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Marstacimab Phase 3 Data Presented at ASH 2023 Demonstrate Significant Bleed Reduction in Hemophilia A and B

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- *Marstacimab reduced annualized bleeding rate by 35% and 92% compared to routine prophylaxis and on-demand treatment in patients with hemophilia A and B without inhibitors, respectively*
- *Consistent reduction in bleeding rates observed after an additional 16 months of follow-up in the trial's long-term extension observational study*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today presented results from the pivotal Phase 3 BASIS clinical trial (NCT03938792) evaluating marstacimab for the treatment of people with severe hemophilia A and moderately severe to severe hemophilia B without inhibitors to Factor VIII (FVIII) or Factor IX (FIX). The results from the BASIS trial demonstrated a statistically significant and clinically meaningful effect on annualized bleeding rate (ABR). The findings were presented today at the 65th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego.

"For more than five decades, the most common treatment for hemophilia A and B has been intravenous infusions that are often administered multiples times per week,"[1] said James Rusnak, M.D., Ph.D., Senior Vice President, Chief Development Officer, Internal Medicine and Infectious Diseases, Research and Development, Pfizer. "Based on these results and if approved, we believe marstacimab could offer a subcutaneous option with a compelling combination of efficacy and safety that may significantly reduce the risk of bleeding. We look forward to potentially bringing this treatment option to people living with hemophilia A and B without inhibitors."

In the BASIS trial, 116 people living with hemophilia were treated with marstacimab during a 12-month active treatment period (ATP) versus a routine prophylaxis (RP) and on-demand (OD) intravenous regimen with FVIII or FIX, administered as part of usual care in a six-month observational period. Marstacimab, a novel, investigational anti-tissue factor pathway inhibitor (anti-TFPI), was administered weekly with flat (not weight-based) dosing as a subcutaneous 300 mg loading dose followed by 150 mg once weekly. The study found:

- Compared to RP, treatment with marstacimab resulted in a 35.2% mean reduction (95% CI: 5.6-55.6; p=0.0376) in ABR over 12 months (mean of 7.85 [5.09-10.61] to 5.08 [3.40-6.77]).
- Marstacimab significantly reduced ABR by 91.6% (95% CI: 88.1-94.1; p<0.0001) compared to OD over 12 months (mean of 38.00 [31.03-46.54] to 3.18 [2.09-4.85]).
- The mean ABR reductions observed with marstacimab were consistent across hemophilia A and B and age groups for OD and were generally consistent across hemophilia A and B and age groups for RP, with all point estimates for a difference <2.5 (non-inferiority margin for the ABR of treated bleeds).

- Following 12 months in the ATP, patients had the option to continue receiving marstacimab in the long-term extension (LTE) study. In the LTE, a consistent reduction in ABR compared to OD (mean ABR of 3.86 [2.02-7.37]) and further numerical reduction compared to RP (mean ABR of 2.27 [1.40-3.67]) were observed after up to an additional 16 months of follow-up (n=87).
- In the OD group, superiority ($p<0.0001$) of marstacimab was demonstrated across all bleeding-related secondary endpoints - spontaneous bleeds, joint bleeds, target joint bleeds, and total bleeds. In the RP group, marstacimab demonstrated non-inferiority to these secondary efficacy endpoints.
- Health-related quality of life parameters showed non-significant improvements vs OD therapy and non-inferiority versus RP therapy.

The safety profile for marstacimab was consistent with Phase 1/2 results and treatment was generally well-tolerated. No deaths were reported and there have been no thromboembolic events or events of consumptive coagulopathy recorded in hemophilia patients in clinical trials investigating marstacimab. The most commonly reported adverse events of special interest among patients treated with marstacimab in BASIS and the LTE (?5% of patients) were COVID-19, hemorrhage, hepatic disorder, hypersensitivity, hypertension and injection site reaction. One treatment-related serious adverse event (SAE) was observed (peripheral swelling), and one patient discontinued from the trial due to a non-treatment-related SAE.

“Recognizing the uncertainty that living with hemophilia can present for patients, the results from the BASIS trial are particularly encouraging as reductions in ABR were seen in the 12-month treatment period and then retained in long-term follow-up,” said Davide Matino, M.D., M.Sc., Assistant Professor of Medicine, McMaster University. “Based on these results, marstacimab has shown the potential to address the diverse needs of appropriate patients with hemophilia A or B without inhibitors with weekly subcutaneous administration in a flat dose that is not weight-based, and with low monitoring requirements.”

