



# U.S. FDA Approves Pfizer's BEQVEZ™ (fidanacogene elaparvovec-dzkt), a One-Time Gene Therapy for Adults with Hemophilia B

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*A one-time dose of BEQVEZ has reduced bleeds post-treatment compared to standard of care with a median of zero bleeds (range 0 to 19) after up to three 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) announced today that the U.S. Food and Drug Administration (FDA) has approved BEQVEZ™ (fidanacogene elaparvovec-dzkt) for the treatment of adults with moderate to severe hemophilia B who currently use factor IX (FIX) prophylaxis therapy, or have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes, and do not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test. BEQVEZ is a one-time treatment that is designed to enable people living with hemophilia B to produce FIX themselves rather than the current standard of care, which requires regular intravenous infusions of FIX that are often administered multiple times a week or multiple times a month.<sup>1,2</sup>

“Many people with hemophilia B struggle with the commitment and lifestyle disruption of regular FIX infusions, as well as spontaneous bleeding episodes, which can lead to painful joint damage and mobility issues,” said Adam Cuker, M.D., M.S., Director, Penn Comprehensive and Hemophilia Thrombosis Program. “A one-time treatment with BEQVEZ has the potential to be transformative for appropriate patients by reducing both

the medical and treatment burden over the long term.”

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.<sup>3,4</sup> 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.<sup>2,4</sup> Despite prophylaxis and regular intravenous infusions, many people living with moderate to severe hemophilia B are at risk of spontaneous bleeding episodes.<sup>5,6,7</sup> The current standard of care also places strain on healthcare systems’ budgets and resource utilization.<sup>6,8,9,10</sup> According to the World Federation of Hemophilia, more than 38,000 people worldwide are living with hemophilia B.<sup>11</sup>

“This milestone is a testament to Pfizer’s continued effort to advance the standard of care for people living with hemophilia, with the delivery of a medicine that has the potential to offer both long-term bleed protection and value to the healthcare system because of its one-time administration,” said Aamir Malik, Chief U.S. Commercial Officer and Executive Vice President, Pfizer. “We are leveraging our expertise that comes with more than 40 years of experience in the hemophilia space, and are proactively working with treatment centers, payers, and the hemophilia community to appropriately help ensure the healthcare system is prepared to readily deliver BEQVEZ to the patients who can benefit from it.”

With BEQVEZ now approved for use, Pfizer is launching an innovative warranty program based on durability of patient response to treatment. The goal of the warranty is to provide greater certainty to payers, maximize access for eligible patients who receive BEQVEZ, and offer financial protection by insuring against the risk of efficacy failure.

“For people living with hemophilia, disease management can interfere with many aspects of their lives. A one-time infusion of BEQVEZ may allow eligible patients more time for the things they love,” said Kim Phelan, Chief Operating Officer, The Coalition for Hemophilia B. “We are excited to have BEQVEZ as a promising treatment option for eligible people living with hemophilia B. We look forward to learning more and celebrating with the community and with Pfizer at our annual conference that is currently taking place.”

BEQVEZ is currently under review with the European Medicines Agency (EMA), and the treatment recently received regulatory approval in Canada. In addition to BEQVEZ, Pfizer currently has two other Phase 3 programs investigating gene therapy in populations where there is a high unmet need: hemophilia A (giiroctocogene fitelparvovec) and

Duchenne muscular dystrophy (fordadistrogene movaparvovec). 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 are currently under review with the FDA and EMA, respectively.

**About BEQVEZ (fidanacogene elaparvovec-dzkt)** BEQVEZ is an adeno-associated virus (AAV)-based gene therapy designed to introduce in the transduced cells a functional copy of the FIX gene encoding a high-activity FIX variant. For eligible patients 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 having to receive frequent infusions of FIX, as is the current standard of care.<sup>1,2,4</sup> It is currently approved in the U.S. for the treatment of adults with moderate to severe hemophilia B (congenital factor IX deficiency) who:

Currently use factor IX prophylaxis therapy, or  
Have current or historical life-threatening hemorrhage, or  
Have repeated, serious spontaneous bleeding episodes, and  
Do not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test.

For eligible patients who are prescribed BEQVEZ, Pfizer offers personalized patient support services including financial assistance resources and logistical support through the Pfizer Gene Together program. More information is available on [www.PfizerGeneTogether.com](http://www.PfizerGeneTogether.com).

