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Pfizer’s ELREXFIO™ Receives U.S. FDA Accelerated Approval for Relapsed or Refractory Multiple Myeloma

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- *The approval of ELREXFIO (elranatamab-bcmm) is based on clinically meaningful response rates and duration of response from Phase 2 MagnetisMM-3 study*
- *ELREXFIO is the first off-the-shelf (ready-to-use) fixed-dose subcutaneous BCMA-directed agent in the U.S. with the option for every-other-week long-term dosing after 24 weeks of weekly treatment*
- *Pfizer continues to advance the MagnetisMM clinical program to expand ELREXFIO into earlier lines of treatment, both as monotherapy and in combination with standard or novel therapies*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE:PFE) today announced the U.S. Food and Drug Administration (FDA) has granted accelerated approval to ELREXFIO™ (elranatamab-bcmm) for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. Approval was based on the results of the single-arm Phase 2 MagnetisMM-3 trial, and continued approval for this indication is contingent upon verification of clinical benefit in a confirmatory trial(s). ELREXFIO is a subcutaneously delivered B-cell maturation antigen (BCMA)-CD3-directed bispecific antibody (BsAb) immunotherapy that binds to BCMA on myeloma cells and CD3 on T-cells, bringing them together and activating the T-cells to kill myeloma cells.

“ELREXFIO reflects our ongoing commitment to developing scientific breakthroughs that meaningfully improve outcomes for people with cancer. Discovered at Pfizer, we advanced this therapy from a first-in-patient trial to approval in less than five years, because we know that time is life for people living with multiple myeloma,” said Angela Hwang, Chief Commercial Officer and President of Global Biopharmaceuticals Business, Pfizer. “With significant responses in a patient population with highly refractory disease, we believe ELREXFIO is poised to potentially become the new standard of care for multiple myeloma, as we plan to build upon this indication with continued development across the expansive MagnetisMM program.”

The approval of ELREXFIO is based on data from response rates and duration of response. Data from cohort A (n=123) of the Phase 2 MagnetisMM-3 study (NCT04649359) showed meaningful responses among heavily pretreated RRMM patients who received ELREXFIO as their first BCMA-directed therapy. Among the patients in this study who received four or more lines of therapy prior to ELREXFIO (n=97), the overall response rate was 58%, with an estimated 82% maintaining the response for at least nine months. The median time to first response was 1.2 months. This study also established ELREXFIO as the first BCMA-directed therapy in the U.S. with once-every-other-week dosing for responding patients after 24 weeks of weekly therapy, which means less time at the clinic and potentially greater long-term treatment tolerability. The label also includes data from MagnetisMM-3 cohort B (n=64). Among the 63 patients in this cohort who received at least four prior lines of therapy, including a BCMA-directed therapy (CAR-T or antibody-drug conjugate), the overall response rate was 33% after a median follow-up of 10.2 months, with an estimated 84% maintaining the response for at least nine

months.

In longer-term efficacy data for cohort A (n=123) presented at the 2023 European Hematology Association meeting, the objective response rate was 61%, and median duration of response, overall survival, and progression-free survival had not yet been reached at 14.7 months median follow-up. For the responding patients, the probability of maintaining a response at 15 months was 72%. Among responding patients who switched to every-other-week dosing at least six months prior to the data cut-off date (n=50), 80% maintained or improved their response after the switch, with 38% attaining a complete response or better after the switch.

“Most multiple myeloma patients will experience relapse or resistance of their disease to treatment, often facing increased symptom burden and lowering their chance of surviving longer with each attempted line of therapy,” said MagnetisMM clinical trial investigator Ajay Nooka, MD, MPH, Director of the Multiple Myeloma Program at Winship Cancer Institute of Emory University. “By offering durable clinical response with an established safety profile and the convenience of subcutaneous administration, ELREXFIO provides a much-needed new option for heavily pre-treated multiple myeloma patients who are struggling with relapsed myeloma.”

