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U.S. FDA Approves Pfizer's VELSIPITY™ for Adults with Moderately to Severely Active Ulcerative Colitis (UC)

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- *Approval of oral, once-daily VELSIPITY based on favorable safety and efficacy data from the ELEVATE UC Phase 3 trials*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) announced today that the U.S. Food and Drug Administration (FDA) has approved VELSIPITY™ (etrasimod), an oral, once-daily, selective sphingosine-1-phosphate (S1P) receptor modulator for adults with moderately to severely active ulcerative colitis (UC). The approved recommended dose for VELSIPITY is 2 mg.

UC is a chronic and often debilitating condition[1] that affects an estimated 1.25 million people in the United States.[2] Symptoms of UC can include chronic diarrhea with blood and mucus, abdominal pain, and urgency.[3,4] However, its impact can span beyond the physical to other aspects of life due to the chronic and unpredictable nature of symptoms.[5,6]

"VELSIPITY provides adults living with moderately to severely active UC the opportunity to achieve steroid-free remission with an oral, once-daily pill that has a favorable benefit-risk profile," said Angela Hwang, Chief Commercial Officer and President of Global Biopharmaceuticals Business, Pfizer. "VELSIPITY's FDA approval today marks a significant milestone for UC patients who need new treatments for this chronic condition and are ready to start advanced therapy."

The U.S. FDA approval was based on results from the ELEVATE UC Phase 3 registrational program (ELEVATE UC 52 and ELEVATE UC 12) that evaluated the safety and efficacy of VELSIPITY 2 mg once-daily on clinical remission in UC patients who had previously failed or were intolerant to at least one conventional, biologic, or Janus kinase (JAK) inhibitor therapy. Nearly two-thirds of patients in ELEVATE UC 52 and ELEVATE UC 12 were naïve to biologic or JAK inhibitor therapy, and these studies were also the only studies for advanced therapies for ulcerative colitis to include patients with isolated proctitis. Both studies achieved all primary and key secondary efficacy endpoints, with a favorable safety profile consistent with previous studies of VELSIPITY.

"Because of the unpredictable nature of UC, people living with the disease can cycle through several different treatments over time. Patients may also be apprehensive about using injectable therapies, like biologics," said Dr. Michael Chiorean, Co-Director of the IBD Center at Swedish Medical Center and an investigator in the ELEVATE Registrational Program. "It's important to have new, effective options like VELSIPITY for those patients who may require an advanced treatment option and prefer the convenience of a once-daily pill. VELSIPITY is a proven advanced treatment with a favorable benefit-risk profile."

"UC can affect patients differently and many people living with this disease struggle with ongoing symptoms," said Michael Osso, President and CEO of the Crohn's & Colitis Foundation. "The introduction of a new

treatment for UC could increase options for patients, and we look forward to seeing the impact of VELSIPITY for patients across the U.S.”

In ELEVATE UC 52, clinical remission was 27.0% for patients receiving VELSIPITY compared to 7.0% for patients receiving placebo at week 12 (20.0% differential, P?.001) and was 32.0% compared to 7.0% at week 52 (26.0% differential, P=?.001). In ELEVATE UC 12, clinical remission was achieved among 26.0% of patients receiving VELSIPITY compared to 15.0% of patients receiving placebo (11.0% differential, P=<.05). All key secondary efficacy endpoints were met at week 12, including endoscopic improvement and mucosal healing. The safety of VELSIPITY was consistent with previous studies, with the most common adverse reactions being headache, elevated liver tests, and dizziness (incidence ? 5%).

Full results from the program were published by The Lancet in March 2023.

View the full Prescribing Information. 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 VELSIPITY™ (Etrasimod)

VELSIPITY is a once-daily, oral, sphingosine 1-phosphate (S1P) receptor modulator that selectively binds with S1P receptor subtypes 1, 4, and 5.

Regulatory applications for VELSIPITY in ulcerative colitis have been submitted to countries around the world for review, including Canada, Australia, Mexico, Russia, Switzerland, and Singapore. The European Medicines Agency (EMA) has accepted the Marketing Authorization Application (MAA) for VELSIPITY, with a decision anticipated in the beginning of 2024.

