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Sangamo Announces Interim Results Of Phase 1/2 CHAMPIONS Study Showing Preliminary Evidence Of In Vivo Genome Editing In Patients With MPS II Treated With SB-913

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- Liver biopsy analysis detected targeted integration of IDS transgene, providing preliminary molecular evidence of in vivo genome editing in humans

- Plasma enzyme activity suggests genome-edited liver cells may be able to generate active IDS enzyme; clinical relevance of observed biochemical changes to be informed by additional data expected later this year

- SB-913 administration was generally well tolerated in 8 patients across 3 dose cohorts

- Second-generation ZFNs incorporating technology improvements for potential increased efficacy are expected to be available for evaluation in the clinic later this year

- Conference call and webcast scheduled for 12:30 p.m. Eastern Time today

BRISBANE, Calif., Feb. 7, 2019 /PRNewswire/ -- Sangamo Therapeutics, Inc. (NASDAQ: SGMO) today reported preliminary molecular and enzymatic evidence of editing of the human genome *in vivo* (inside the body). These findings are part of the interim results from the Phase 1/2 CHAMPIONS Study evaluating SB-913, a zinc finger nuclease (ZFN) *in vivo* genome editing product candidate for the treatment of patients with Mucopolysaccharidosis Type II (MPS II). These interim results were presented today at the WORLD*Symposium* 2019 being held in Orlando, Florida. Also reported today were interim results from the EMPOWERS Study (announced separately) evaluating SB-318 for the treatment of MPS I. Sangamo believes data from these two studies provide complementary evidence supportive of a favorable safety profile and of the activity of the ZFN *in vivo* genome editing technology used in both SB-913 and SB-318. The two WORLD*Symposium* presentations have been made available on the Sangamo website.

MPS II, also known as Hunter syndrome, is a rare genetic disorder caused by a deficiency of iduronate-2-sulfatase (IDS), a lysosomal enzyme which is required to break down or recycle the toxic buildup of glycosaminoglycans (GAGs). Without IDS enzyme activity, GAGs accumulate in cells throughout the body, leading to widespread tissue and organ damage. The current standard-of-care treatment for MPS II is enzyme replacement therapy (ERT), given weekly as intravenous infusions. SB-913 is an investigational product candidate being evaluated to treat MPS II using ZFNs, which are designed to insert a normal copy of the IDS gene into a precise location in the DNA of liver cells. The goal of SB-913 treatment is to enable a patient's liver to produce a continuous supply of functional IDS enzyme.

"The interim results from the CHAMPIONS Study provide preliminary evidence that *in vivo* genome editing occurred and that genome-edited liver cells are able to generate active IDS enzyme in patients with MPS II," said Dr. Joseph Muenzer, a professor of pediatrics and genetics at the University of North Carolina School of Medicine in Chapel Hill and a lead study investigator. "More data are needed to understand whether the small increases in IDS enzyme activity observed can translate into improved outcomes in MPS II patients treated with this first generation of SB-913. I look forward to reviewing additional data later this year from the five patients who have received the high-dose of SB-913."

In the CHAMPIONS Study, liver biopsies have been analyzed for three eligible patients – one from the low-dose cohort and two from the mid-dose cohort. Sangamo scientists developed an assay using reverse transcription polymerase chain reaction (RT-qPCR), a standard laboratory method used to amplify and detect specific molecular signals. The assay was designed to detect gene integration by identifying albumin-IDS chimeric mRNA transcripts, which can only be made if the IDS gene has successfully integrated at the expected site within the endogenous albumin gene. This assay detected albumin-IDS chimeric mRNA transcript in both mid-dose cohort patients, providing preliminary evidence of ZFN-mediated targeted integration of the IDS gene. Genome editing in mid-dose cohort patients appears to be occurring at a low frequency, as a parallel liver tissue analysis for minor genome edits conducted using MiSeq DNA sequencing, which is a less sensitive assay (lower limit of quantification of 0.1%), did not detect editing in samples from the low and mid-dose cohort patients. Liver biopsies from patients who received the high dose of SB-913 will be available for analysis later this year.

"The SB-913 and SB-318 data presented today represent an encouraging first step in the translation of genome editing technology from basic research to genomic medicine. Further data will be available throughout 2019 and will help inform our understanding of these early results," said Sandy Macrae, Sangamo's Chief Executive Officer. "With our expertise in zinc finger protein design and our understanding of the factors that contribute to efficient genome editing, our scientists have been able to engineer a second-generation of ZFNs. In preclinical studies, these have demonstrated the potential for greater potency and higher enzyme expression than our first generation ZFNs. We believe these improvements have the potential to provide greater benefit for patients."

Sangamo has developed second-generation, potentially more potent ZFN constructs designed to increase editing efficiency. Preclinical data of these second-generation ZFNs were reviewed by U.S. regulators. The preclinical data showed three potential advantages for use in the clinic: (1) a 5- to 30-fold improvement in efficiency and potency due to structural changes; (2) the ability to function equally well in the patients who have a single nucleotide polymorphism (SNP) in the target locus in the albumin gene (approximately 20% of the population); (3) improved specificity. The second-generation ZFNs are already being manufactured and are expected to be ready for evaluation in the clinic later this year. Additional data from Sangamo's *in vivo* genome editing programs will be assessed before potential integration plans for the second-generation ZFNs are finalized.

Interim CHAMPIONS Study Results Presented at WORLD*Symposium*

The primary objective of the CHAMPIONS Study is the safety and tolerability of SB-913, and secondary objectives include evaluation of change from baseline in plasma IDS activity and urine GAG levels. Biochemical measurements of urinary GAGs and plasma IDS are obtained at screening and baseline visits, every two weeks for an initial phase, and then every four weeks.

