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European Commission Approves Pfizer's DURVEQTIX® (fidanacogene elaparvovec), a One-Time Gene Therapy for Adults with Hemophilia B

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- *A one-time dose of DURVEQTIX has reduced bleeds post-treatment compared to standard of care with a median annualized bleed rate (ABR) of zero bleeds (range 0 to 9.9) after up to four years of follow-up, providing sustained bleed protection and potentially avoiding years of treatment burden with prophylaxis for many patients.*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced that the European Commission (EC) has granted conditional marketing authorization for DURVEQTIX® (fidanacogene elaparvovec), a gene therapy for the treatment of severe and moderately severe hemophilia B (congenital factor IX deficiency) in adult patients without a history of factor IX inhibitors and without detectable antibodies to variant AAV serotype Rh74. DURVEQTIX is designed to enable people living with hemophilia B to produce factor IX (FIX) themselves via a one-time dose, rather than multiple intravenous FIX infusions weekly or biweekly with the current standard of care.[1,2,3]

"There is a substantial medical and treatment burden for people with hemophilia B that receive standard of care today, with frequent infusions and many remaining at risk of breakthrough bleeds that can lead to pain and restricted mobility," said Alexandre de Germay, Chief International Commercial Officer and Executive Vice President, Pfizer. "DURVEQTIX has shown the potential to offer long-term bleed protection in a one-time dose, reducing or eliminating bleeds for the appropriate patients with hemophilia B. These outcomes and their impact could become potentially transformative for hemophilia B care in the European Union."

Hemophilia B is a rare genetic bleeding disorder that prevents normal blood clotting because of a deficiency in FIX that causes those with the disease to bleed more frequently and longer than others.[1,4] The standard of care for hemophilia B treatment is prophylactic infusions of FIX replacement therapy that temporarily replace or supplement low levels of blood-clotting factor.[1,2] Despite prophylaxis and regular intravenous infusions, many people living with moderate to severe hemophilia B are at risk of spontaneous bleeding episodes.[5,6,7] The current standard of care also places strain on healthcare systems' budgets and resource utilization.[6,8,9,10] According to the World Federation of Hemophilia, more than 42,000 people worldwide are living with hemophilia B.[11]

The conditional marketing authorization is based on results from the pivotal Phase 3 BENEGENE-2 study (NCT03861273) evaluating the efficacy and safety of DURVEQTIX in adult male participants (age 18–62) with moderately severe to severe hemophilia B. BENEGENE-2 met its primary efficacy endpoint of non-inferiority and demonstrated a statistically significant decrease in annualized bleeding rate (ABR) for total bleeds (treated and untreated) post-DURVEQTIX infusion versus prophylaxis regimen with FIX, administered as part of usual

care. Efficacy, based on ABR, also remained stable during year two to year four after treatment. DURVEQTIX was generally well-tolerated, with a safety profile consistent with Phase 1/2 results.

This conditional marketing authorization is valid in all 27 European Union (EU) member states, as well as in Iceland, Liechtenstein, and Norway. The EC approval follows recent regulatory approvals by the U.S. Food and Drug Administration (FDA) and Health Canada, where it is marketed as BEQVEZ™.

This milestone builds on Pfizer's more than 40-year commitment to delivering breakthrough solutions to improve the lives of people living with hemophilia. In addition to DURVEQTIX, Pfizer recently reported positive results from a Phase 3 program investigating a gene therapy in hemophilia A (giroctocogene fitelparvovec). Additionally, a Phase 3 trial is investigating marstacimab, a novel, investigational, anti-tissue factor pathway inhibitor for the treatment of people with hemophilia A and B with and without inhibitors. A Biologics License Application and European Marketing Authorization Application for marstacimab for eligible patients without inhibitors are currently under review with the FDA and European Medicines Agency (EMA), respectively.

About DURVEQTIX® (fidanacogene elaparvovec)

DURVEQTIX is a gene therapy that contains a bio-engineered adeno-associated virus (AAV) capsid and a high-activity variant of human coagulation FIX gene. For people living with hemophilia B, the goal of this gene therapy is to enable them to produce FIX themselves via this one-time treatment rather than needing regular intravenous infusions of FIX, as is the current standard of care.[1,2,3]

In December 2014, Pfizer licensed DURVEQTIX from Spark® Therapeutics. Under the agreement, Pfizer assumed responsibility for pivotal studies, any regulatory activities, and potential global commercialization of this gene therapy.

About BENEGENE-2

The BENEGENE-2 study is a Phase 3, open-label, single-arm study to evaluate the efficacy and safety of DURVEQTIX in adult male participants (age 18–65) with moderately severe to severe hemophilia B (defined as FIX circulating activity of 2% or less). The main objective of the study is to evaluate the ABR for participants treated with gene therapy versus FIX prophylaxis replacement regimen, administered as part of usual care.

The study enrolled and dosed 45 participants. Eligible study participants have completed a minimum six months of routine FIX prophylaxis therapy during the lead-in study (NCT03587116) and received one intravenous dose of DURVEQTIX at a dose of 5×10^{11} vg/kg. Participants in the BENEGENE-2 study were screened with a validated assay designed to identify individuals who test negative for neutralizing antibodies to the gene therapy vector.

