Somavaratan, a Long-Acting Recombinant Human Growth Hormone (rhGH), for the Treatment of Adults with Growth Hormone Deficiency (AGHD): Results of VITAL, an Open-Label, Dose-Finding, International, Phase 2 Study (NCT02526420)

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Daily rhGH injections for AGHD represent a treatment burden associated with noncompliance and loss of treatment effect in 65% of adult patients (1). Some AGHD patients opt not to initiate therapy due to the onus of daily injections, thereby missing the opportunity to mitigate consequences associated with GHD. Somavaratan is a novel long-acting rhGH under development for treatment of GHD in adults and children. A Phase 1 PK/PD study of somavaratan in AGHD demonstrated an extended elimination $t_{1/2}$, as well as durable IGF-I response after a single dose (2). Here we present preliminary data from VITAL, an open-label, international, multicenter, Phase 2 study evaluating safety, starting dose, and dose titration for monthly somavaratan administration in AGHD. Eligible subjects were adults aged 24–70 years, with documented GHD. Subjects were stratified into 3 cohorts with different starting doses based on expected requirements for rhGH: Cohort A) 0.6 mg/kg/month for subjects ≥ 35 years of age; Cohort B) 0.8 mg/kg/month for subjects < 35 years of age; and Cohort C) 1.0 mg/kg/month for female subjects on oral estrogen, regardless of age. Subjects received 5 monthly SC doses of somavaratan, with 4 dose adjustments permitted until 2 consecutive means of pre-dose and Day 8 IGF-I SDS values were within the target range of 0 to 1.5. Results are presented as mean ± SD. Of 36 subjects enrolled in the study (18 female and 18 male; mean age, 46.1 ± 13.1 years), 33 completed all 5 doses. Somavaratan was well tolerated; most adverse events (AEs) were mild or moderate in severity, and no severe AEs were deemed related to somavaratan. The most common related AEs were injection site reactions (19.4%) and headache (11.1%). Mean IGF-I SDS increased from -1.32 ± 1.73 at baseline to 2.31 ± 2.54 at 7 days after the first dose in the study (Day 8 IGF-I SDS: 3.45 ± 1.85,

1.37 ± 3.01, -0.10 ± 1.99 for Cohorts A, B, and C, respectively). Although all subjects within a cohort received the same weight-based starting dose (mg/kg), subjects who received higher total doses (mg) tended to have higher IGF-I responses (r^2 = 0.43, 0.71, and 0.12 for Cohorts A, B, and C, respectively). Following the last study dose, IGF-I SDS returned to pre-dose values by Day 22 (*P* = 0.18, 0.13, and 0.39 for Cohorts A, B, and C). In conclusion, somavaratan was well tolerated and induced a robust IGF-I response in AGHD, with sustained effect for at least 2 weeks. More frequent, twice-monthly administration of a lower, non-weight-based starting dose may allow for optimal individual patient titration, while providing adequate drug exposure throughout the dosing interval. Starting somavaratan dose and administration frequency are being investigated further in the extension study (NCT02719990) and will be used in a new Phase 3 study.

Disclosure: BMKB: Principal Investigator, Novo Nordisk, Ad Hoc Consultant, Novo Nordisk, Ad Hoc Consultant, Pfizer, Inc., Principal Investigator, Opko, Principal Investigator, Versartis, Inc., Ad Hoc Consultant, Versartis, Inc.. DR: Employee, Versartis, Inc., Employee, Versartis, Inc.. TR: Employee of CRO, Versartis, Inc.. SAY: Employee, Versartis, Inc., Employee, Versartis, Inc.. RWC: Employee, Versartis, Inc., Employee, Versartis, Inc.. BB: Employee, Versartis, Inc., Employee, Versartis, Inc.. MK: Consultant, Versartis, Inc.. EH: Employee, Versartis, Inc., Employee, Versartis, Inc.. TSB: Investigator, Dexcom, Investigator, Elcelyx, Investigator, Glysens, Investigator, Insulet, Investigator, Jansen Pharmaceuticals, Investigator, Lexicon Pharmaceuticals, Inc., Investigator, Lifescan, Investigator, Eli Lilly & Company, Investigator, Medtronic Minimed, Investigator, Merck & Co., Investigator, Novo Nordisk, Investigator, Sanofi, Investigator, Senseonics, Investigator, Versartis, Investigator, Yofimeter, Ad Hoc Consultant, Ascensia, Ad Hoc Consultant, Astra Zeneca, Ad Hoc Consultant, BD, Ad Hoc Consultant, Calibra, Ad Hoc Consultant, Eli Lilly & Company, Ad Hoc Consultant, Medtronic Minimed, Ad Hoc Consultant, Novo Nordisk, Ad Hoc Consultant, Sanofi, Speaker, Abbott Laboratories, Speaker, Insulet, Speaker, Medtronic Minimed, Speaker, Novo Nordisk, Speaker, Sanofi, Investigator, Companion Medical, Investigator, Boehringer Ingelheim, Investigator, BD, Investigator, Ascensia, Investigator, ACON, Investigator, Abbott Laboratories. KH: Medical Advisory Board Member, Pfizer, Inc., Medical Advisory Board Member, Versartis, Inc, Speaker Bureau Member, Ipsen, Speaker Bureau Member, Novartis Pharmaceuticals, Speaker Bureau Member, Pfizer, Inc., Investigator, Novo Nordisk, Investigator, Versartis, Inc.. LK: Medical Advisory Board Member, Pfizer, Inc., Medical Advisory Board Member, Versartis, Inc., Investigator, Versartis, Inc.. KM: Investigator, Novo Nordisk, Investigator, Pfizer, Inc.. SM: Ad Hoc Consultant, Novartis Pharmaceuticals, Planning Group Member, Ipsen, Principal Investigator, Pfizer, Inc., Advisory Group Member, chiasma, Ad Hoc Consultant, ionis. SN: Investigator, Novo Nordisk, Investigator, Versartis, Inc.. DJT: Medical Advisory Board Member, Eisai, Medical Advisory Board Member, Genzyme Corporation, Educational Seminar, Eli Lilly & Company, Principal Investigator, Eisai, Principal Investigator, Janssen-Cilag, Principal Investigator, Novo Nordisk, Principal Investigator, Versartis, Inc.. WWW: Investigator, Novo Nordisk, Investigator, Versartis, Inc., Medical Advisory Board Member, Ipsen, Medical Advisory Board Member, Chiasma, Medical Advisory Board Member, Versartis, Inc.. KCJY: Investigator, Pfizer, Inc., Investigator, Opko, Investigator, Novo Nordisk, Investigator, Versartis, Medical Advisory Board Member, Pfizer, Inc., Medical Advisory Board Member, Novo Nordisk, Medical Advisory Board Member, Sandoz, Medical Advisory Board Member, Versartis, Inc.. MB: Investigator, Pfizer, Inc., Investigator, OPKO, Investigator, Genexine, Investigator, IDS, Speaker, Pfizer, Inc., Speaker, Sandoz, Speaker, Diasorin, Ad Hoc Consultant, Versartis, Inc., Ad Hoc Consultant, OPKO, Ad Hoc Consultant, Sandoz, Ad Hoc Consultant, Genexine. CJS: Medical Advisory Board Member, Versartis, Inc., Investigator, Versartis, Inc.. Nothing to Disclose: KSD

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