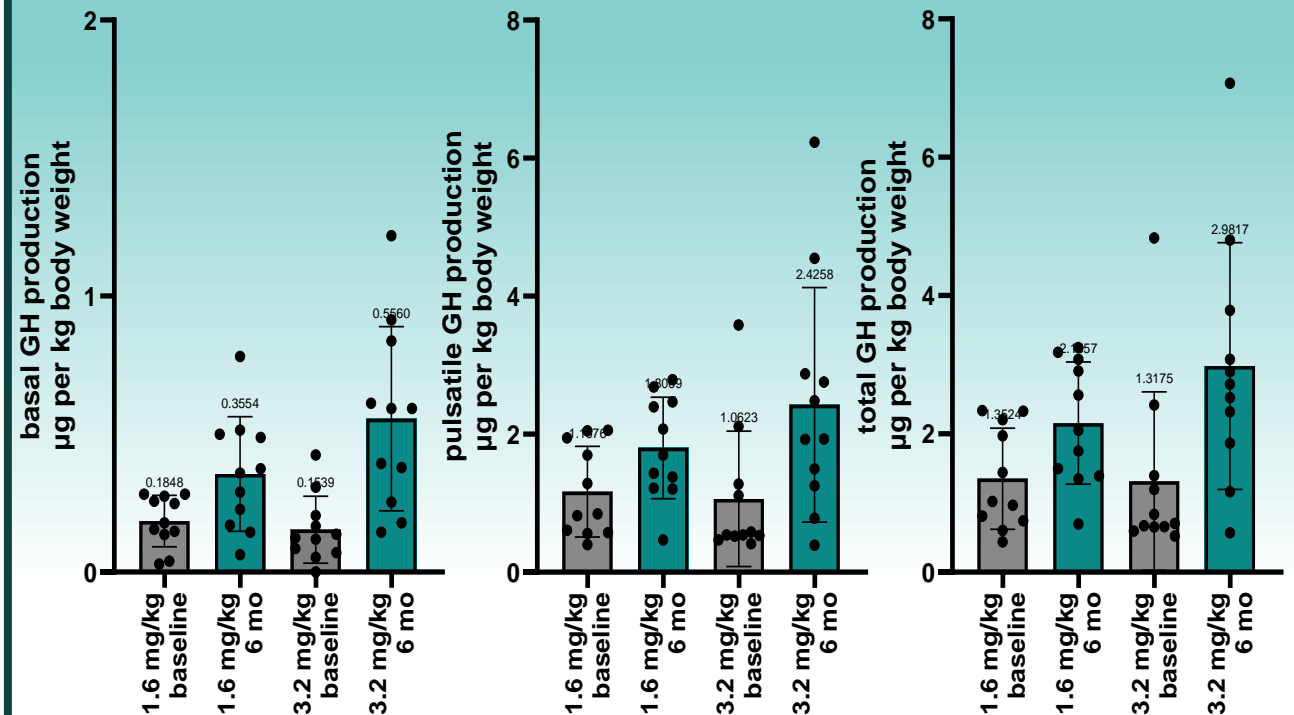
1. Bright 2021 JES
2. Figure 'Long-Acting Growth Hormone: An Update' Paul H. Saenger & Jorge Mejia-Corletto In: Advanced Therapies in Pediatric Endocrinology and Diabetology. Endocr Dev. Basel, Karger, 2016, vol 30, pp 79-97

Background

- In children, growth rates have been linked to both the amount and the pattern of GH secretion in pulse profiles
- In OraGrowthH212, GH pulse profiles, based on 10-minute blood sampling over 12 hours (8 am-8 pm), showed significant increases in GH secretion with 1.6 and 3.2 mg/kg/day of LUM-201 over 6 months, with no difference between doses [FC14.3, ESPE 2023].
- Oral LUM-201 normalizes growth rates in moderate PGHD over 12 months (Phase 2 Trials: OraGrowthH210 & OraGrowthH212) [FC 7.6, ESPE 2024]

PK/PD: N=22, Open label LUM-201 1.6 & 3.2mg/kg daily
Objectives: Assess LUM-201 effect on endogenous GH pulsatility, Assess Height Velocity, Evaluate PK/PD

Changes in GH secretion at baseline and at 6 months on LUM-201 treatment



Objective

To characterize relationships between GH pulse profiles with growth and IGF-1 responses to oral LUM-201 (doses combined).

