Sangamo Therapeutics Logo

# Sangamo Announces Gene Therapy and Ex Vivo Gene-Edited Cell Therapy Data Presentations at the American Society of Hematology Annual Meeting

November 6, 2019

BRISBANE, Calif.--(BUSINESS WIRE)--Nov. 6, 2019-- Sangamo Therapeutics, Inc. (NASDAQ: SGMO), a genomic medicine company, today announced that hemophilia A gene therapy clinical data and hemoglobinopathies *ex vivo* gene-edited cell therapy data will be featured in poster presentations at the 61st Annual Meeting of the American Society of Hematology (ASH). The ASH abstracts, which were submitted on August 3, 2019, were released online this morning. The conference will take place in Orlando, FL, from December 7-10, 2019.

**Gene Therapy**

- Abstract #2060: "Updated Follow-up of the Alta Study, a Phase 1/2, Open Label, Adaptive, Dose-Ranging Study to Assess the Safety and Tolerability of SB-525 Gene Therapy in Adult Patients with Severe Hemophilia A"
  Presenter: Barbara Konkle, M.D., Bloodworks Northwest, Professor of Medicine at University of Washington
  *December 7th, 2019, 5:30-7:30pm Eastern Time*

The SB-525 poster will show updated Alta study data including durability of Factor VIII (FVIII) levels, bleeding rate, factor usage, and safety, for all five patients in the high dose cohort of 3e13 vg/kg, with approximately 4 months to 11 months of follow-up after treatment with SB-525.

As of the abstract submission date, four patients in the 3e13 vg/kg cohort achieved FVIII levels within the normal range with no bleeding events reported up to 24 weeks post-administration. These patients did not require FVIII replacement therapy following the initial prophylactic period of up to approximately 3 weeks post-SB-525 administration. The fifth patient in the 3e13 vg/kg cohort had only recently undergone treatment with SB-525 at the time of the abstract submission. As previously reported, one patient had treatment-related serious adverse events (SAEs) of hypotension and fever, which occurred approximately 6 hours after completion of the vector infusion and resolved with treatment within 24 hours, with no loss of FVIII expression. SB-525 is being developed as part of a global collaboration between Sangamo and Pfizer.

"The rapid kinetics of Factor VIII expression, durability of response, and the relatively low intra-cohort variability in the context of a complete cessation of bleeding events and elimination of exogenous Factor VIII usage continues to suggest SB-525 is a differentiated hemophilia A gene therapy," said Bettina Cockroft, M.D., M.B.A., Chief Medical Officer of Sangamo, commenting on the published abstract. "We are pleased with the progress of the program toward a registrational Phase 3 study led by Pfizer, who announced it has enrolled its first patient in the 6-month Phase 3 lead-in study. We have recently completed the manufacturing technology transfer to Pfizer and initiated the transfer of the IND."

***Ex Vivo* Gene-Edited Cell Therapy**

- Abstract #3544: "Preliminary Results of a Phase 1/2 Clinical Study of Zinc Finger Nuclease-Mediated Editing of BCL11A in Autologous Hematopoietic Stem Cells for Transfusion-Dependent Beta Thalassemia"
  Presenter: Angela Smith, MD, Associate Professor in the Division of Pediatric Blood and Marrow Transplantation at the University of Minnesota
  *December 9th, 2019, 6:00-8:00pm Eastern Time*
- Abstract #974: "Zinc Finger Nuclease-Mediated Disruption of the BCL11A Erythroid Enhancer Results in Enriched Biallelic Editing, Increased Fetal Hemoglobin, and Reduced Sickling in Erythroid Cells Derived from Sickle Cell Disease Patients"
  Presenter: Samuel Lessard, Ph.D., Scientist, Sanofi

The ST-400 beta thalassemia poster will show preliminary results from the first three patients enrolled in the Phase 1/2 THALES study. In this study, hematopoietic stem progenitor cells (HSPCs) are apheresed from the patient, edited to knock out the erythroid specific enhancer of the *BCL11A* gene, and cryopreserved prior to infusion back into the patient following myeloablative conditioning with busulfan. The first three patients all have severe beta thalassemia genotypes: $\beta^0/\beta^0$, homozygous for the severe $\beta^+$ IVS-I-5 (G>C) mutation, and $\beta^0/\beta^+$ genotype including the severe IVS-II-654 (C>T) mutation, respectively.

As of the abstract submission date, Patient 1 and Patient 2 had experienced prompt hematopoietic reconstitution. Patient 1 had increasing fetal hemoglobin (HbF) fraction that contributed to a stable total hemoglobin. After being free from packed red blood cell (PRBC) transfusions for 6 weeks, the patient subsequently required intermittent transfusions. Patient 2 had rising HbF levels observed through 90 days post-infusion. For both patients, as of the most recent follow-up reported in the abstract, on-target insertions and deletions (indels) were present in circulating white blood cells. Patient 3 had just completed ST-400 manufacturing at the time of abstract submission. As previously disclosed, Patient 1 experienced an SAE of hypersensitivity during ST-400 infusion considered by the investigator to be related to the product cryoprotectant, DSMO, and which resolved by the end of the infusion. No other SAEs related to ST-400 have been reported and all other AEs have been consistent with myeloablation. No clonal hematopoiesis has been observed. Longer follow-up will be required to assess the clinical significance of these early results. ST-400 is being developed as part of a global collaboration between Sangamo and Sanofi, along with support through a grant from the California Institute for Regenerative Medicine (CIRM).

