# Treatment Adherence with Weekly, Twice-Monthly and Monthly Dosing of Somavaratan (VRS-317), a Long-Acting Growth Hormone Treatment for Children with Growth Hormone Deficiency (GHD), After 24 Months of At-Home Dosing in the VISTA Study

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# Disclosures

- Eric Humphriss, MBA, and F. Naureen Sheikh, PhD, are employees of Versartis, Inc
- David Ng, PhD, and Morgan Seaman are employees of ResearchPoint Global, a CRO receiving funding from Versartis, Inc
- George Bright, MD, is a consultant to Versartis and holds equity interests in Versartis, Inc
- Somavaratan (VRS-317) is an investigational agent

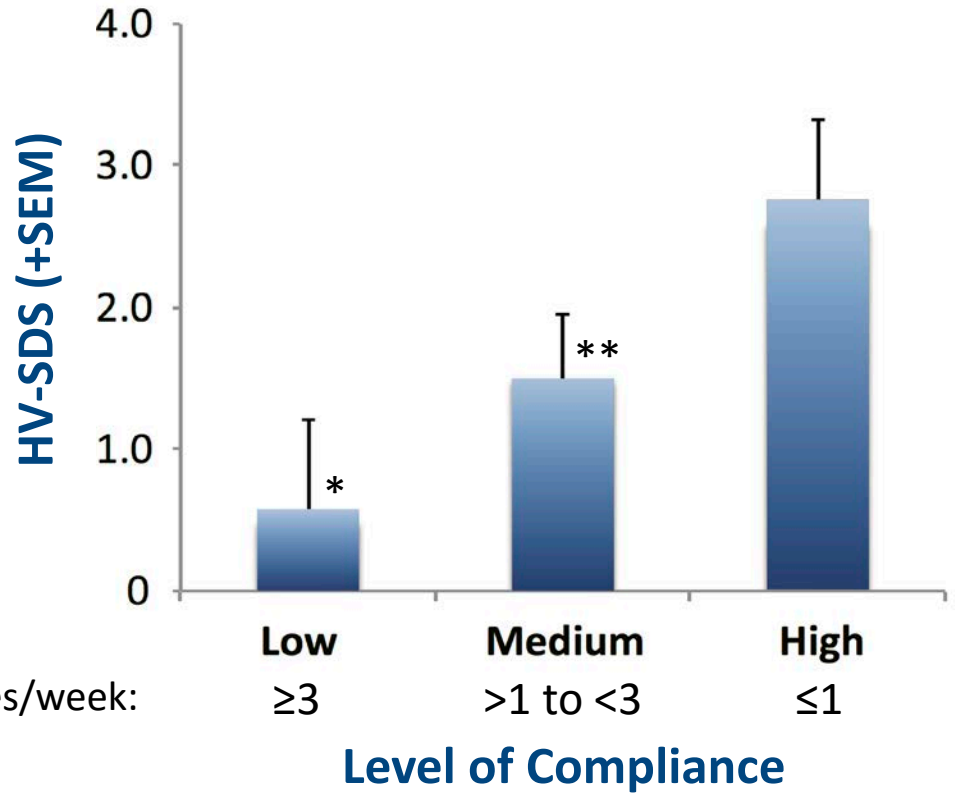
# Challenges With Adherence to Daily Growth Hormone Treatment

- Children with growth hormone deficiency (GHD) are often treated for multiple years with daily injections of recombinant human growth hormone (rhGH) replacement therapy, currently the only treatment available in North America and Europe
- Treatment adherence to daily subcutaneous rhGH is a known burden for these patients, with poor adherence negatively impacting treatment outcome[1]
- Noncompliance to daily injections has been reported in up to 66%–77% of adults and children with GHD,[2] and is significantly associated with reduced annual height velocity[3]

1. De Pedro et al, *Gr Horm IGF Res.* 2016; 26:32-35; 2. Rosenfeld and Bakker. *Endocr Pract.* 2008;14:143-54; 3. Cutfield et al, *PLOS One*. 2011;6:e16223.