Methods

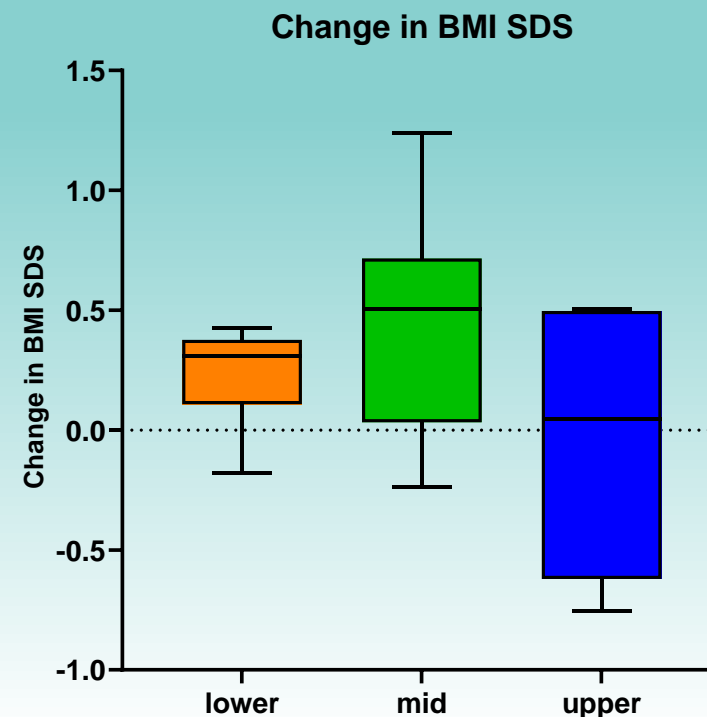
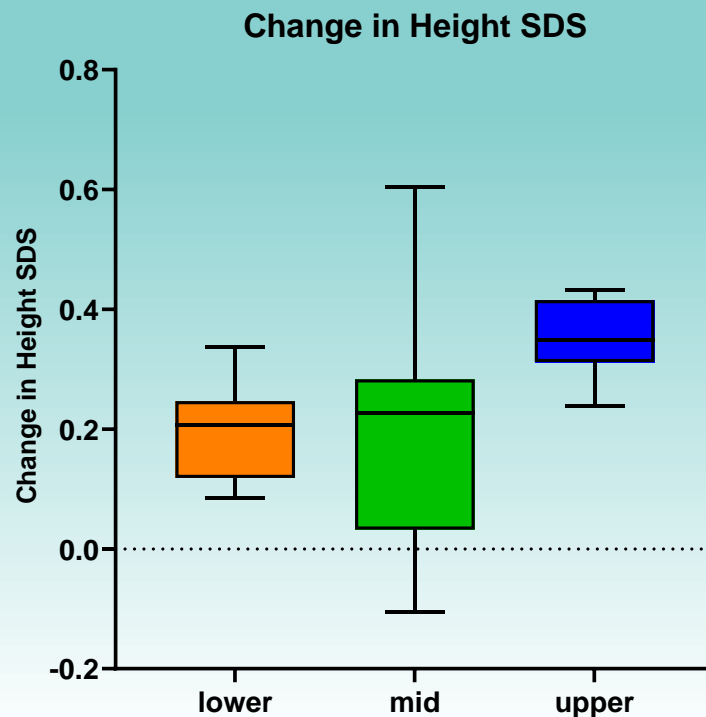
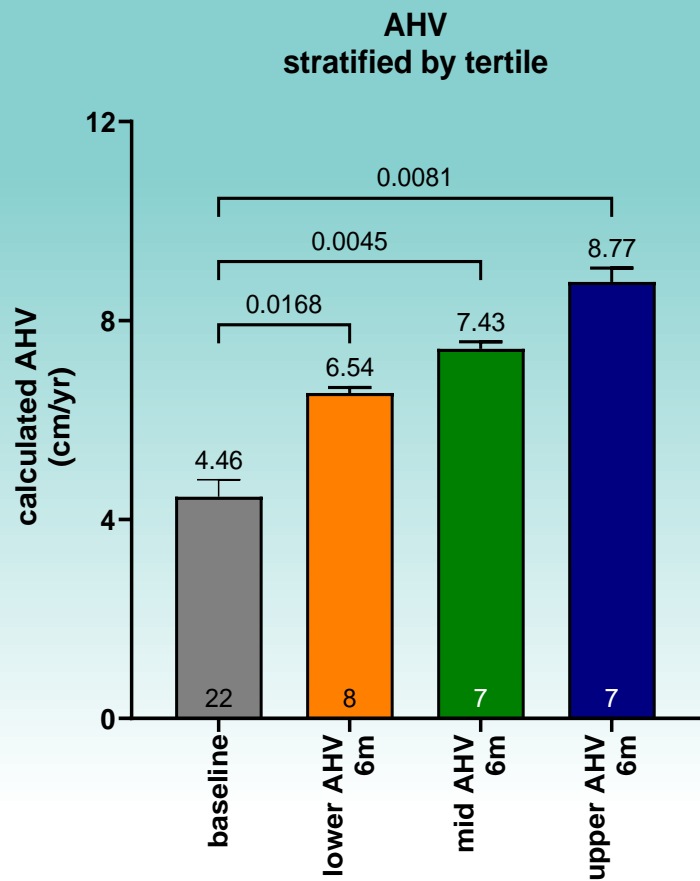
22 prepubertal children with moderate PGHD were included.

