Safety and Efficacy of Somavaratan (VRS-317), a Long-Acting Recombinant Human Growth Hormone (rhGH), in Children with Growth Hormone Deficiency (GHD): 3-Year Update of the Vertical & VISTA Trials (NCT01718041, NCT02068521)

Number: OR31-1
Category: Pediatric Endocrinology

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rhGH has been the mainstay for treatment of pediatric GHD for over three decades, but the burden of daily subcutaneous injections required for current formulations significantly compromises treatment effects (1). Somavaratan is a novel long-acting rhGH fusion protein with $t_{1/2}$ > 100 hours in clinical development for treatment of GHD in children and adults (2). In a multi-center, randomized Phase 1b/2a study initiated in 2013, somavaratan treatment resulted in clinically meaningful improvements in height velocity (HV) and IGF-I (measured by mass spectrometry) in pre-pubertal children with GHD (3). Following an initial Phase 1b single dose PK/PD study in PGHD, 64 subjects were randomized in a Phase 2a study (VERTICAL) to receive 5.0 mg/kg/month for 6 months divided weekly, twice-monthly, or monthly. Subjects were permitted to continue somavaratan treatment in the long-term safety study, VISTA; 60 subjects elected to continue. Based on early growth and IGF-I responses from treatment, all subjects were transitioned to a uniform frequency and higher dose of 3.5 mg/kg given twice-monthly by the beginning of Year 2 of treatment. Bone age was interpreted by a central reader using the Fels method. Here we present preliminary efficacy and safety findings of somavaratan in a subset of 30 subjects (15 male, 15 female; mean baseline age, 7.5 years) who have completed 3 years of treatment. IGF-I SDS increased from -1.7 ± 0.8 at baseline to 1.1 ± 1.6 at peak (3–5 days post-injection) and -0.2 ± 0.9 at trough (end of dosing cycle) in Year 3; 8 subjects had transient IGF-I SDS excursions > 2.0, of which 3 events were > 3.0 (range, 2.3–3.9). During Years 1, 2, and 3, mean HV remained consistent at 8.5 ± 1.8, 8.5 ± 1.7, and 8.1 ± 1.5 cm/year, and height-SDS continued to increase from -2.6 ± 0.5 at baseline to -1.9 ± 0.6, -1.4 ± 0.7, and -1.0 ± 0.7. The mean difference in years between bone age and chronological age improved from -1.53 ± 0.85 at baseline to -0.6 ± 0.83 in Year 3. Treatment-related AEs were generally mild and transient. In conclusion, somavaratan showed continued increases in IGF-I, HV, height-SDS, and bone age through 3 years of treatment in pre-pubertal children with GHD. Increasing the somavaratan dose to 3.5 mg/kg twice-monthly resulted in consistent growth rates through 3 years of treatment, and

overall growth at year 3 in line with US registry data reported for daily rhGH (4-6). The somavaratan 3.5 mg/kg twice-monthly dose is currently under evaluation in a Phase 3 study in treatment-naïve GHD children (NCT02339090).

Disclosure: WVM: Investigator, Versartis, Inc.. PYF: Investigator, Versartis, Inc.. HJN: Investigator, Versartis, Inc.. QLV: Investigator, Versartis, Inc.. JSF: Investigator, Versartis, Inc.. BSM: Principal Investigator, Alexion, Coinvestigator, Armagen, Principal Investigator, Endo Pharmaceuticals, Ad Hoc Consultant, Ferring Pharmaceuticals, Advisory Group Member, Abbvie, Principal Investigator, Genentech, Inc., Coinvestigator, BioMarin, Principal Investigator, Novo Nordisk, Coinvestigator, Armagen, Ad Hoc Consultant, Novo Nordisk, Ad Hoc Consultant, Pfizer, Inc., Principal Investigator, Alexion, Ad Hoc Consultant, Sandoz, Principal Investigator, Endo Pharmaceuticals, Principal Investigator, Sandoz, Scientific Content Contributor, Up To Date, Coinvestigator, BioMarin, Advisory Group Member, Abbvie, Ad Hoc Consultant, Ferring Pharmaceuticals, Principal Investigator, Versartis, Principal Investigator, Genentech, Inc., Ad Hoc Consultant, Versartis, Coinvestigator, Shire, Principal Investigator, Novo Nordisk, Principal Investigator, Tolmar, Coinvestigator, Eli Lilly & Company, Ad Hoc Consultant, Novo Nordisk, Ad Hoc Consultant, Pfizer, Inc., Ad Hoc Consultant, Sandoz, Principal Investigator, Sandoz, Scientific Content Contributor, Up To Date, Principal Investigator, Versartis, Ad Hoc Consultant, Versartis, Coinvestigator, Shire, Principal Investigator, Tolmar, Coinvestigator, Eli Lilly & Company. DN: Employee of CRO, Versartis, Inc.. EH: Employee, Versartis, Inc., Employee, Versartis, Inc.. RWC: Employee, Versartis, Inc., Employee, Versartis, Inc.. GMB: Consultant, Versartis, Inc..

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