ELREXFIO’s label contains a Boxed Warning for cytokine release syndrome (CRS) and neurologic toxicity (NT), including immune effector cell-associated neurotoxicity syndrome (ICANS), in addition to warnings and precautions for infections, neutropenia, hepatotoxicity and embryo-fetal toxicity. The most common adverse reactions to ELREXFIO (incidence ?20%) are CRS, fatigue, injection site reaction, diarrhea, upper respiratory tract infection, musculoskeletal pain, pneumonia, decreased appetite, rash, cough, nausea, and fever (pyrexia). The most common Grade 3 to 4 laboratory abnormalities (?20%) are decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased white blood cells, and decreased platelets. The step-up dose regimen (12/32/76 mg), combined with acetaminophen, dexamethasone, and diphenhydramine pre-treatment, is intended to reduce the incidence and severity of CRS. As a precaution, patients should be hospitalized for 48 hours following the first step-up dose and for 24 hours following the second step-up dose. No hospitalization is required for the third step-up dose. Given the risk of CRS and NT, including ICANS, ELREXFIO is available only through a restricted program called the ELREXFIO Risk Evaluation and Mitigation Strategy (REMS). A confirmatory trial (MagnetisMM-5) in the double-class exposed relapsed or refractory population involving 854 patients was initiated in 2022 to gather additional safety and efficacy data. Data will be shared as available.

“Accessibility is key to unlocking the potential impact of new treatment options. Unfortunately, novel therapies for triple-class-exposed multiple myeloma can be out of reach for medically underserved populations,” said Jenny Ahlstrom, Founder and Chief Executive Officer of the HealthTree Foundation for Multiple Myeloma. “With the approval of ELREXFIO, patients have a new off-the-shelf treatment option that can be delivered on an ongoing basis in community clinics, where the majority of patients with multiple myeloma receive their care.”

For patients who are prescribed ELREXFIO, Pfizer offers the support of Patient Access Navigators, through our Pfizer Oncology Together program, who provide personalized services for all aspects of treatment, including financial assistance resources, treatment support, and resources to navigate potential insurance and coverage issues.

ELREXFIO received Breakthrough Therapy Designation and Orphan Drug Designations and was approved under the FDA’s Accelerated Approval Program, which is designed to shorten the time of FDA review for drugs that treat serious conditions and fill an unmet medical need. The FDA review was also conducted under Project Orbis, a framework for the concurrent submission and review of oncology drugs among international partners to potentially expedite approvals. Currently, five countries (Switzerland, Brazil, Canada, Australia, and Singapore) are participating. A new drug application for ELREXFIO is being evaluated by the Japanese Ministry of Health, Labour and Welfare. Additionally, a marketing authorization application for ELREXFIO is currently being evaluated under the PRIME scheme by the European Medicines Agency (EMA).

The extensive MagnetisMM clinical development program is investigating ELREXFIO's use across the entire spectrum of myeloma progression, from newly diagnosed multiple myeloma to RRMM. Ongoing registrational-intent trials are exploring ELREXFIO both as monotherapy and in combination with standard or novel therapies. These include the Phase 3 MagnetisMM-5 trial in the double-class exposed setting and MagnetisMM-7 with ELREXFIO as maintenance treatment in newly diagnosed patients after transplant.

View the full Prescribing Information, including the Boxed Warning and patient Medication Guide. 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 Multiple Myeloma
Multiple myeloma (MM) is an aggressive and currently incurable blood cancer that affects plasma cells made in the bone marrow. Healthy plasma cells make antibodies that help the body fight infection.[1] MM is the second most common type of blood cancer, with over 35,000 new cases of MM diagnosed annually in the U.S. and 176,000 globally.[2,3] About half of those diagnosed with MM won't survive beyond five years, and most will receive four or more lines of therapy due to relapse.[4] While disease trajectory varies for each person, relapses are nearly inevitable.[5] Real-world evidence shows that people with RRMM often become resistant to the three main classes of treatment – proteasome inhibitors, immunomodulatory agents and anti-CD38 monoclonal antibodies – after just a few rounds of therapy, and re-treating with these classes was common.[6] The goal of therapy for people with RRMM is to achieve disease control with acceptable toxicity and improved quality of life.[7]

What is the most important information I should know about ELREXFIO?
ELREXFIO (elranatamab-bcmm) may cause side effects that are serious, life-threatening, or can lead to death, including cytokine release syndrome (CRS) and neurologic problems.