Subjects grouped into tertiles based on 6 months (M6) Annualized Height Velocity (AHV).

Pulsatile GH secretion profiles were characterized using

- (1) Approximate Entropy (ApEn, scale 0-1) examining degree of orderliness over the whole profile and
- (2) Functional Principal Component Analysis (FPCA) identifying where within the 12hr profile, divided into 4hr periods, the dominant variation occurred.

Results (1) AHV, Change in Height & BMI SDS at 6m treatment with LUM-201, stratified by AHV tertiles



Paired test to Δ Ht sds/ Δ BMI sds 0 p value:

<0.001

0.04

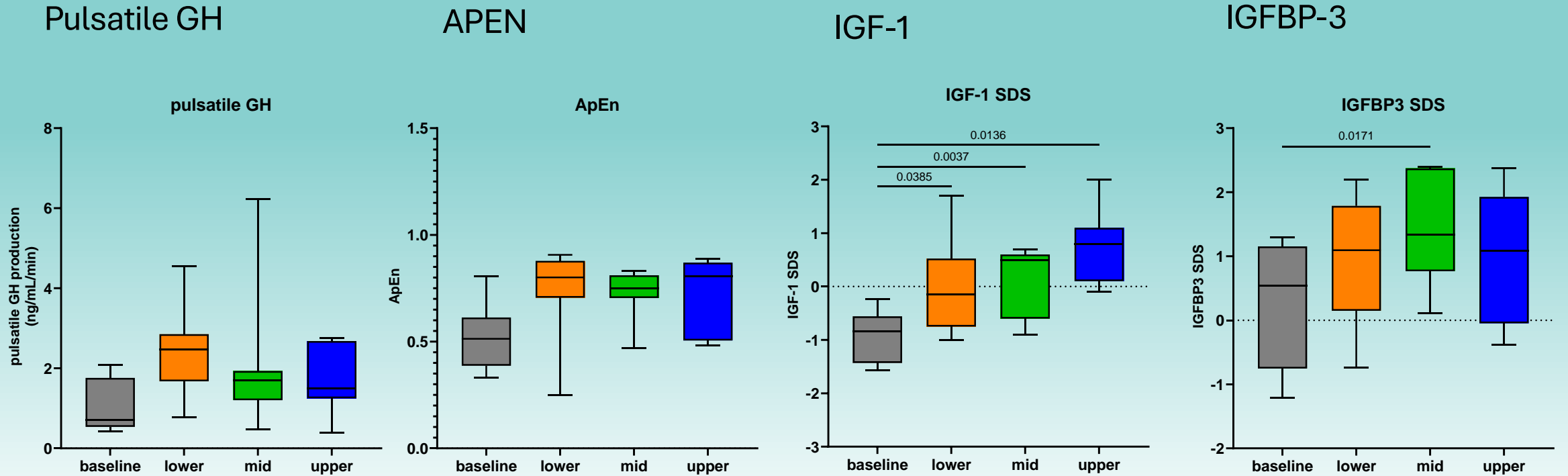
<0.001

0.01

0.05

NS

Results (2) Pulsatile GH, APEN, IGF-1 and IGFBP-3 SDS at 6m treatment with LUM-201, stratified by AHV tertiles.



