Sangamo Therapeutics Announces Updated Preliminary Phase 1/2 Data in Fabry Disease Clinical Study Showing Continued Tolerability and Sustained Elevated α-gal A Enzyme Activity in Five Longest Treated Patients

August 30, 2022

- Isaralgagene civaparvovec, or ST-920, continued to be generally well tolerated across three dose cohorts in the six treated patients

- The five longest treated patients exhibited elevated α-Gal A activity, ranging from nearly 3-fold to nearly 17-fold above mean normal, up to 15 months as at the last date of measurement

- One patient was withdrawn from enzyme replacement therapy (ERT) and demonstrated significantly elevated levels of α-Gal A activity at 12 weeks post withdrawal

- Since the cutoff date, an additional five patients have been dosed and an additional four patients in the dose escalation phase have been withdrawn from ERT. The Phase 1/2 STAAR study has progressed into the dose expansion phase.

BRISBANE, Calif.--(BUSINESS WIRE)--Aug. 30, 2022-- Sangamo Therapeutics, Inc. (Nasdaq: SGMO), a genomic medicine company, today announced updated preliminary results from the Phase 1/2 STAAR clinical study evaluating isaralgagene civaparvovec, or ST-920, a wholly owned gene therapy product candidate for the treatment of Fabry disease. These latest data show that, as of the February 14, 2022 cutoff date, the investigational treatment continued to be generally well tolerated, with no treatment-related adverse events above Grade 1 (mild). The five longest treated patients continued to exhibit elevated alpha-galactosidase A (α-Gal A) activity, sustained up to 15 months as of the last date of measurement. The sixth patient exhibited elevated α-Gal A activity to within normal range at two weeks post dosing.

These updated data will be presented at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Meeting on August 31, 2022, from 6:45pm-8:15pm Central European Time (Ref: SSIEM22-2517). These data are also available on Sangamo's website on the Events & Presentations page.

"These updated preliminary results continue to demonstrate the potential of isaralgagene civaparvovec gene therapy to safely address the most challenging symptoms of Fabry disease," said Jaya Ganesh, MD, Division of Medical Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai and investigator of the Phase 1/2 study. "I am excited to see whether these encouraging trends continue into the next dose cohort and beyond, as we progress this potential treatment for a very challenging illness."

As of the cutoff date, the first five patients treated, across three dose cohorts (0.5e13 vg/kg, 1e13 vg/kg and 3e13 vg/kg), sustained elevated α-Gal A activity ranging from nearly 3-fold to nearly 17-fold above mean normal at the last date of measurement.

- *Cohort 1, Patient 1 [on ERT at the cutoff date]:* α-Gal A activity measured at ERT trough was 12.4-fold above mean normal at Month 15
- *Cohort 1, Patient 2 [not on ERT]:* α-Gal A activity was 2.7-fold above mean normal at Month 15
- *Cohort 2, Patient 1 [not on ERT]:* α-Gal A activity was 3.5-fold above mean normal at Week 48
- *Cohort 2, Patient 2 [began the study on ERT and was subsequently withdrawn from ERT at week 24]:* α-Gal A activity was 10.3-fold above mean normal at Week 36. This represents a sustained α-Gal A expression compared with the 10-fold above mean normal levels previously exhibited as of November 9, 2021, with α-Gal A expression one week post ERT withdrawal.
- *Cohort 3, Patient 1 [on ERT at the cutoff date]:* α-Gal A activity measured at ERT trough was 16.7-fold above mean normal at Week 16
- *Cohort 3, Patient 2 [on ERT at the cutoff date]:* α-Gal A activity measured at ERT trough increased to within normal range at Week 2

"We are excited by the strong progress of our wholly owned Fabry program, which we believe places us in a leading position to offer patients a compelling potential therapy for their underlying disease," said Nathalie Dubois-Stringfellow, Ph.D, Sangamo's newly appointed Senior Vice President, Chief Development Officer. "We look forward to sharing an update on the additional patients dosed and continue to actively prepare for a potential Phase 3 trial."

As of the cutoff date, isaralgagene civaparvovec was generally well tolerated across three dose cohorts in the six treated patients, with no treatment-related adverse events higher than Grade 1 (mild) and no treatment-related serious adverse events. No patients experienced liver enzyme elevations requiring steroid treatment, and no prophylactic steroid treatments had been used.

Three patients have anecdotally reported improvements in their symptoms, including improvements in the ability to sweat, a primary and common Fabry disease symptom. No progression of Fabry cardiomyopathy was observed in those patients who presented with signs of cardiomyopathy on cardiac MRI at baseline. The first patient in Cohort 2 with the most significant elevation in plasma globotriaosylsphingosine (lyso-Gb3) pre-treatment, showed a significant reduction of approximately 40% from baseline levels of plasma lyso-Gb3 within 10 weeks after dosing which was sustained through Week 48. The second patient in Cohort 2 demonstrated a moderate increase in lyso-Gb3 levels since the withdrawal of ERT. The other four patients with lower baseline levels of lyso-Gb3 sustained steady levels through the cutoff date.

