# Pfizer Announces Positive Topline Results From Phase 3 Study of Hemophilia A Gene Therapy Candidate

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

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced positive topline results from the Phase 3 AFFINE study (NCT04370054) evaluating giroctocogene fitelparvovec, an investigational gene therapy for the treatment of adults with moderately severe to severe hemophilia A.

The AFFINE study 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 study, among all dosed participants, one participant (1.3%) returned to prophylaxis post-infusion.

In the AFFINE study, giroctocogene fitelparvovec was generally well tolerated. Transient 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, providing bleed protection and reducing the need for routine prophylaxis with intravenous (IV) infusions or injections.1,2,3,4

“We are very pleased with these positive results from the Phase 3 AFFINE study demonstrating the safety and efficacy of our one-time gene therapy candidate for people with hemophilia A,” said James Rusnak, M.D., Ph.D., Senior Vice President, Chief Development Officer, Internal Medicine and Infectious Diseases, Research and Development, Pfizer. “We look forward to advancing this latest innovation to help address the medical and treatment burden associated with frequent and time-consuming IV infusions or injections, building on Pfizer’s more than 40-year effort to advance hemophilia treatment.”

In this Phase 3 study, eligible study participants were initially enrolled in a lead-in study (NCT03587116) and upon successful completion, were enrolled into the AFFINE study where they received a one-time 3e13 vg/kg dose of giroctocogene fitelparvovec by IV infusion. Participants in the AFFINE study were screened with a validated assay designed to identify individuals who test negative for neutralizing antibodies to the gene therapy vector. Clinical study 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 study.

Analyses of the full Phase 3 dataset from the AFFINE study 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 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. BEQVEZ is also approved in Canada and is awaiting a decision from the European Commission following a positive opinion from the EMA's Committee for Medicinal Products for Human Use in May 2024. Additionally, regulatory submissions for marstacimab are currently under review by the FDA and the EMA. Marstacimab is a potential novel subcutaneous therapy being studied for the treatment of people with hemophilia A and B with and without inhibitors. Pfizer announced the acceptance of the regulatory filings for the without inhibitors cohort in December 2023.

**About the AFFINE Study**

The Phase 3 AFFINE (NCT04370054) study is an open-label, multicenter, single-arm study 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. Study 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 annualized bleeding rate (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 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.5

Hemophilia A occurs in approximately 25 in every 100,000 male births worldwide.6 Approximately 55-75% of males with hemophilia A have a moderate to severe form of the disease.7 For people who live with hemophilia A, there is an increased risk of spontaneous bleeding as well as bleeding following injuries or surgery.5 It is a lifelong disease that requires constant monitoring and therapy.8

**About Pfizer: Breakthroughs that Change Patients' Lives**

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For 175 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on X at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

***Disclosure Notice***

*The information contained in this release is as of July 24, 2024. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.*

*This release contains forward-looking information about giroctocogene fitelparvovec, an investigational gene therapy for hemophilia A, including its potential benefits and topline results from a Phase 3 study, and Pfizer's hemophilia portfolio, that involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data, including results from the AFFINE study and the long-term follow-up study; 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 our clinical studies; whether and when drug applications may be filed in any jurisdictions for any potential indication for giroctocogene fitelparvovec or any other hemophilia product candidates; whether and when any such applications that may be pending or filed may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether giroctocogene fitelparvovec or any such other product candidates will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of giroctocogene fitelparvovec or any such other product candidates; uncertainties regarding the commercial success of Pfizer's hemophilia products; uncertainties regarding the impact of COVID-19 on our business, operations and financial results; and competitive developments.*

*A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.*

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Media Contact: +1 (212) 733-1226 PfizerMediaRelations@pfizer.com

Investor Contact: +1 (212) 733-4848 IR@pfizer.com

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