Tell your healthcare provider or get medical help right away if you develop any signs or symptoms of CRS or neurologic problems at any time during your treatment with ELREXFIO.

Cytokine release syndrome (CRS). Symptoms of CRS may include:

- fever of 100.4°F (38ºC) or higher
- trouble breathing
- chills
- dizziness or light-headedness
- fast heartbeat
- headache
- increased liver enzymes in your blood

Due to the risk of CRS, you will receive ELREXFIO on a "step-up" dosing schedule and should be hospitalized for 48 hours after the first "step-up" dose and for 24 hours after the second "step-up" dose of ELREXFIO.

- During the "step-up" dosing schedule:
  - For your first dose, you will receive a smaller "step-up" dose of ELREXFIO on day 1 of treatment
  - For your second dose, you will receive a larger "step-up" dose of ELREXFIO, which is usually given on day 4 of treatment
  - For your third dose, you will receive the first treatment dose of ELREXFIO, which is usually given on day 8 of treatment
- If your dose of ELREXFIO is delayed for any reason, you may need to repeat the "step-up" dosing schedule

- Before each dose of ELREXFIO you receive during the "step-up" dosing schedule, you will receive medications to help reduce your risk of CRS. Your healthcare provider will decide if you need to receive medications to help reduce your risk of CRS with future doses

Neurologic problems. Symptoms of neurologic problems may include:

- headache
- agitation, trouble staying awake, confusion or disorientation, or seeing or hearing things that are not real (hallucinations)
- trouble speaking, thinking, remembering things, paying attention, or understanding things
- problems walking, muscle weakness, shaking (tremors), loss of balance, or muscle spasms
- numbness and tingling (feeling like "pins and needles")
- burning, throbbing, or stabbing pain
- changes in your handwriting

Your healthcare provider will monitor you for signs and symptoms of CRS and neurologic problems during treatment with ELREXFIO, as well as other side effects, and will treat you as needed. Your healthcare provider may temporarily stop or completely stop your treatment with ELREXFIO if you develop CRS, neurologic problems, or any other severe side effects.

If you have any questions about ELREXFIO, ask your healthcare provider.

See **"What are the possible side effects of ELREXFIO?"** section for more information about side effects.

ELREXFIO is available only through the ELREXFIO Risk Evaluation and Mitigation Strategy (REMS) Program due to the risk of CRS and neurologic problems. You will receive an ELREXFIO Patient Wallet Card from your healthcare provider. **Carry the ELREXFIO Patient Wallet Card with you at all times and show it to all of your healthcare providers.** The ELREXFIO Patient Wallet Card lists signs and symptoms of CRS and neurologic problems. **Get medical help right away if you develop any of the signs and symptoms listed on the ELREXFIO Patient Wallet Card.** You may need to be treated in a hospital.

Before taking ELREXFIO, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection
- are pregnant or plan to become pregnant. ELREXFIO may harm your unborn baby. **Females who are able to become pregnant:**
  - Your healthcare provider should do a pregnancy test before you start treatment with ELREXFIO
  - You should use effective birth control (contraception) during treatment and for 4 months after your last dose of ELREXFIO
  - Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with ELREXFIO
- are breastfeeding or plan to breastfeed. It is not known if ELREXFIO passes into your breast milk. Do not breastfeed during treatment and for 4 months after your last dose of ELREXFIO

Tell your healthcare provider about all of the medications you take, includingprescription and over-the-counter medications, vitamins, and herbal supplements.