Since the cutoff date, an additional five patients have been dosed in the Phase 1/2 STAAR study, resulting in a total of eleven patients dosed to date – one additional patient in Cohort 3, two patients in Cohort 4 at the 5e13 vg/kg dose level and the first two patients in the expansion phase at the 5e13 vg/kg dose level. There are multiple additional patients in screening, including both male and female candidates. Out of the five treated patients in the dose escalation phase who began the STAAR study on ERT, an additional four have been withdrawn from ERT since the cutoff date, completing ERT withdrawal for all patients in this dose escalation phase of the study. Sangamo expects to provide additional results from the STAAR study in the second half of 2022 and is currently planning for a potential Phase 3 clinical trial.

A Current Report on Form 8-K summarizing the updated preliminary results from the Phase 1/2 STAAR clinical study in more detail will be filed by Sangamo, and this press release is subject to the further detail provided in the Form 8-K.

About the STAAR Study

The Phase 1/2 STAAR study is a global open-label, single-dose, dose-ranging, multicenter clinical study designed to evaluate the safety and tolerability of isaralgagene civaparvovec, or ST-920, a gene therapy product candidate in patients with Fabry disease. Isaralgagene civaparvovec requires a one-time infusion without preconditioning. The STAAR study is enrolling patients who are on ERT, are ERT pseudo-naïve (defined as having been off ERT for six or more months), or who are ERT-naïve. The age range of the six patients dosed as of the cutoff date is 22 to 48 years. The U.S. Food and Drug Administration has granted Orphan Drug designation to isaralgagene civaparvovec, which has also received Orphan Medicinal Product designation from the European Medicines Agency.

About Fabry Disease

Fabry disease is a lysosomal storage disorder caused by mutations in the galactosidase alpha gene (*GLA*), which leads to deficient alpha-galactosidase A (α-Gal A) enzyme activity, which is necessary for metabolizing globotriaosylceramide (Gb3). The buildup of Gb3 in the cells can cause serious damage to vital organs, including the kidney, heart, nerves, eyes, gut and skin. Symptoms of Fabry disease can include decreased or absent sweat production, heat intolerance, angiokeratoma (skin blemishes), vision problems, kidney disease, heart failure, gastrointestinal disturbance, mood disorders, neuropathic pain and tingling in the extremities.

About Sangamo Therapeutics

Sangamo Therapeutics is a clinical-stage biopharmaceutical company with a robust genomic medicines pipeline. Using ground-breaking science, including our proprietary zinc finger genome engineering technology and manufacturing expertise, Sangamo aims to create new genomic medicines for patients suffering from diseases for which existing treatment options are inadequate or currently don't exist. To learn more, visit www.sangamo.com and connect with us on LinkedIn and Twitter.

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 therapeutic potential of isaralgagene civaparvovec (ST-920), including its potential to address the most challenging symptoms of Fabry disease and to become a compelling potential therapy for patients with Fabry disease, the potential for the favorable trends exhibited by treated patients in the Phase 1/2 STAAR study to continue, Sangamo's expectation for reporting updated results from the Phase 1/2 STAAR study and the expected timing thereof, plans to discontinue patients on ERT, plans for conducting a Phase 3 clinical trial of isaralgagene civaparvovec, and other statements that are not historical fact. These statements are not guarantees of future performance and are subject to risks and uncertainties that are difficult to predict. Sangamo's actual results may differ materially and adversely from those expressed. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties related to: the uncertain timing and unpredictable nature of clinical trials and clinical trial results, including the risks that therapeutic effects observed in preliminary clinical trial results will not be durable in patients and that final Phase 1/2 STAAR study data will not validate the safety and efficacy of isaralgagene civaparvovec; reliance on results of early clinical trials, such as the Phase 1/2 STAAR study, which results are not necessarily predictive of future clinical trial results, including the results of any Phase 3 trial of isaralgagene civaparvovec; the research and development process, including the enrollment, operation and results of clinical trials and the presentation of clinical data; the effects of the evolving COVID-19 pandemic and the impacts of the pandemic on the global business environment, healthcare systems and business and operations of Sangamo, including the initiation and operation of clinical trials; the unpredictable regulatory approval process for product candidates across multiple regulatory authorities; the manufacturing of products and product candidates; the commercialization of approved products; the potential for technological developments that obviate technologies used by Sangamo in isaralgagene civaparvovec; Sangamo's lack of resources to fully develop, obtain regulatory approval for and commercialize its product candidates; and those risks and uncertainties described in Sangamo's filings with the U.S. Securities and Exchange Commission, including its Annual Report on Form 10-K for the year ended December 31, 2021 as supplemented by Sangamo's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022. The information contained in this release is as of August 30, 2022, and Sangamo undertakes no duty to update forward-looking statements contained in this release except as required by applicable laws.

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