The European Marketing Authorization Application was based on the primary analysis of BENEGENE-2, which was conducted when 41 participants had reached 15 months of follow-up, with a subsequent data cut provided during review, which monitored some patients up to four years. Clinical trial participants will be followed for up to a total of 15 years, including six years in the BENEGENE-2 study and up to an additional nine years as part of a separate Phase 3 study (NCT05568719) to learn about the long-term safety and efficacy of DURVEQTIX.

Results show that DURVEQTIX significantly reduced the frequency of bleeding compared with usual care. At the 15-month follow-up period, DURVEQTIX patients had a model-based ABR (total bleeds) of 1.44 compared to 4.50 during the lead-in period ($p=0.0084$), resulting in a 68% reduction. DURVEQTIX eliminated bleeds in 62.2% of patients.

DURVEQTIX was generally well-tolerated, with a safety profile consistent with Phase 1/2 results. The most common adverse reaction (incidence ?5%) reported in Phase 3 and 1/2 clinical studies was an increase in liver enzymes (transaminases), which was treated with corticosteroids. No serious adverse events related to treatment or associated with infusion reactions, thrombotic events, or FIX inhibitors were reported.

BEQVEZ (fidanacogene elaparvovec-dzkt) U.S. Important Safety Information

What is BEQVEZ?
BEQVEZ is a one-time gene therapy used for the treatment of adults with moderate to severe hemophilia B who are receiving routine prophylaxis, have a current life-threatening bleed or a history of life-threatening bleeds, or have repeated serious spontaneous bleeds.

Before treatment with BEQVEZ, your healthcare professional will conduct a blood test to check for antibodies to the AAVRh74var virus. The results of this testing will help determine if you may receive BEQVEZ.

Before receiving BEQVEZ, tell your healthcare professional about all your medical conditions, including if you:

- Have kidney or liver problems, including hepatitis
- Have factor IX inhibitors or a history of factor IX inhibitors
- Have an active infection

BEQVEZ may cause serious side effects, including:
Increased Liver Enzymes. Most patients treated with BEQVEZ developed elevated liver enzyme levels and most did not experience any symptoms.

Your healthcare professional will **monitor liver enzymes and factor IX activity levels** before administration of BEQVEZ and frequently following the administration to detect and identify possible elevations in liver enzymes and to monitor your response to BEQVEZ. Your doctor may prescribe a corticosteroid for the treatment of elevated liver enzymes.

Avoid or limit alcohol consumption during the first year following BEQVEZ infusion, as alcohol may reduce the effect of BEQVEZ and may increase liver enzyme levels.

Infusion reactions, including hypersensitivity and severe allergic reactions (anaphylaxis) may occur. Alert your healthcare professional right away if you get any symptoms of hypersensitivity, which may include but are not limited to low blood pressure, fever, heart palpitation, nausea, vomiting, chills, or headache.

BEQVEZ can insert itself into the DNA of cells in the human body. The effect that insertion may have on those cells is unknown but **may contribute to a theoretical risk of cancer**. There have been no reported cases of cancer caused by treatment with BEQVEZ.

The most common side effect of BEQVEZ is increased liver enzymes. These are not all the possible side effects of BEQVEZ. For more information, ask your healthcare professional.

Talk to your healthcare professional before receiving any vaccinations if you are taking a corticosteroid.

Talk to your doctor about any medications you plan to take including over the counter medications, herbal supplements, and vitamins as certain substances can affect the liver and may reduce the effectiveness of BEQVEZ.

Your healthcare professional will test your factor IX activity levels and for factor IX inhibitors.

After receiving BEQVEZ, your doctor will discuss whether and when you are able to stop prophylaxis, if you need to resume prophylaxis, and actions you may need to take for surgeries, procedures, injuries, and bleeding events.

Do not donate blood, organs, tissues, or cells for transplantation following administration of BEQVEZ.

BEQVEZ is not intended for administration to women. **Males should not donate sperm and should use a male condom or not have sexual intercourse** for up to 6 months after receiving BEQVEZ.

Patients and caregivers should ensure proper handling of any materials that have come into contact with the patient's urine, feces, saliva, mucus, or semen in the first 6 months after BEQVEZ infusion.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 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/.

Disclosure notice

The information contained in this release is as of July 25, 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 DURVEQTIX , a gene therapy, including its potential benefits and an approval in the EU of DURVEQTIX for the treatment of adult patients with hemophilia B, and Pfizer's hemophilia portfolio , 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 DURVEQTIX and Pfizer's hemophilia portfolio ; 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 BENEGENE-2 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 particular jurisdictions for DURVEQTIX or

any other hemophilia product candidates ; whether and when any applications that may be pending or filed for DURVEQTIX or any other hemophilia 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 DURVEQTIX or any other hemophilia 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 DURVEQTIX or any other hemophilia product candidates ; uncertainties regarding the impact of COVID-19 on Pfizer's 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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