Baseline to 6m in whole group, p value: 0.005

<0.001

<0.001

0.04

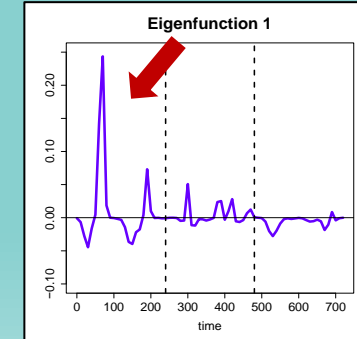
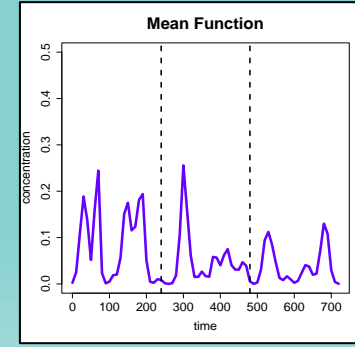
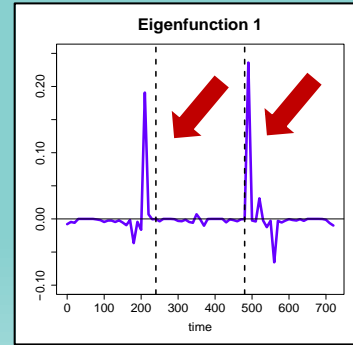
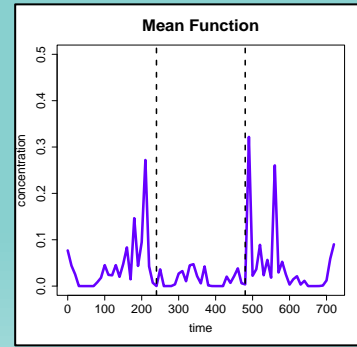
Results (3)

Functional Principal Component Analysis

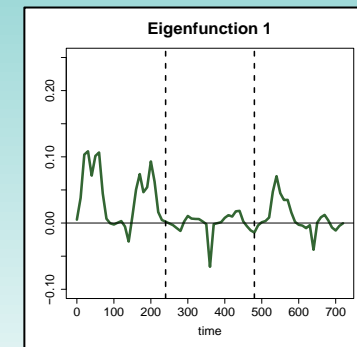
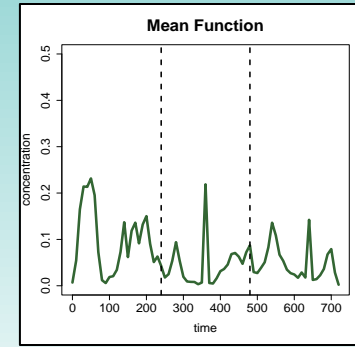
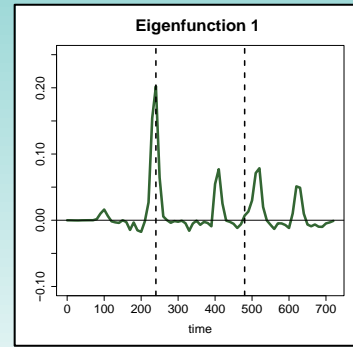
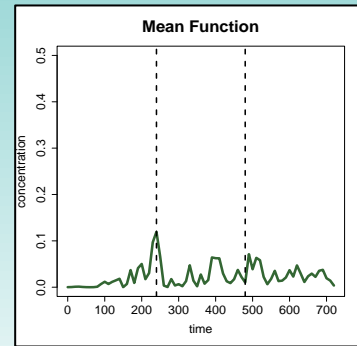
Baseline