# Noncompliance to Daily rhGH Associated With Suboptimal Response

- In a national survey of GH compliance by children in New Zealand (N=177), overall rate of noncompliance (≥1 missed injection/week, based on returned GH vials) was 66%[1]
- Height velocity (HV) SDS and linear growth increased with treatment compliance, whereas missing ≥1 dose/week significantly reduced linear growth ($P<0.05$)[1]




*$P<0.01$, **$P<0.001$ vs. High using non-parametric Spearman's rank correlation


[1]Cutfield et al, *PLOS One*. 2011;6:e16223.

# Poor Adherence to rhGH Therapy Results in Suboptimal Growth

## ONE OF THE PRIMARY CAUSES OF GH THERAPY FAILURE IS PATIENT NON-ADHERENCE TO THE PRESCRIBED DRUG THERAPY

- Longitudinal study with 158 children between 4-16 years with GHD or SGA
- 33.5% Moderate-to-poor adherence
  - Defined as taking <92% of prescribed rhGH medication
- Decreased adherence significantly associated with
  - Treatment duration (p=0.001)
  - Mother's educational level (p=0.007)
  - Decreased HV (p=0.002)
  - IGF-I levels (p<0.0001)

| | | Good Adherence | Moderate-Poor Adherence | *P* |
|---|---|---|---|---|
| **Age (years)** | | 10.5 ± 2.7 | 11.5 ± 2.8 | 0.041 |
| **Sex** | **Male** | 62 (61.4) | 39 (38.6) | 0.072 |
| | **Female** | 43 (75.4) | 14 (24.6) | |
| **Pubertal stage N (%)** | **Pre-pubertal** | 56 (73.7) | 20 (26.3) | 0.064 |
| | **Pubertal** | 49 (59) | 33 (40.2) | |
| **Duration of treatment (yrs)** | | 2.78 ± 1.71 | 3.78 ±1.80 | 0.001 |
| **Daily Dose (mg/day)** | | 0.98 ± 0.29 | 1.08 ± 0.32 | 0.038 |
| **IGF-1 SDS** | | **1.3 ± 1.03** | **0.48 ± 1.09** | **<0.0001** |
| **HV-SDS** | | **1.57 ± 1.90** | **0.61 ± 1.50** | **0.002** |

## Height Velocity SDS & IGF-I Levels Impacted by Lack of Adherence

De Pedro, S. et al. Growth Hormone & IGF Research 26 (2016) 32-35

# Clinical Need for Long-Acting Growth Hormone

*"Long-acting growth hormone compounds may represent an advance over daily GH injections because of increased convenience and differing pharmacodynamic properties, providing the potential for improved adherence and outcomes."*

– Growth Hormone Research Society Consensus Statement[1]

- There is a clinical need for a safe and effective long-acting growth hormone treatment for which improved treatment adherence is attainable
- Development of a long-acting form of rhGH with long-term effectiveness may potentially reduce treatment burden, improve adherence issues, and improve overall treatment outcomes

