Sangamo Therapeutics Reports on Pfizer's Announcement of Positive Topline Results From Phase 3 Trial of Hemophilia A Gene Therapy Candidate

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Giroctocogene fitelparvovec trial meets primary and key secondary objectives of superiority compared to prophylaxis

RICHMOND, Calif.--(BUSINESS WIRE)--Jul. 24, 2024-- Sangamo Therapeutics, Inc. (Nasdaq: SGMO), a genomic medicine company, today reported on Pfizer Inc.'s announcement of positive topline results from the Phase 3 AFFINE trial (NCT04370054) evaluating giroctocogene fitelparvovec, an investigational gene therapy that Sangamo is co-developing with and licensing to Pfizer for the treatment of adults with moderately severe to severe hemophilia A.

Sangamo is eligible to earn from Pfizer up to $220 million in milestone payments upon the achievement of certain regulatory and commercial milestones for giroctocogene fitelparvovec and product sales royalties of 14% - 20% if giroctocogene fitelparvovec is approved and commercialized, subject to certain reductions.

Pfizer reported that the AFFINE trial achieved its primary objective of non-inferiority, as well as superiority, of total annualized bleeding rate (ABR) from Week 12 through at least 15 months of follow up post-infusion compared with routine Factor VIII (FVIII) replacement prophylaxis treatment. Following a single 3e13 vg/kg dose, giroctocogene fitelparvovec demonstrated a statistically significant reduction in mean total ABR compared to the pre-infusion period (1.24 vs 4.73; one-sided p-value=0.0040).

Key secondary endpoints as defined by the trial protocol were met and also demonstrated superiority compared to prophylaxis. 84% of participants maintained FVIII activity >5% at 15 months post-infusion (one-sided p-value = 0.0086) with the majority of participants having FVIII activity ≥15%, and the mean treated ABR showed a statistically significant 98.3% reduction from 4.08 in the pre-infusion period to 0.07 post-infusion (from Week 12 up to at least 15 months [15-44 months]; one-sided p-value < 0.0001). Throughout the trial, among all dosed participants, one participant (1.3%) returned to prophylaxis post-infusion.

In the AFFINE trial, giroctocogene fitelparvovec was generally well tolerated. Transiently elevated FVIII levels ≥150% were observed in 49.3% of dosed participants, as measured via chromogenic assay, with no impact on efficacy and safety results. Serious adverse events were reported in 15 patients (20%), including 13 events reported by 10 patients (13.3%) assessed as related to treatment. Treatment-related adverse events generally resolved in response to clinical management.

"For people living with hemophilia A, the physical and emotional impact of needing to prevent and treat bleeding episodes through frequent IV infusions or injections cannot be underestimated," said Professor Andrew Leavitt M.D., AFFINE lead investigator, Departments of Laboratory Medicine and Medicine Division of Hematology/Oncology Director, Adult Hemophilia Treatment Center, University of California, San Francisco, CA. "I'm excited by the strength of these positive results from the AFFINE trial that show giroctocogene fitelparvovec was generally well tolerated, and demonstrate the transformative potential of this gene therapy candidate to provide superior bleed protection compared with routine FVIII prophylaxis, while helping relieve the treatment burden for people living with hemophilia A."

Giroctocogene fitelparvovec is a novel, investigational gene therapy that contains a bio-engineered AAV6 capsid and a modified B-domain deleted human coagulation FVIII gene. The goal of this investigational treatment for people living with hemophilia A is that a single infusion of giroctocogene fitelparvovec may allow them to produce FVIII themselves for an extended period of time, provide bleed protection and reduce the need for routine prophylaxis with intravenous (IV) infusions or injections.[i,ii,iii,iv]

"We are thrilled with the positive topline results from the Phase 3 AFFINE trial, which demonstrated the potential of giroctocogene fitelparvovec as a one-time gene therapy for people with hemophilia A and provide a potential alternative to the current burden of disease management," said Nathalie Dubois-Stringfellow, Ph.D, Chief Development Officer at Sangamo. "These impressive results further validate the power of our genomic technologies and take us one step closer towards what could become Sangamo's first medicine commercially available to patients. We greatly appreciate Pfizer's strong leadership of this important program and look forward to their discussions of these data with regulatory authorities."

In this Phase 3 trial, eligible trial participants were initially enrolled in a lead-in study (NCT03587116) and upon successful completion, were enrolled into the AFFINE trial where they received a one-time 3e13 vg/kg dose of giroctocogene fitelparvovec by IV infusion. Participants in the AFFINE trial were screened with a validated assay designed to identify individuals who test negative for neutralizing antibodies to the gene therapy vector. Clinical trial participants will be evaluated in AFFINE over the course of five years, and up to a total of 15 years as part of a long-term follow-up trial.