Pfizer currently has three Phase 3 programs investigating novel treatment options for people living with hemophilia. In addition to the BASIS study, fidanacogene elaparvovec and giroctocogene fitelparvovec are investigational gene therapy treatments being studied for the treatment of adults living with hemophilia B and hemophilia A, respectively. Updated data from both gene therapy programs, including an oral presentation of four-year results from Pfizer’s Phase 1/2 study of giroctocogene fitelparvovec in adults living with severe hemophilia A, will be presented at the ASH meeting.

About the BASIS study

BASIS is a global Phase 3, open-label, multicenter study evaluating ABR through 12 months of treatment with marstacimab, an investigational, novel subcutaneous therapy option, in approximately 145 adolescent and adult participants ages 12 to <75 years with severe hemophilia A (defined as FVIII <1%) or moderately severe to severe hemophilia B (defined as FIX activity ?2%) with or without inhibitors. Approximately 15% of participants are adolescents (ages 12 to <18 years old). This study is comparing treatment with a run-in period for patients prescribed factor replacement therapy or bypass therapy during a six-month observational period with a 12-month ATP, during which participants receive prophylaxis (a 300 mg subcutaneous loading dose of marstacimab, followed by 150 mg subcutaneously once weekly) with potential for dose escalation to 300 mg once weekly.

The inhibitor cohort of the BASIS trial has completed enrollment and is expected to read out as early as late 2024. Pfizer is also conducting BASIS KIDS, an open-label study investigating the safety and efficacy of marstacimab in children 1 to <18 years of age with severe hemophilia A or moderately severe to severe hemophilia B with or without inhibitors. The study will compare 12 months of historical standard treatment to marstacimab prophylaxis.

About Marstacimab

Marstacimab is a human monoclonal immunoglobulin G isotype, subclass 1 (IgG1) that targets the Kunitz 2 domain of tissue factor pathway inhibitor (TFPI), a natural anticoagulation protein that functions to prevent the formation of blood clots. Marstacimab is in development as a prophylactic treatment to prevent or reduce the frequency of bleeding episodes in individuals with severe hemophilia A or moderately severe to severe hemophilia B with or without inhibitors.

About Hemophilia

Hemophilia is a family of rare genetic blood diseases caused by a clotting factor deficiency (FVIII in hemophilia A, FIX in hemophilia B), which prevents normal blood clotting. Hemophilia is diagnosed in early childhood and impacts more than 400,000 people worldwide.[2] The inability of the blood to clot properly can increase the risk of painful bleeding inside the joints, which can cause joint scarring and damage. People living with hemophilia can suffer permanent joint damage following repeated bleeding episodes.[1,2]

For decades, the most common treatment approach for hemophilia A and B has been factor replacement therapy, which replaces the missing clotting factors. Factor replacement therapies increase the amount of clotting factor in the body to levels that improve clotting, resulting in less bleeding.[3,4] Approximately 25%-30% of people with hemophilia A and 3%-5% of people with hemophilia B are unable to continue taking factor replacement therapies because they develop inhibitors to FVIII and FIX.[5,6]

In a survey of people in the U.S. receiving prophylaxis for hemophilia A or B, nearly one-third of those that receive treatment and have high compliance — defined as taking 75% or more of their prescribed infusions — stated that the time-consuming nature of prophylaxis was the most significant challenge of the regimen.[7,8] Nearly 60% of those that took the less than the prescribed number of infusions reported that the time commitment was the primary reason for missing infusions.

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 more than 170 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 Twitter 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 December 9, 2023. 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 marstacimab, an investigational anti-tissue factor pathway inhibitor, and Pfizer's hemophilia programs for fidanacogene elaparvovec and giroctocogene fitelparvovec, including their potential benefits, that involves 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; whether or when the inhibitor cohort of the BASIS trial will be successful; 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 any applications may be filed with regulatory authorities in particular jurisdictions for marstacimab, fidanacogene elaparvovec or giroctocogene fitelparvovec; whether and when any such applications that may be pending or filed for marstacimab, fidanacogene elaparvovec or giroctocogene fitelparvovec 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 marstacimab, fidanacogene elaparvovec and giroctocogene fitelparvovec 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 marstacimab, fidanacogene elaparvovec and giroctocogene fitelparvovec; 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, 2022 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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