Sangamo Announces Preliminary Results From the First Three Patients in a Phase 1/2 Study Evaluating ST-400 Ex Vivo Gene-edited Cell Therapy in Beta Thalassemia

December 9, 2019

- *First three patients experienced prompt hematopoietic reconstitution, and no clonal hematopoiesis*
- *Early first-in-human data provide insights into relationship between product specific characteristics, including cell dose, editing efficiency, and fetal hemoglobin induction*
- *Additional study results expected in late 2020 once enrollment is complete and all six patients have longer follow-up*

BRISBANE, Calif.--(BUSINESS WIRE)--Dec. 9, 2019-- Sangamo Therapeutics, Inc. (Nasdaq: SGMO), a genomic medicine company, today announced preliminary results from the first three patients treated in the Phase 1/2 THALES study evaluating investigational ST-400 *ex vivo* gene-edited cell therapy in transfusion-dependent beta thalassemia (TDT). The data are featured in a poster presentation on December 9, 2019 at the 61st Annual Meeting of the American Society of Hematology (ASH) in Orlando, FL. The ST-400 ASH poster will be available on Sangamo's website in the Investors and Media section under Events and Presentations at the beginning of the poster session at 10am Eastern Time.

"The prompt hematopoietic reconstitution and on-target indels in circulating white blood cells observed in the three patients treated with ST-400 indicate successful editing with zinc finger nuclease technology," said Angela Smith, MD, Associate Professor in the Division of Pediatric Blood and Marrow Transplantation at the University of Minnesota, and a Principal Investigator of the THALES study. "As is the case in other myeloablative conditioning studies of stem cell transplants for beta thalassemia patients, the full effects of the treatment may take as long as 12 to 18 months or more to manifest. Longer-term follow-up, including from additional patients, will be necessary to understand the safety profile and potential clinical benefit of ST-400 in beta thalassemia. The emerging tolerability and safety profile of ST-400, as well as the induction of fetal hemoglobin and presence of indels, suggest that further exploration of this novel gene-edited cell therapy is merited."

Beta thalassemia is a rare blood disorder caused by a mutation in the beta-globin gene that results in impaired production of red blood cells. ST-400 is an autologous cell therapy candidate that uses gene editing to modify a patient's own hematopoietic stem cells (HSCs) to produce functional progeny red blood cells by increasing fetal hemoglobin.

In the THALES study, hematopoietic stem and progenitor cells (HSPCs) are collected from the patient, modified using zinc finger nuclease (ZFN) gene editing technology to disrupt the erythroid specific enhancer (ESE) of the *BCL11A* gene, and cryopreserved prior to infusion back into the patient following myeloablative conditioning with busulfan. To date, ST-400 has been manufactured for five patients, three of whom had been treated at the time of the ASH data cut. ST-400 is being developed as part of a global collaboration between Sangamo and Sanofi, and with the support of a grant from the California Institute for Regenerative Medicine (CIRM).

The three patients treated with ST-400 experienced prompt hematopoietic reconstitution, demonstrating neutrophil engraftment in 14-22 days and platelet engraftment in 22-35 days (Table 1). No emerging clonal hematopoiesis has to date been observed by on-target indel pattern monitoring in the three treated patients. Reported adverse events (AEs) are consistent with the known toxicities of mobilization, apheresis, and myeloablative busulfan conditioning. One serious adverse event (SAE) related to ST-400 was reported. As previously disclosed, Patient 1 experienced hypersensitivity during ST-400 infusion considered by the investigator to be likely related to the product cryoprotectant excipient, DMSO, and which resolved by the end of the infusion.

"The early experiences with the first three patients enrolled in this first-in-human study of ST-400 are providing useful insights into the patient characteristics, product characteristics and outcomes, including the relationship between patient genotype, phenotype, age, CD34+ cell dose, editing efficiency, and induction of fetal hemoglobin," said Adrian Woolfson, BM., B.Ch., Ph.D., Head of Research and Development at Sangamo. "Our understanding of ST-400 will continue to evolve as we follow the progress of these and additional patients in the coming year, and those dosed in Sanofi's BIVV003 clinical trial, which is evaluating the same gene-editing approach in sickle cell disease."

Patient 1

Patient 1, age 36, has a β^0/β^0 genotype, the most severe form of TDT, and had 27 annualized packed red blood cell (PRBC) events prior to enrollment into the study. The patient underwent a second cycle of mobilization and apheresis due to the low cell dose and potency achieved in the first cycle. In both ST-400 lots, editing efficiency was approximately 25%, which was lower than the other patients enrolled in the study and 12 trial-run lots manufactured at clinical scale (71% median editing efficiency).

On-target indels in the infused ST-400 product were 23%, and the CD34+ cell dose was 5.4 x 10^6 cells/kg. Indels have persisted in peripheral leukocytes through Month 9. Following ST-400 infusion, fetal hemoglobin levels increased to approximately 2.7 g/dL at Day 56 and remained elevated compared to baseline at 0.9 g/dL at week 39, the most recent measurement at the time of the ASH data cut. After an initial transfusion-free duration of 6 weeks, the patient resumed intermittent PRBC transfusions, with an overall 33% reduction in annualized PRBC units transfused since engraftment.