What should I avoid while receiving ELREXFIO?
Do not drive or operate heavy or potentially dangerous machinery for 48 hours after completing each of the 2

doses of ELREXFIO that are part of the “step-up" dosing schedule and the first treatment dose and at any time during treatment with ELREXFIO if you develop any new neurologic symptoms until the symptoms go away.

What are the possible side effects of ELREXFIO?
ELREXFIO may cause serious side effects, including:

- **Infections.** Upper respiratory tract infection and pneumonia are common during treatment with ELREXFIO. ELREXFIO can cause bacterial and viral infections that are severe, life-threatening, or that may lead to death. Your healthcare provider will monitor you for symptoms of infection before and during treatment with ELREXFIO
    - Your healthcare provider may prescribe medications for you to help prevent infections and treat you as needed if you develop an infection during treatment with ELREXFIO
    - Tell your healthcare provider right away if you develop any signs or symptoms of an infection during treatment with ELREXFIO, including:

- fever of 100.4°F (38ºC) or higher
- chills
- cough
- shortness of breath
- chest pain
- sore throat
- pain during urination
- feeling weak or generally unwell
    - People with active infections should not start ELREXFIO

- **Decreased white blood cell counts.** Decreased white blood cell counts are common during treatment with ELREXFIO and can also be severe. A fever can occur with low white blood cell counts and may be a sign that you have an infection. Your healthcare provider will treat you as needed
- **Liver problems.** ELREXFIO can cause increased liver enzymes and bilirubin in your blood. These increases can happen with or without you also having CRS. Tell your healthcare provider if you develop any of the following signs or symptoms of a liver problem:
    - tiredness
    - loss of appetite
    - pain in your right upper stomach-area (abdomen)
    - dark urine
    - yellowing of your skin or the white part of your eyes

Your healthcare provider will check your blood and monitor you for signs and symptoms of these serious side effects before you start and during treatment with ELREXFIO and may temporarily or completely stop treatment with ELREXFIO if you develop certain side effects.

The most common side effects of ELREXFIO include:

- tiredness
- injection site reaction, such as redness, itching, pain, bruising, rash, swelling, and tenderness
- diarrhea
- muscle and bone pain decreased appetite rash
- cough
- nausea
- fever

The most common severe abnormal lab test results with ELREXFIO include decreased white blood cells, red blood cells, and platelets.

These are not all of the possible side effects of ELREXFIO.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

What is ELREXFIO?
ELREXFIO is a prescription medication used to treat adults with multiple myeloma who have already received at least four treatment regimens (including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody) to treat their multiple myeloma, **and** their cancer has come back or did not respond to prior treatment.

ELREXFIO is approved based on patient response. Data are not yet available to show if ELREXFIO improves survival or symptoms.

It is not known if ELREXFIO is safe and effective in children.

Please read full Prescribing Information , including BOXED WARNING, for ELREXFIO.

About Pfizer in Hematology
At Pfizer, we have an industry-leading portfolio of 24 approved innovative cancer medicines and biosimilars, generating $12 billion in revenues in 2022. This includes eight therapies to treat hematologic malignancies where we have taken bold new approaches over the past decade to translate scientific research into transformative medicines for people living with blood cancer. For the millions living with blood cancer today and for those diagnosed tomorrow, we work tirelessly to deliver on our mission: Breakthroughs that change patients' lives.

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 August 14, 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 ELREXFIO (elranatamab-bcmm), a B-cell maturation antigen (BCMA) CD3-targeted bispecific antibody, including its potential benefits, pending regulatory applications and the MagnetisMM clinical program to potentially expand ELREXFIO into earlier lines of treatment, as monotherapy and in combination with standard or novel therapies, 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; 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 for any potential indications for ELREXFIO may be filed in any particular jurisdictions; whether and when the EMA may approve the pending application for ELREXFIO for the treatment of people with relapsed or refractory multiple myeloma (RRMM) and whether and when regulatory authorities in any jurisdictions may approve any such other applications that may be pending or filed for ELREXFIO, 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 ELREXFIO 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 ELREXFIO; 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, 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 .

Category: Prescription Medicines

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