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Sangamo, Pfizer announce updated Phase 1/2 results for SB-525 investigational Hemophilia A gene therapy

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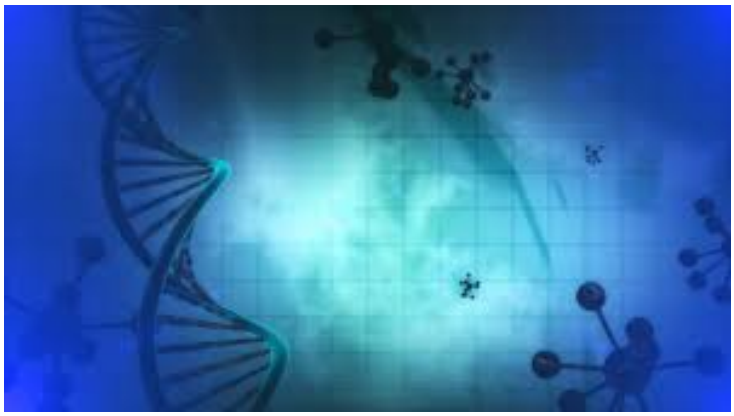
In addition to the collaboration for the development and commercialization of gene therapies for hemophilia A, Sangamo and Pfizer are also working together on the development of gene therapies for amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) using Sangamo's proprietary zinc finger protein transcription-factor technology (ZFP-TF).



Sangamo Therapeutics, a genomic medicine company, and Pfizer has announced updated results from the Phase 1/2 Alta study evaluating investigational SB-525 gene therapy for severe hemophilia A. The data showed that SB-525 was generally well-tolerated and demonstrated a dose-dependent increase in Factor VIII (FVIII) activity levels. The first two patients treated at the 3e13 vg/kg dose rapidly achieved normal levels of FVIII activity as measured using a chromogenic assay, with no reported bleeding events, and the response continues to be durable for as long as 24 weeks, the extent of follow-up. The two patients more recently treated at the 3e13 vg/kg dose level are demonstrating FVIII activity kinetics that appear consistent with the first two patients treated in this dose cohort at similar early time points. Data from 10 patients treated with SB-525 were presented during an oral presentation on July 6 at the XXVII Congress of the International Society on Thrombosis and Haemostasis (ISTH), in Melbourne, Australia.

"The initial results with SB-525 gene therapy for patients with severe hemophilia A continue to look very promising," said Barbara Konkle, M.D., Bloodworks Northwest, Professor of Medicine at University of Washington and a Principal Investigator of the Alta study. "It is encouraging that patients in the 3e13 vg/kg cohort have attained normal Factor VIII levels within 5-7 weeks of treatment with SB-525 gene therapy and have sustained Factor VIII activity with no bleeding episodes. It will be important to continue to follow these patients to understand the potential long-term durability of this gene therapy."

Alta study data presented at ISTH included 10 patients treated across four ascending dose cohorts: 9e11 vg/kg (2 patients), 2e12 vg/kg (2 patients), 1e13 vg/kg (2 patients) and 3e13 vg/kg (4 patients). Factor VIII activity data presented at ISTH included results through June 18, 2019. All other data presented at ISTH were as of May 30, 2019.

Across the dose cohorts, patients demonstrated a dose-dependent increase in FVIII levels and a dose-dependent reduction in the use of FVIII replacement therapy. In the two patients treated with the 1e13 vg/kg dose, FVIII activity levels have been durable through weeks 52 and 32. For the four patients in the 3e13 vg/kg cohort, FVIII activity data were available through

24, 19, 6, and 4 weeks of follow-up, respectively. The first two patients treated in the 3e13 vg/kg cohort (Patients 7 and 8) remained in the normal range, as measured using a chromogenic assay, through 24 and 19 weeks of follow-up, respectively. The next two patients in the 3e13 vg/kg cohort (Patients 9 and 10), with 6 and 4 weeks of follow-up, respectively, demonstrated rapid FVIII activity kinetics that appear consistent with Patients 7 and 8 at similar early time points. Also noted in the presentation at ISTH, Patient 9 attained normal FVIII activity levels at week 7, subsequent to the data transfer for the conference. No patient in the 3e13 vg/kg dose cohort has experienced bleeding events as of the data cut-off date, nor have patients in this dose cohort required factor replacement following initial use of prophylactic factor.

SB-525 was generally well tolerated. Patients in the Alta study were not treated with prophylactic steroids. One treatment-related serious adverse event (SAE) was reported. This patient experienced hypotension and fever six hours after completion of SB-525 infusion; this fully resolved with treatment and the patient was discharged as planned within 24 hours. No similar hypotension event was observed in the three subsequent patients dosed. Adverse events observed in 10% (n=1) or more patients included: increased alanine aminotransferase (30%) and aspartate aminotransferase (10%), pyrexia (30%), fatigue (10%), hypotension (10%), myalgia (10%), and tachycardia (10%). No patients treated with SB-525 have experienced an alanine aminotransferase (ALT) elevation associated with a loss of Factor VIII expression. In the 3e13 vg/kg cohort, two subjects experienced a transient grade 1 ALT elevation (>1.5 x baseline) managed with a tapering course of oral steroids.

“The initial results of the Alta study presented at ISTH demonstrate that SB-525 has the potential to be a predictable and reliable treatment that may bring clinical benefit to patients with hemophilia A,” said Adrian Woolfson, M.D., Ph.D., Executive Vice President of Research and Development, Sangamo. “The results show that SB-525 is well tolerated, that Factor VIII levels in the first two patients in the 3e13 vg/kg cohort reached normal, sustained levels as measured using a chromogenic assay, and that variability of Factor VIII activity is low, both within each patient and within each dose cohort. We look forward to continuing to follow these patients to further understand the durability of response to SB-525 gene therapy and to working with Pfizer to potentially advance a registrational study.”

Based on the accumulating results from the Alta study, the U.S. Food and Drug Administration (FDA) has granted regenerative medicine advanced therapy (RMAT) designation for SB-525 gene therapy to treat severe hemophilia A. RMAT designation is granted to regenerative medicine therapies intended to treat, modify, reverse, or cure a serious condition, for which preliminary clinical evidence indicates that the medicine has the potential to address an unmet medical need. The RMAT designation includes all the benefits of the fast track and breakthrough therapy designation programs, including early interactions with FDA.

“We are encouraged by the initial clinical data suggesting safety, tolerability, and efficacy of SB-525 and are beginning preparations, including manufacturing, to potentially advance into a registrational study. We are also encouraged by our interactions with regulators and by the FDA’s recent RMAT designation,” said Seng Cheng, Senior Vice President and Chief Scientific Officer of Pfizer’s Rare Diseases Research Unit. “If FVIII levels are sustained, and patients continue to have no bleeding episodes and remain off factor replacement therapy, we believe that this gene therapy may potentially represent a transformative treatment paradigm for severe hemophilia A.”

The fifth patient in the 3e13 vg/kg cohort (Patient 11) is expected to be treated soon. Sangamo and Pfizer are working on plans to advance SB-525 to a registrational study. Pfizer will assume responsibility for SB-525 late-stage development and manufacturing. Transfer of the SB-525 manufacturing process from Sangamo to Pfizer has been initiated.

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