Patient 2

Patient 2, age 30, is homozygous for the severe β+ IVS-I-5 (G>C) mutation and had 18 annualized PRBC events prior to enrollment into the study. On-target indels in the ST-400 product were 73%, with a CD34+ cell dose of 3.9 x 10^6 cells/kg, the lowest seen across the ST-400 lots manufactured for the 5 enrolled patients. Indels have persisted in peripheral leukocytes through Month 6. Following ST-400 infusion, fetal hemoglobin levels increased as compared with baseline, but have been <1 g/dL through to 26 weeks, the lowest induction level observed in the three patients treated to date. The patient is currently receiving intermittent PRBC transfusions.

Patient 3

Patient 3, age 23, has a β0/β+ genotype that includes the severe IVS-II-654 (C>T) mutation and had 15 annualized PRBC events prior to enrollment into the study. On-target indels in the ST-400 product were 54%, with a CD34+ cell dose of 10.3 x 10^6 cells/kg. At the time of the ASH data cut indels have persisted in peripheral leukocytes through Day 56. Following ST-400 infusion, fetal hemoglobin levels have increased as compared to baseline and were continuing to rise as of the latest measurement of 2.8 g/dL at Day 90. Following an initial transfusion-free period of 7 weeks, the patient has received two PRBC transfusions commencing at 62 days post-infusion.

Patient 4, age 18 with a β^{WT} (αα)/β^o (αααα) genotype, and Patient 5, age 35 with a β^o/β+ (severe IVS-I-110 G>A) genotype, were dosed after the time of the ASH data cut. Sangamo expects to enroll a sixth and final patient in the study in the coming months. Results from additional patients and longer-term follow-up data are expected in the second half of 2020. Sanofi is running a parallel clinical trial with BIVV003, which uses a similar approach in sickle cell disease.

"We look forward to longer-term data and data from additional treated patients next year, where we will be in a better position to assess safety and the observed clinical effects," said Karin Knobe, M.D., Ph.D., Therapeutic Head of Development, Rare Blood Disorders, Sanofi. "We also look forward to exploring the potential of BIVV003 as a gene-edited cell therapy for sickle cell disease, a debilitating disease with significant unmet patient needs. We are currently enrolling patients."

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). The age range for the 5 patients enrolled is 18-36 years. 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 (β^0/β^0 or non- β^0/β^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 recently granted Orphan Drug status to ST-400.

Table 1: ST-400 Product Characteristics and Hematopoietic Reconstitution

Patient	Cell Dose (10^6/kg)	CD34+ (%)	CFU Dose (10^5/kg)	On-target Indels[a] (%)	Neutrophil Engraftment[b] Day(s)	Platelet Engraftment[c] Day(s)
1[d]	5.9	91	6.2	23[e]	14	25
2[d]	4.5	87	4.0	73	15	22
3[f]	11.4	90	14.8	54	22	35
4	5.4	86	7.3	80	Pre-Infusion	Pre-Infusion
5	9.5	98	10.5	76	Pre-Infusion	Pre-Infusion

[a]Percentage of all *BCL11A* ESE alleles with an indel; this is not equivalent to the percent of all cells with at least one edited *BCL11A* ESE allele.

[b]Neutrophil engraftment defined as occurring on the first of 3 consecutive days on which the patient's neutrophil count was ≥500 cells/μL.

[c]Platelet engraftment defined as occurring on the first of 3 consecutive measurements spanning a minimum of 3 days (in the absence of platelet transfusion in the preceding 7 days) on which the patient's platelet count was ≥20,000 cells/μL.

[d]Patients 1 and 2 received G-CSF from day +5 through neutrophil engraftment per site's standard operating procedure.

[e]Patient 1 underwent 2 cycles of apheresis and manufacturing of ST-400; on-target indel percentage for the lot not shown was 26%. All other patients underwent only one cycle of apheresis and manufacturing.

[f]Patient 3 received G-CSF from day +21 through neutrophil engraftment per site's standard operating procedure.

About Sangamo Therapeutics

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

Sangamo Forward Looking Statements

This press release contains forward-looking statements regarding Sangamo's current expectations. These forward-looking statements include, without limitation, statements relating to the investigational beta thalassemia ex vivo gene-edited cell therapy*, ST-400, including its potential therapeutic benefits; the potential long-term impacts of ST-400; ST-400 having the potential to be a predictable and reliable treatment that may bring clinical benefit to patients with beta thalassemia; plans to advance ST-400 into a potential registrational study; and other statements that are not historical fact. These statements are not guarantees of future performance and are subject to risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties related to: the research and development process; additional data, including the risk that the data reported from the THALES study to date may not be indicative of the final results from the study or that such final results may not validate and support the safety and efficacy of ST-400; the completion of the THALES study; the possibility of unfavorable new clinical data from the THALES study and further analyses of existing clinical data from the study that may material change clinical outcomes; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from the clincal studies relating to ST-400, any potential registrational studies or any other clinical studies of ST-400; Sangamo's*

reliance on third-parties to meet their clinical and manufacturing obligations; Sangamo's ability to maintain strategic partnerships; and the potential for technological developments by Sangamo's competitors that will obviate Sangamo's cell therapy technology. Further, there can be no assurance that the necessary regulatory approvals will be obtained for ST-400 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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