In December 2014, Pfizer licensed BEQVEZ 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 FDA approval is based on the results from the pivotal BENEGENE-2 study, a Phase 3, open-label, single-arm study to evaluate the efficacy and safety of BEQVEZ 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 annualized bleeding rate (ABR) for participants treated with gene therapy versus FIX prophylaxis replacement regimen, administered as part of usual care.

The study enrolled 45 participants. Eligible study participants have completed a minimum of six months of routine FIX prophylaxis therapy during the lead-in study (NCT03587116) and received a single intravenous infusion of BEQVEZ at a dose of  $5 \times 10^{11}$  vg/kg of body weight. Clinical trial participants will be followed for up to a total of 15 years, including six

years in the BENEENE-2 study and an additional nine years as part of a separate Phase 3 study (NCT05568719) to learn about the long-term safety and efficacy of BEQVEZ.

BENEENE-2 met its primary endpoint of non-inferiority in the ABR of total bleeds post-BEQVEZ infusion versus prophylaxis regimen with FIX, administered as part of usual care. A mean ABR of 2.5 was observed among patients who received BEQVEZ in the efficacy evaluation period – defined as between week 12 and data cutoff (median 1.8 years of follow-up) – after receiving the one-time dose compared to a mean ABR of 4.5 during the lead-in pre-treatment period of at least six months (median 1.2 years of follow-up). Bleeds were eliminated in 60% of patients compared to 29% in the prophylaxis arm. A median ABR of zero (range of 0 to 19) was observed during the efficacy evaluation period compared to the prophylaxis arm in which a median ABR of 1.3 (range of 0 to 53.9) was observed.

BEQVEZ was generally well-tolerated in patients who received it. The most common adverse reaction (incidence  $\geq 5\%$ ) reported in Phase 3 and 1/2 clinical studies was an increase in transaminases. No deaths, serious adverse events related to treatment or associated with infusion reactions, thrombotic events, or FIX inhibitors were reported. Elevated transaminases were observed in 26 out of 60 patients treated at the recommended dose and 31 out of 60 patients received corticosteroids.

In addition to the Phase 3 trial, BEQVEZ patients have been followed up to six years in a Phase 1/2a study and its corresponding Phase 2a long-term follow-up study. Pfizer is continuing to monitor for long-term treatment durability and safety in its clinical program over the course of 15 years.

**About Hemophilia B** Hemophilia is a rare genetic bleeding disorder that prevents normal blood clotting because of a deficiency in one of several blood clotting factors and is predominately found in males.<sup>3,4</sup> People with hemophilia are at risk for excessive and recurrent spontaneous and/or post-traumatic bleeding, which can be life-threatening, particularly in those with severe hemophilia.<sup>3,4</sup> People with severe hemophilia often bleed spontaneously into their muscles or joints, or rarely into other critical closed spaces such as the intracranial space, where bleeding can be fatal.<sup>3,4</sup>

According to the World Federation of Hemophilia, more than 38,000 people worldwide are living with hemophilia B.<sup>11</sup> People with hemophilia B have a deficiency in clotting FIX, a specific protein in the blood. Hemophilia B is also called congenital FIX deficiency or Christmas disease. The current standard of care requires recurrent intravenous infusions of either plasma-derived or recombinant FIX to control and prevent bleeding

episodes.1,2,4

## **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 neutralizing 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](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

The full Prescribing Information can be found here. If it is not currently available via this link, it will be visible as soon as possible as we work to finalize the document. Please check back for the full information shortly.

**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](http://www.Pfizer.com). In addition, to learn more, please visit us on [www.Pfizer.com](http://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/](http://www.facebook.com/Pfizer/).

Category: Prescription Medicines

**Disclosure notice** *The information contained in this release is as of April 26, 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 BEQVEZ, a gene therapy, including its potential benefits and an approval in the U.S. of BEQVEZ for the treatment of adult patients with hemophilia B, and Pfizer's other investigational gene therapy and hemophilia candidates 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 BEQVEZ; 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; 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 BEQVEZ or any other product candidates; whether and when any applications that may be pending or filed for BEQVEZ or any other 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 BEQVEZ 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 BEQVEZ or any other 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](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).

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