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European Commission Approves Pfizer's HYMPAVZI™ (marstacimab) for the Treatment of Adults and Adolescents with Severe Hemophilia A or B Without Inhibitors

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- *In the EU, HYMPAVZI is the first once-weekly subcutaneous treatment approved for eligible people living with severe hemophilia B and the first to be administered via a pre-filled pen or syringe for people living with severe hemophilia A or B*
- *HYMPAVZI's approval is based on Phase 3 study results demonstrating non-inferiority and superiority compared to routine prophylaxis in eligible patients with hemophilia A or B without inhibitors*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) announced today that the European Commission (EC) has granted marketing authorization for HYMPAVZI™ (marstacimab) for the routine prophylaxis of bleeding episodes in patients 12 years of age and older weighing at least 35 kg with severe hemophilia A (congenital factor VIII [FVIII] deficiency, FVIII <1%) without FVIII inhibitors or severe hemophilia B (congenital factor IX [FIX] deficiency, FIX <1%) without FIX inhibitors.

HYMPAVZI is the first and only anti-tissue factor pathway inhibitor (anti-TFPI) approved in the European Union (EU) for the treatment of hemophilia A or B and the first hemophilia medicine approved in the EU to be administered via a pre-filled, auto-injector pen. HYMPAVZI offers a subcutaneous treatment option with a once-weekly dosing schedule and minimal preparation required for each individual administration.

"There is a considerable treatment burden associated with the standard-of-care options for hemophilia A and B, including time-consuming preparation and administration of infusions and injections potentially causing missed doses and an increased risk of bleeding," said Dr. Laurent Frenzel, Head of the Hemophilia Treatment and Research Center at the Necker-Enfants malades Hospital (Paris Cité). "HYMPAVZI is a significant advancement for eligible patients in that it may provide bleed prevention as well as once-weekly subcutaneous administration via a pre-filled pen."

Hemophilia is a family of rare genetic blood diseases caused by a clotting factor deficiency (FVIII in hemophilia A, FIX in hemophilia B), impacting more than 800,000 people globally. [1] Diagnosed in early childhood, hemophilia inhibits the blood's ability to clot properly, increasing the risk of repeated bleeding inside the joints, which can lead to permanent joint damage. [2,3] Despite significant progress in hemophilia treatment in recent years, many people living with the disease continue to experience bleeding episodes and manage their condition with frequent intravenous infusions that may need to be administered multiple times a week. [4]

"HYMPAVZI offers a first-in-class treatment option for people living with hemophilia, a disease that often leads to recurring joint bleeds and can impact daily activities as simple as climbing stairs," said Alexandre de Germay, Chief International Commercial Officer and Executive Vice President, Pfizer. "This approval builds on Pfizer's

more than four-decade commitment to improve the standard of care in hemophilia, and we look forward to delivering this medicine that reduced bleeds as compared to factor prophylaxis and, importantly, requires limited preparation, meeting a key need for eligible patients."

The marketing authorization is based on results from the pivotal Phase 3 BASIS study (NCT03938792) that evaluated the efficacy and safety of marstacimab in adults and adolescents 12 years and older with severe hemophilia A or B without inhibitors. In the study, HYMPAVZI significantly reduced the annualized bleeding rate (ABR) for treated bleeds by 35% (ABR of 5.08 vs. 7.85, p-value 0.0376) during the 12-month active treatment period, demonstrating non-inferiority and superiority compared to routine prophylaxis (RP) with FVIII or FIX administered as part of usual care. The safety profile for HYMPAVZI was consistent with Phase 1/2 results, and the most commonly reported adverse events in the study were injection site reactions, headache, pruritus, and hypertension.

This marketing authorization is valid in all 27 EU member states, as well as in Iceland, Liechtenstein, and Norway. The EC approval follows the regulatory approval of HYMPAVZI in the United States in October.

Pfizer's more than 40-year effort to advance hemophilia treatment began with the introduction of recombinant treatments and has extended to the introduction of newer, advanced treatment modalities. In addition to recent regulatory approvals for HYMPAVZI, Pfizer reported positive results from a Phase 3 program investigating a gene therapy candidate in hemophilia A (giroctocogene fitelparvovec) in July and received regulatory approvals in Europe and the U.S. for its hemophilia B gene therapy BEQVEZ™ (fidanacogene elaparvovec).

About HYMPAVZI (marstacimab)
Discovered by Pfizer scientists, HYMPAVZI is a rebalancing agent 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 and restore hemostasis.

HYMPAVZI is approved by the EC for the routine prophylaxis of bleeding episodes in patients aged 12 years and older weighing at least 35 kg with severe hemophilia A (congenital factor VIII [FVIII] deficiency, FVIII <1%) without FVIII inhibitors or severe hemophilia B (congenital factor IX [FIX] deficiency, FIX <1%) without FIX inhibitors.

About the BASIS study
The pivotal BASIS study is a global Phase 3, open-label, multicenter study to evaluate the efficacy and safety of HYMPAVZI in 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.