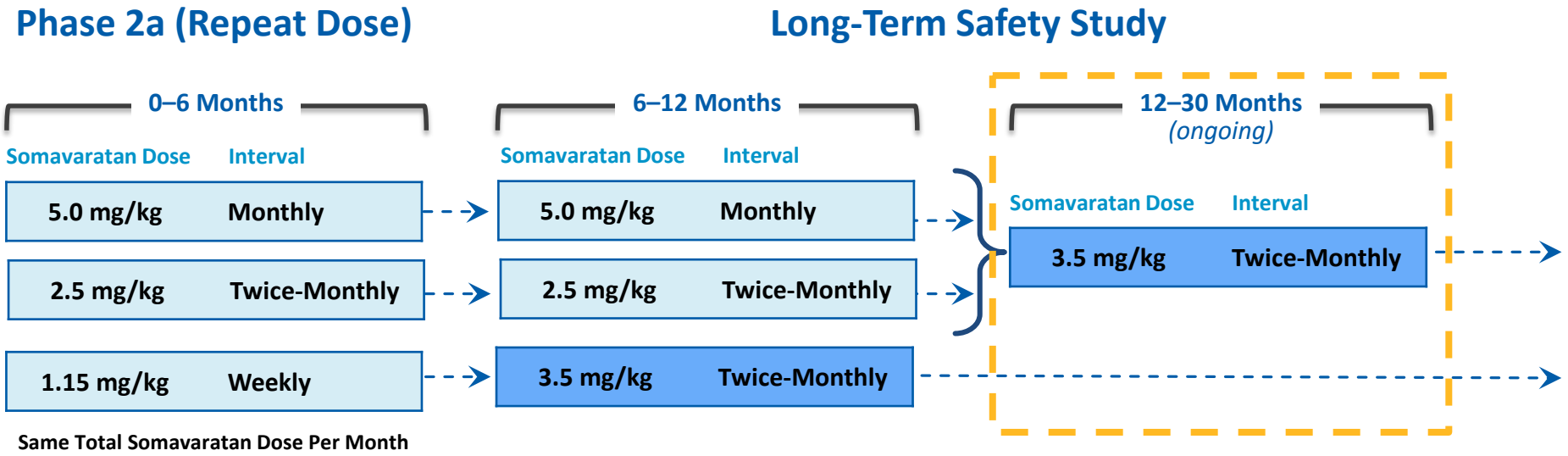

1. Christiansen et al. *Eur J Endocrinol*. 174;C1-C8

# Methods: Monitoring Treatment Adherence

- Dosing events were reported by the caregiver using a smartphone-compatible electronic patient-reported outcome diary (eDiary)
- Prior to at-home dosing (initiated at beginning of extension study), caregivers were trained on:
  - Preparation of somavaratan
  - Subcutaneous injection technique
  - eDiary use
- In-clinic visits were conducted quarterly for patient follow-up, eDiary reprogramming, and re-supply of somavaratan and ancillary supplies
- The eDiary was programmed to provide both assigned injection volume and timing of injection. Caregivers used the eDiary to report injection volume administered and date of administration
- Notifications sent to research nurse for late or missed injections

# VISTA Study Design

## NAÏVE TO TREATMENT PRE-PUBERTAL CHILDREN WITH GHD* IN US




*GHD confirmed by short stature (height-SDS), 2 or more growth hormone stimulation tests, IGF-I SDS, and delayed bone age

- From the beginning of the second treatment year, all subjects received 3.5 mg/kg somavaratan twice-monthly, based on growth and IGF-I responses observed in Year 1[1]
- As of April 2015, dose formulation changed from 50 to 100 mg/mL


[1]Moore et al. *J Clin Endocrinol Metab.* 2016;101(3):1091-1097.

# Patient Demographics and Baseline Characteristics

| | Subjects Enrolled in Extension Study (n=60) |
|---|---|
| **Baseline age, Mean (SD)** | 7.8 (2.4) |
| **Gender, n (%)** | |
| **Female** | 26 (43%) |
| **Male** | 34 (57%) |
| **Race, n (%)** | |
| **White** | 50 (83%) |
| **Asian** | 4 (7%) |
| **Black or African American** | 3 (5%) |
| **American Indian or Alaska native** | 1 (2%) |
| **Other** | 2 (3%) |

**Baseline characteristics are consistent with a pediatric population with moderate GHD**

# Results: Reported Treatment Adherence after 30 Months Somavaratan Exposure

| Parameter | Somavaratan Starting Regimen | | | Somavaratan Phase 3 Regimen |
|---|---|---|---|---|
| | 5.0 mg/kg Monthly (n=22) | 2.5 mg/kg Twice-Monthly (n=18) | 1.15 mg/kg Weekly[a] (n=20) | 3.5 mg/kg Twice-Monthly (n=58) |
| Doses | | | | |
| Completed/Expected | 131/131 | 213/213 | 195/195 | **2266/2276** |
| Event adherence rate (%) | 100 | 100 | 100 | **99.6** |

[a]Expected doses in the weekly dosing group were lower than the 2.5 mg/kg twice-monthly group due to earlier switch to Phase 3 dosing

NOTE: As of April 2015, dose formulation changed from 50 to 100 mg/mL somavaratan.

**Reported adherence to somavaratan occurred at nearly 100% over 24 months of at-home dosing**

# Conclusions

- Use of an eDiary device/application simplifies parent tracking of timing for and recording of at-home dosing events in this clinical trial
- With at-home dosing and over 2200 doses administered at the Phase 3 dose, treatment adherence rate was 99.6%
- With nearly 100% reported adherence for all dosing schedules over 24 months of at-home therapy, this study provides evidence that long-term adherence to treatment may be improved with long-acting growth hormone preparations in children with GHD

**A Phase 3 study of somavaratan using the eDiary to monitor treatment adherence is ongoing (NCT02339090)**

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