Patients with attenuated (cognitively intact) MPS II receiving ERT weekly were enrolled and treated in three dose cohorts:

- Cohort 1 (low-dose) — 5e12 vector genomes per kilogram body weight (vg/kg) of SB-913
- Cohort 2 (mid-dose) — 1e13 vg/kg of SB-913 (2x the starting dose)
- Cohort 3 (high-dose) — 5e13 vg/kg of SB-913 (5x the mid-dose)

Two patients are enrolled in each cohort, along with an additional three patients, all of whom have received the high dose, in an expanded cohort.

Safety data on eight patients were collected and analyzed. Administration of SB-913 was generally well tolerated in these patients. Of the 18 total adverse events (AEs) reported as related to study drug, 16 were mild (Grade 1), two were moderate (Grade 2), and all AEs resolved. There were no treatment-related serious adverse events (SAEs) reported.

The results of biochemical measurements were available in the first six patients who had sufficient length of follow-up for interpretation.

A newly developed sensitive quantitative assay (lower limit of quantification of 0.78 nmol/hour/mL) was used to measure plasma IDS activity. Small increases in IDS enzyme activity compared to baseline were recorded in the two patients receiving the mid-dose and in one patient receiving the high-dose. At 24 weeks these measurements remained within the expected range for baseline values (less than 10 nmol/hour/mL, as compared to the normal range which is estimated at greater than 82 nmol/hour/mL).

A more substantial increase in plasma IDS activity was measured in the second patient in the high dose cohort, with levels rising to approximately 50 nmol/hour/mL by week 6 following SB-913 administration. The plasma IDS activity levels subsequently decreased in the context of development of a mild transaminitis — a known risk of AAV-based therapies — due to a suspected immune response. Grade 1 elevations in liver function tests were measured at Day 62, 111 and 128. The patient was hospitalized on Day 121 for an incarcerated umbilical hernia considered unrelated to the study drug. As of the most recent observation, the patient's plasma IDS activity measured 14 nmol/hour/mL, above the baseline value but below the normal range.

Baseline urine GAG measurements for all six patients were in a range considered at or slightly above normal, except for heparan sulfate which was elevated in all patients at baseline. At 24 weeks, urine GAG results did not show a meaningful change.

The clinical relevance of the biochemical changes observed following administration of SB-913 will be assessed as clinical data and patient outcomes are analyzed following a trial of withdrawal from ERT. To date, two mid-dose and one high-dose patients have initiated ERT withdrawal. One mid-dose patient was recommended to resume ERT approximately 3 months after initiation of ERT withdrawal due to fatigue and increasing GAGs. Analyses from these withdrawals will be available later in 2019.

Conference Call
Sangamo will host a conference call today, February 7, 2019, at 12:30 p.m. Eastern Time, which will be open to the public. The call will also be webcast live and can be accessed via a link on the Sangamo Therapeutics website in the Investors and Media section under Events and Presentations.

The conference call dial-in numbers are (877) 377-7553 for domestic callers and (678) 894-3968 for international callers. The conference ID number for the call is 4387585. For those unable to listen in at the designated time, a conference call replay will be available for one week following the call. The conference call replay numbers for domestic and international callers are (855) 859-2056 and (404) 537-3406, respectively. The conference ID number for the replay is 4387585.

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

Forward-Looking Statements

This press release contains forward-looking statements based on Sangamo's current expectations. These forward-looking statements include, without limitation, statements relating to the potential therapeutic applications for SB-913 and SB-318, the potential for SB-913 to treat MPS II, including the potential for IDS enzyme activity increases observed in the CHAMPIONS Study to date to potentially translate into improved outcomes and for SB-913 to potentially cause the liver to produce a continuous supply of functional IDS enzyme, the timing and nature of additional data from SB-913, the potential advantages of second-generation ZFNs and the timing of the use of the second-generation ZFNs, Sangamo's belief that the second-generation ZFNs have the potential for greater benefit for patients, and other statements that are not historical fact. 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, risks and uncertainties related to early data, including the risk that the early data from the CHAMPIONS Study may not be representative of final results after all patients are treated in the study and all data are collected and analyzed; Sangamo's ability to complete the CHAMPIONS Study and the EMPOWERS Study; whether the final results from the CHAMPIONS Study and the EMPOWERS Study will validate and support interim results and the overall safety and efficacy of SB-913 and SB-318, respectively, including the risk that the early efficacy data from the CHAMPIONS Study and the EMPOWERS Study to date may not be maintained or replicated; whether Sangamo will be able to effectively deliver its ZFNs to produce a beneficial therapeutic effect, including the risks that the second-generation ZFNs may not be successfully integrated into Sangamo's product candidates and even if successfully integrated, the second-generation ZFNs may not have any advantages over Sangamo's first-generation ZFNs or otherwise may not produce any beneficial therapeutic effect; Sangamo's reliance on partners and other third-parties to meet their clinical and manufacturing obligations, and its ability to maintain strategic partnerships. Further, there can be no assurance that the necessary regulatory approvals for SB-913 or SB-318 will be obtained or that Sangamo and its partners will be able to develop commercially viable product candidates for the treatment of MPS II, MPS I and other diseases. These risks and uncertainties are described more fully in Sangamo's Quarterly Report on Form 10-Q for the quarter ended September 30, 2018 as filed with the Securities and Exchange Commission.

Forward-looking statements contained in this press release 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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