Pfizer reported that analyses of the full Phase 3 dataset from the AFFINE trial are ongoing and additional data will be presented at upcoming medical meetings. Giroctocogene fitelparvovec has been granted Fast Track and Regenerative Medicine Advanced Therapy designations from the U.S. Food and Drug Administration (FDA), as well as Orphan Drug designations in the U.S. and the European Union. Pfizer reported that it will discuss these data with regulatory authorities in the coming months. Pfizer recently received FDA approval for BEQVEZ™ (fidanocogene elaparvovec), its hemophilia B gene therapy for eligible patients.

About the AFFINE Trial

The Phase 3 AFFINE (NCT04370054) trial is an open-label, multicenter, single-arm trial to evaluate the efficacy and safety of a single infusion of giroctocogene fitelparvovec in adult male participants (n=75 dosed participants) with moderately severe to severe hemophilia A. Trial participants included in the assessments of the key endpoints of the primary efficacy analysis (n=50) completed a minimum six months of routine FVIII replacement prophylaxis therapy during the lead-in study (NCT03587116) providing data to compare with post giroctocogene fitelparvovec treatment.

The primary endpoint measures the total ABR (spontaneous and traumatic bleedings, treated and untreated) from Week 12 through at least 15 months

following treatment with giroctocogene fitelparvovec compared to total ABR on prior FVIII prophylaxis replacement therapy. For more information, visit clinicaltrials.gov.

Giroctocogene fitelparvovec is being developed as part of a collaboration agreement for the global development and commercialization of gene therapies for hemophilia A between Sangamo Therapeutics and Pfizer. In late 2019, Sangamo transferred the manufacturing technology and the Investigational New Drug application to Pfizer. Under the agreement, Pfizer assumed responsibility for pivotal studies, any regulatory activities, and potential global commercialization of giroctocogene fitelparvovec.

About Hemophilia A

Hemophilia is an inherited, rare bleeding disorder that causes people to bleed for longer than normal due to a deficiency of a protein required for normal blood clotting, known as clotting Factor VIII (FVIII) in hemophilia A. The severity of hemophilia is determined by the amount of the factor in the blood. The lower the amount of the factor, the more likely it is that bleeding will occur, which can lead to serious health problems.[v]

Hemophilia A occurs in approximately 25 in every 100,000 male births worldwide.[vi] Approximately 55-75% of males with hemophilia A have a moderate to severe form of the disease.[vii] For people who live with hemophilia A, there is an increased risk of spontaneous bleeding as well as bleeding following injuries or surgery.[v] It is a lifelong disease that requires constant monitoring and therapy.[viii]

About Sangamo Therapeutics

Sangamo Therapeutics is a genomic medicine company dedicated to translating ground-breaking science into medicines that transform the lives of patients and families afflicted with serious neurological diseases who do not have adequate or any treatment options. Sangamo believes that its zinc finger epigenetic regulators are ideally suited to potentially address devastating neurological disorders and that its capsid discovery platform can potentially expand delivery beyond currently available intrathecal delivery capsids, including in the central nervous system. Sangamo's pipeline also includes multiple partnered programs and programs with opportunities for partnership and investment. To learn more, visit www.sangamo.com and connect with us on LinkedIn and Twitter/X.

Forward-Looking Statements

This release contains forward-looking statements regarding Sangamo's current expectations. These forward-looking statements include, without limitation, statements regarding, the potential of giroctocogene fitelparvovec to provide superior bleed protection compared with routine FVIII replacement therapy, that a single infusion of giroctocogene fitelparvovec may allow patients to produce FVIII themselves for an extended period of time, Pfizer's continued advancements of the giroctocogene fitelparvovec program, the potential for Pfizer to complete clinical development, regulatory interactions, manufacturing and global commercialization of any resulting products, the potential for Sangamo to receive development and commercial milestone payments and royalties, 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 in these forward-looking statements. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties related to: the global business environment, healthcare systems and the business and operations of Sangamo and Pfizer,; the research and development process, including the results of preclinical studies and clinical trials; the 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 and its partners; the potential for Pfizer to breach or terminate its collaboration agreement with Sangamo; the potential for Sangamo to fail to realize its expected benefits from the Pfizer collaboration; and Sangamo's need for substantial additional funding to operate as a going concern. There can be no assurance that Sangamo will earn any milestone or royalty payments under the Pfizer agreement or obtain regulatory approvals for product candidates arising from this agreement. Actual results may also differ from those projected in forward-looking statements due to risks and uncertainties that exist in Sangamo's and Pfizer's operations and businesses. These risks and uncertainties are described more fully in Sangamo's Securities and Exchange Commission, or SEC, filings and reports, including in its Annual Report on Form 10-K for the year ended December 31, 2023, as supplemented by its Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, each filed with the SEC, and future filings and reports that Sangamo makes from time to time with the SEC. Forward-looking statements contained in this release are made as of July 24, 2024, and Sangamo undertakes no duty to update such information except as required under applicable law.

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[viii] Brod M, Bushnell DM, Neergaard JS, et al. Understanding treatment burden in hemophilia: development and validation of the Hemophilia Treatment Experience Measure (Hemo-TEM). J Patient Rep Outcomes. 2023;7(1):17.

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