Sangamo Therapeutics Announces Evidence of Clinical Benefit in Phase 1/2 STAAR Study in Fabry Disease

February 22, 2023

- Sustained, elevated expression of alpha-galactosidase A (α-Gal A) activity observed in 13 patients for over two years for the longest treated patient as of cutoff date.

- Achieved 78% globotriaosylceramide (Gb3) substrate clearance at 6-months and 77% reduction in urine podocyte loss in one of the first kidney biopsies.

- All dose escalation patients had been withdrawn from enzyme replacement therapy (ERT) and remain off ERT today.

- Reported a clinically meaningful and statistically significant increase in mean general health scores, as measured by the SF-36 General Health survey.

- Since the cutoff date, four additional patients have been dosed in the expansion phase, and a further two patients have been withdrawn from ERT.

- The Phase 1/2 STAAR study expansion phase is ongoing and preparations for a potential Phase 3 trial actively progress, with a trial start anticipated by the end of 2023.

BRISBANE, Calif.--(BUSINESS WIRE)--Feb. 22, 2023-- Sangamo Therapeutics, Inc. (Nasdaq: SGMO), a genomic medicine company, today announced updated preliminary data as of the October 20, 2022 cutoff date 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 data, which present new biomarker data and results from the first kidney biopsies in this study, indicate evidence of clinical benefit for isaralgagene civaparvovec in Fabry disease.

As of the November 15, 2022 supplemental cutoff date, 13 patients across the dose escalation and expansion phases exhibited supraphysiological levels of α-Gal A activity, sustained for over two years for the patient with the longest follow-up. All five patients who began the dose escalation phase on ERT had been successfully withdrawn from ERT and continued to exhibit supraphysiological levels of α-Gal A activity following withdrawal. No patient has required the resumption of ERT treatment to date.

Importantly, there is evidence of significant Gb3 substrate reduction at six months in one of the first kidney biopsies taken from this study, along with a significant reduction in urine podocyte loss. In addition, the study observed a clinically meaningful and statistically significant increase in mean general health scores, as measured by the SF-36 General Health survey.

These updated data will be shared at the 19th Annual WORLD*Symposium* on Friday, February 24, 2023 via an oral presentation in the session from 8:00-9:00am Eastern Time and a poster presentation from 3:00-4:00pm Eastern Time (Poster Ref: 169). These data will also be available on Sangamo's website on the Presentations page.

"Fabry is a debilitating disease with life-long impact," said Dr. Robert Hopkin, MD, Cincinnati Children's Hospital Medical Center, and investigator of the Phase 1/2 study. "The combination of the first kidney biopsy results and the associated urine podocyte data are highly encouraging and compelling. As a whole, this exciting dataset shows that ST-920 has the potential to improve the lives of patients without the need for burdensome ERT treatment."

As of the November 15, 2022 supplemental cutoff date, all nine patients treated in the dose escalation phase across the four dose cohorts ($0.5x10^{13}$ vg/kg, $1x10^{13}$ vg/kg, $3x10^{13}$ vg/kg and $5x10^{13}$ vg/kg) exhibited elevated α-Gal A activity ranging from nearly 4-fold to 68-fold of mean normal, sustained for over two years for the patient with the longest follow-up, at the last date of measurement. ERT withdrawal was completed for all five patients who began the study on ERT, with continued supraphysiological levels of α-Gal A activity following ERT withdrawal. All five patients remain off ERT as of February 22, 2023. For naïve and pseudo-naïve patients in the dose escalation phase, patients in the highest dose cohort exhibited significantly higher levels of α-Gal A activity compared to those patients in lower dose cohorts.

As of the November 15, 2022 supplemental cutoff date, the first three patients dosed in the expansion phase at the highest dose level exhibited a rapid increase in α-Gal A activity, sustained for up to 14 weeks for the patient with the longest follow-up, at the last date of measurement. The fourth patient had increased to within normal range at four weeks of dosing. The first female patient dosed in the study demonstrated a similar response profile to males as of the supplemental cutoff date.

Gb3 is a fatty substrate that accumulates in the cells of Fabry disease patients and can result in damage to multiple organs, including the kidneys, heart and central nervous system. As of the October 20, 2022 cutoff date, the kidney biopsy for patient 9 in the dose escalation phase – who demonstrated a high number of Gb3 inclusions and high levels of plasma globotriaosylsphingosine (lyso-Gb3) at baseline – exhibited a notable 78% clearance in Gb3 inclusions per peritubular capillary (or PTC) from an average of 8.7 inclusions per PTC at baseline to 1.9 inclusions per PTC, 6 months after dosing. This assessment was made by two blinded pathologists who independently scored digital images of the sectioned kidney from baseline and 6-month biopsies, adjudicated by a third independent pathologist. In addition, this patient exhibited a 77% reduction in urinary podocyte loss after 6 months. The significant decrease in renal Gb3 inclusions and the reduction in urine podocyte loss supports a potentially favorable impact on progression of Fabry nephropathy.