"The first three patients enrolled in the THALES study all have severe beta thalassemia genotypes that result in almost no endogenous beta globin production. The increases in fetal hemoglobin and presence of on-target indels in circulating blood cells suggests successful editing using zinc finger nucleases. The results are preliminary and will require additional patients and longer-term follow-up to assess their clinical significance," said Adrian Woolfson, BM., B.Ch., Ph.D., Head of Research and Development. "It is important to note that myeloablative hematopoietic stem cell transplantation reboots the hematopoietic system, and that sufficient time is required for the stem cells to fully repopulate the marrow and for new blood cells to form. In other myeloablative conditioning studies in a similar patient population, full manifestation of the effects of gene modification in the red blood cell

compartment has taken as long as 12 months or more to become evident."

Sanofi's *in vitro* sickle cell disease poster details a similar approach to ST-400, using mobilized HSPCs from normal donors and SCD patients and utilizing the same zinc finger nuclease for gene editing, delivered as transient non-viral RNA, and designed to disrupt the erythroid specific enhancer of the *BCL11A* gene, which represses the expression of the gamma globin genes, thereby switching off HbF synthesis. Results from *ex vivo* studies demonstrated enriched biallelic editing, increased HbF, and reduced sickling in erythroid cells derived from non-treated sickle cell disease patients. Sanofi has initiated a Phase 1/2 trial evaluating BIVV003, an *ex vivo* gene-edited cell therapy using ZFN gene editing technology to modify autologous hematopoietic stem cells using fetal hemoglobin to produce functional red blood cells with higher BhF content that are resistant to sickling in patients with severe sickle cell disease. Recruitment is ongoing.

**About the Alta study**

The Phase 1/2 Alta study is an open-label, dose-ranging clinical trial designed to assess the safety and tolerability of SB-525 gene therapy in patients with severe hemophilia A. SB-525 was administered to 11 patients in 4 cohorts of 2 patients each across 4 ascending doses (9e11 vg/kg, 2e12 vg/kg, 1e13vg/kg and 3e13vg/kg) with expansion of the highest dose cohort by 3 additional patients. The U.S. Food and Drug Administration (FDA) has granted Orphan Drug, Fast Track, and regenerative medicine advanced therapy (RMAT) designations to SB-525, which also received Orphan Medicinal Product designation from the European Medicines Agency.

**About the THALES study**

The Phase 1/2 THALES study is a single-arm, multi-site study to assess the safety, tolerability, and efficacy of ST-400 autologous hematopoietic stem cell transplant in 6 patients with transfusion-dependent beta thalassemia (TDT). ST-400 is manufactured by *ex vivo* gene editing of a patient's own (autologous) hematopoietic stem cells using non-viral delivery of zinc finger nuclease technology. The THALES study inclusion criteria include all patients with TDT ($\beta^0/\beta^0$ or non- $\beta^0/\beta^0$) who have received at least 8 packed red blood cell transfusions per year for the two years before enrollment in the study. The FDA has granted Orphan Drug status to ST-400.

**About Sangamo Therapeutics**

Sangamo Therapeutics, Inc. is focused on translating ground-breaking science into genomic medicines with the potential to transform patients' lives using gene therapy, *ex vivo* gene-edited cell therapy, *in vivo* genome editing, and gene regulation. For more information about Sangamo, visit www.sangamo.com.

*Forward-Looking Statements*

*This press release contains forward-looking statements regarding Sangamo's current expectations. These forward-looking statements include, without limitation, statements regarding the Company's ability to develop and commercialize product candidates to address genetic diseases with the Company's proprietary technologies, as well as the timing of commencement of clinical programs and the anticipated benefits therefrom. These statements are not guarantees of future performance and are subject to certain risks, uncertainties and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, the outcomes of clinical trials, the uncertain regulatory approval process, uncertainties related to the execution of clinical trials, Sangamo's reliance on partners and other third-parties to meet their clinical and manufacturing obligations, and the ability to maintain strategic partnerships. Further, there can be no assurance that the necessary regulatory approvals will be obtained or that Sangamo and its partners will be able to develop commercially viable product candidates. Actual results may differ from those projected in forward-looking statements due to risks and uncertainties that exist in Sangamo's operations and business environments. These risks and uncertainties are described more fully in Sangamo's Annual Report on Form 10-K for the year ended December 31, 2018 as filed with the Securities and Exchange Commission and Sangamo's most recent Quarterly Report on Form 10-Q. Forward-looking statements contained in this announcement are made as of this date, and Sangamo undertakes no duty to update such information except as required under applicable law.*

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