6 months treatment

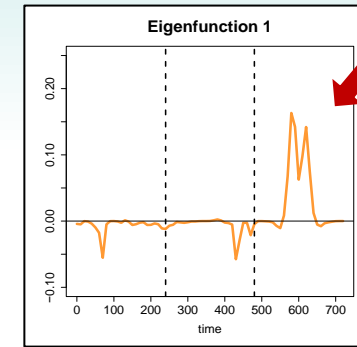
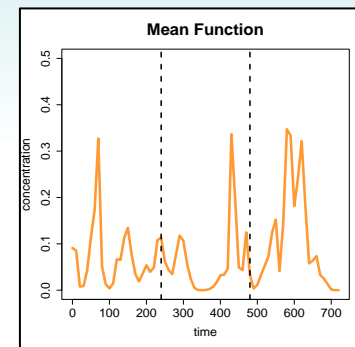
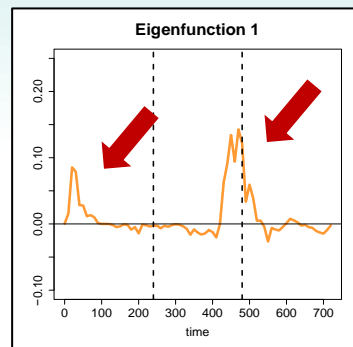
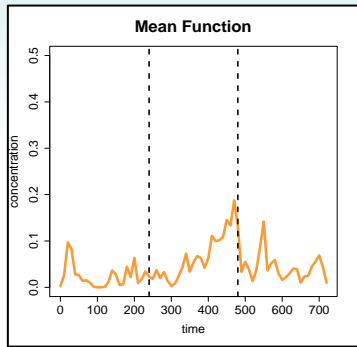
Upper AHV



Middle AHV

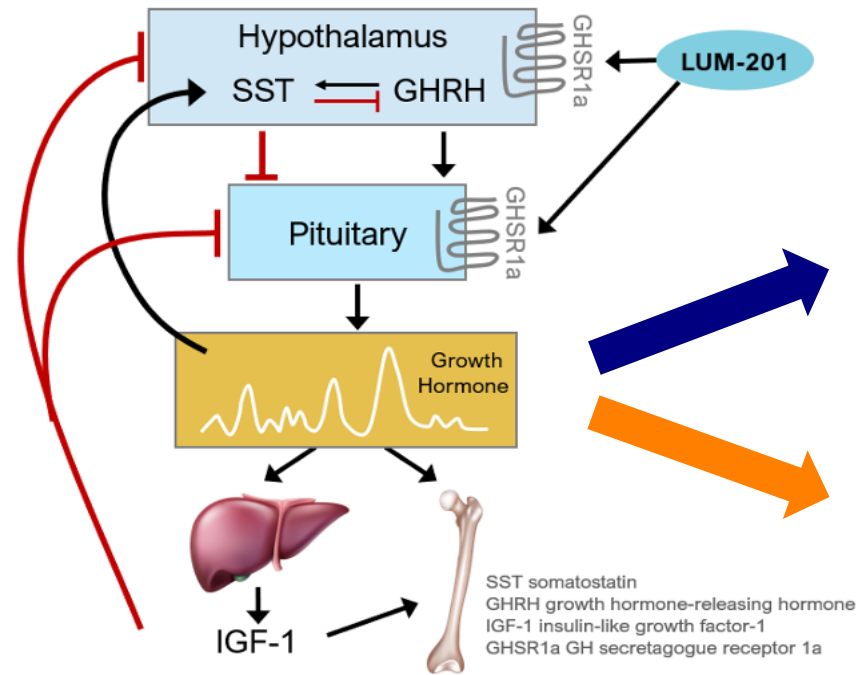


Lower AHV

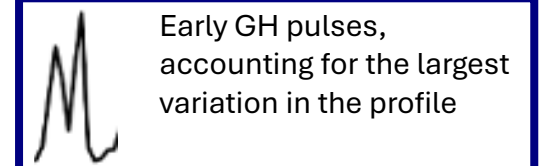


Conclusions

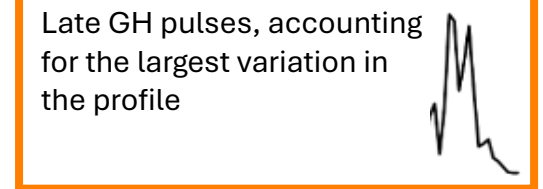
- In response to oral LUM-201, pulsatile GH secretion, ApEn, growth, serum IGF-1 and IGFBP-3 increased.
- In addition, LUM-201 induced both an increase in disorderliness (ApEn) of the pulse profiles and an alteration in times at which the greatest variation occurred, which differed between higher and lower responders.



Higher Growth Response



12hr daytime GH pulse profile



Lower Growth Response

Both amount and pattern of GH secretion are important for growth and IGF-1 responses to LUM-201