As of the October 20, 2022 cutoff date, the kidney biopsy for patient 8 – who exhibited a lower number of Gb3 inclusions and lower levels of plasma lyso-Gb3 at baseline – demonstrated stable PTC inclusions 6-months post dosing. This patient exhibited a notable 97% reduction in urinary podocyte loss after 6-months which, coupled with the significant increase in a-Gal A activity along with reduction in lyso-Gb3 after dosing, provides evidence of a potentially favorable effect on Fabry nephropathy.

In addition, changes in General Health Scores for patients in the dose escalation phase from baseline at Week 52 were statistically significant with a mean increased General Health Score of 19.6, further demonstrating the potential clinical benefit of isaralgagene civaparvovec. For context, a 3- to 5-point change on any SF-36 score is the minimally clinically important difference.

“We are thrilled with these data, which we believe demonstrate the importance of ST-920 as a potential gene therapy to treat the underlying pathology of Fabry disease. Taken together, the updated biomarker data, kidney biopsy improvements and SF-36 results suggest a promising path forward in our efforts to develop a gene therapy that has the potential to transform the lives of patients living with Fabry disease,” said Nathalie Dubois-Stringfellow, Ph.D, Sangamo’s Senior Vice President, Chief Development Officer. “We believe that we have a potential best-in-class gene therapy and are excited to advance this program into a Phase 3 clinical trial as the next step in our mission to deliver an important potential treatment to patients as quickly as possible.”

For naïve and pseudo-naïve patients in the dose escalation and expansion phases, where levels of lyso-Gb3 started high at baseline (>80 ng/mL), patients experienced a 40-65% reduction in levels following treatment as of the October 20, 2022 cutoff date. For the first time, and at the highest dose level, a 54% reduction in plasma lyso-Gb3 levels was observed where baseline levels started below 25 ng/mL. For patients in the dose escalation and expansion phases who began the study on ERT, plasma lyso-Gb3 levels following ERT withdrawal remained within the range of levels and variability normally observed in patients treated with ERT as of the cutoff date. In these patients, α-Gal A activity remained elevated, and no patient experienced symptoms requiring the resumption of ERT to date.

As of the October 20, 2022 cutoff date, isaralgagene civaparvovec was generally well tolerated in the 13 treated patients across four dose cohorts and the expansion groups. No treatment-related adverse events greater than a Grade 2 were reported and there were no treatment-related serious adverse events. No prophylactic corticosteroids or other immune modulating agents were administered.

Since the October 20, 2022 cutoff date, a further four patients have been dosed in the expansion phase to achieve a total of 17, and an additional two patients have been withdrawn from ERT. Dosing of the remaining patients in the expansion phase of the Phase 1/2 STAAR study is ongoing, with a total of 20 sites active and recruiting. We expect dosing to conclude by the end of 2023. Preparations for a potential Phase 3 trial actively progress, with a trial start anticipated by the end of 2023, depending on regulatory interactions. Dosing of the first patient in the Phase 3 trial could begin as early as the first part of 2024.

Our Annual Report on Form 10-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 10-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 13 patients dosed as of the cutoff date is 22 to 67 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 improve the lives of patients without the need for ERT and to have a favorable effect on Fabry nephropathy, Sangamo’s expectation for, and timelines related to, the completion of dosing in the Phase 1/2 STAAR study, the planning for and the anticipated commencement of and dosing in a potential Phase 3 trial, depending on regulatory interactions, and the anticipated timing thereof, 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, including data from kidney biopsies, will not be durable in patients and that final Phase 1/2 STAAR study data will not validate the potential safety and efficacy of isaralgagene civaparvovec and that the patients withdrawn from ERT will remain off ERT; 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 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, or the SEC, including its Annual Report on Form

10-K for the year ended December 31, 2021, as supplemented in its Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, and future filings and reports that Sangamo makes from time to time with the SEC. The information contained in this release is as of February 22, 2023, and Sangamo undertakes no duty to update forward-looking statements contained in this release except as required by applicable laws.

View source version on businesswire.com: https://www.businesswire.com/news/home/20230222005671/en/

Investor Relations & Media Inquiries
Louise Wilkie
ir@sangamo.com
media@sangamo.com

Source: Sangamo Therapeutics, Inc.