The marketing authorization is based on data from 116 people living with severe hemophilia without inhibitors who were treated with marstacimab during a 12-month active treatment period (ATP) versus a RP regimen with FVIII or FIX, administered as part of usual care in a 6-month observational period. During the ATP, participants received 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 in patients weighing ? 50 kg when control of bleeding events is judged to be inadequate by the healthcare professional.

HYMPAVZI reduced the ABR for treated bleeds by 35% after a 12-month ATP compared to RP treatment in patients with hemophilia A or B without inhibitors. In an interim analysis of the long-term extension study, a consistent reduction in mean ABR for treated bleeds of 2.79 (95% CI 1.90-4.09) was observed in up to an additional 16 months of follow-up (n=87). HYMPAVZI demonstrated non-inferiority across all bleeding-related secondary endpoints: spontaneous bleeds, joint bleeds, target joint bleeds, and total bleeds.

The safety profile for HYMPAVZI was consistent with Phase 1/2 results and treatment was generally well-tolerated. The most commonly reported adverse events were injection site reactions, headache, pruritus, and hypertension.

The inhibitor cohort of the BASIS study is ongoing, with results expected in the third quarter of 2025. 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.

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 800,000 people worldwide. [1] 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. [2,3]

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. [5,6]

The burden of intravenous infusions is believed to be a barrier to treatment adherence for some people living with hemophilia due in part to inconvenience, time constraints, and poor venous access. [7,8,9,10] In a patient/physician/specialist nurse survey across six European countries, lack of time for treatment and convenience were among the leading reasons for not using the prescribed amount of clotting factor or skipping treatment administration. [7]

HYMPAVZI (marstacimab) U.S. Important Safety Information

Important: Before you start using HYMPAVZI, it is very important to talk to your healthcare provider about using factor VIII and factor IX products (products that help blood clot but work in a different way than HYMPAVZI). You may need to use factor VIII or factor IX medicines to treat episodes of breakthrough bleeding during treatment with HYMPAVZI. Carefully follow your healthcare provider's instructions regarding when to use factor VIII or factor IX medicines and the prescribed dose during your treatment with HYMPAVZI.

Before using HYMPAVZI, tell your healthcare provider about all of your medical conditions, including if you:

- have a planned surgery. Your healthcare provider may stop treatment with HYMPAVZI before your surgery. Talk to your healthcare provider about when to stop using HYMPAVZI and when to start it again if you have a planned surgery.
- have a severe short-term (acute) illness such as an infection or injury.
- are pregnant or plan to become pregnant. HYMPAVZI may harm your unborn baby.

Females who are able to become pregnant:
- Your healthcare provider will do a pregnancy test before you start your treatment with HYMPAVZI.
- You should use effective birth control (contraception) during treatment with HYMPAVZI and for at least 2 months after the last dose of HYMPAVZI.
- Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with HYMPAVZI.
- are breastfeeding or plan to breastfeed. It is not known if HYMPAVZI passes into your breast milk.

Tell your healthcare provider about all the medicines you take , including prescription medicines, over?the? counter medicines, vitamins, and herbal supplements.

What are the possible side effects of HYMPAVZI?

HYMPAVZI may cause serious side effects, including:

- **blood clots (thromboembolic events).** HYMPAVZI may increase the risk for your blood to clot. Blood clots may form in blood vessels in your arm, leg, lung, or head and can be life?threatening. Get medical help right away if you develop any of these signs or symptoms of blood clots:
  - swelling or pain in arms or legs
  - redness or discoloration in your arms or legs
  - shortness of breath
  - pain in chest or upper back
  - fast heart rate
  - cough up blood
  - feel faint
  - headache
  - numbness in your face
  - eye pain or swelling
  - trouble seeing
- **allergic reactions.** Allergic reactions, including rash and itching have happened in people treated with HYMPAVZI. Stop using HYMPAVZI and get medical help right away if you develop any of the following symptoms of a severe allergic reaction:
  - swelling of your face, lips, mouth, or tongue
  - trouble breathing
  - wheezing
  - dizziness or fainting
  - fast heartbeat or pounding in your chest
  - sweating

The most common side effects of HYMPAVZI are injection site reactions (itching, swelling, hardening, redness, bruising, pain at the injection site), headache, and itching.

These are not all the possible side effects of HYMPAVZI. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

The full Prescribing Information can be found here.

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

www.facebook.com/Pfizer/.

Category: Prescription Medicines

Disclosure notice
The information contained in this release is as of November 20, 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 HYMPAVZI™ (marstacimab), an anti-tissue factor pathway inhibitor, and Pfizer's other hemophilia approved and investigational products, 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, uncertainties regarding the commercial success of HYMPAVZI and Pfizer's other hemophilia products; 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 HYMPAVZI or any other products or product candidates; whether and when any such applications that may be pending or filed for HYMPAVZI or any other products or product candidates 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 HYMPAVZI or any such other products or 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 HYMPAVZI or any such other products or product candidates; 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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