About ELEVATE UC 52 and ELEVATE UC 12

ELEVATE UC 52 and ELEVATE UC 12 are pivotal trials that are part of the ELEVATE UC Phase 3 registrational program.[7]

ELEVATE UC 52 is a randomized, double-blind, placebo-controlled trial that utilized a treat-through design comprising of a 12-week induction period followed by a 40-week maintenance period. Subjects were randomized to VELSIPITY or placebo and continued on treatment without re-randomization for the entire duration of the study. Beginning at week 12, all patients could continue their randomized treatment; patients whose disease had not improved or had worsened compared to baseline could discontinue and, if eligible, enroll in an open-label extension study. The primary objective of this trial was to assess the safety and efficacy of etrasimod 2 mg once daily on clinical remission after both 12 and 52 weeks. The primary endpoint is based on the 3-domain, modified Mayo score (MMS). In ELEVATE UC 52, clinical remission was 27.0% for patients receiving etrasimod compared to 7.0% for patients receiving placebo at week 12 (20.0% differential, P?.001) and was 32.0% compared to 7.0% at week 52 (26.0% differential, P??.001). Statistically significant improvements were attained in all key secondary endpoints, including endoscopic improvement and mucosal healing at weeks 12 and 52, and corticosteroid-free remission and sustained clinical remission at week 52.

ELEVATE UC 12 is a randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of etrasimod 2 mg once-daily in subjects with moderately to severely active UC. The primary objective of this trial was to assess the safety and efficacy of etrasimod on clinical remission at 12 weeks assessed by the FDA-required, 3-domain, MMS. In ELEVATE UC 12, clinical remission was achieved among 26.0% of patients receiving etrasimod compared to 15.0% of patients receiving placebo (11.0% differential, P<.05). All key secondary endpoints were met at week 12, including endoscopic improvement and mucosal healing.

In ELEVATE UC 12, a similar proportion of patients experienced treatment-emergent adverse events (AEs) between etrasimod 2 mg and placebo treatment groups, while in ELEVATE UC 52, it was higher in the etrasimod 2 mg group compared to placebo. The proportion of patients experiencing serious AEs was similar between treatment groups in both trials. The most common treatment-emergent AEs in 3% or more of etrasimod-treated patients and greater than placebo up to week 52 in either trial were headache, elevated liver tests, worsening of UC, COVID-19 infection, dizziness, pyrexia, arthralgia, abdominal pain and nausea. Data support that initiation of etrasimod treatment does not require a complex up-titration regimen.

Nearly two-thirds of patients in ELEVATE UC 52 and ELEVATE UC 12, respectively, were naïve to biologic or JAK inhibitor therapy.

IMPORTANT SAFETY INFORMATION & INDICATION

Do not take VELSIPITY if you:

- have had a heart attack, chest pain (unstable angina), stroke or mini stroke (transient ischemic attack or TIA), and certain types of heart failure requiring hospitalization in the last 6 months
- have or have had a history of unusual heartbeats (arrhythmia) that is not corrected by a pacemaker

Talk to your healthcare provider before taking VELSIPITY if you have any of these conditions or do not know if you have any of these conditions.

VELSIPITY can cause serious side effects, including:

- **Infections:** VELSIPITY can increase your risk of serious infections. These infections can be life-threatening and cause death. VELSIPITY lowers the number of white blood cells (lymphocytes) in your blood. This usually returns to normal within 4 to 5 weeks after you stop taking VELSIPITY. Your healthcare provider will test your blood before you start taking VELSIPITY. Your healthcare provider may delay or stop your VELSIPITY treatment if you have an infection. Call your healthcare provider right away if you have any of these symptoms of an infection during treatment with VELSIPITY, and for 5 weeks after you stop taking VELSIPITY: fever or high temperature, pain when peeing or peeing more often than usual as these can be signs of a urinary tract infection, tiredness, flu-like symptoms, or headache with fever, neck stiffness, sensitivity to light, nausea, or confusion as these may be symptoms of meningitis, an infection of the lining around your brain and spine.
- **Slow heart rate (also known as bradyarrhythmia) when you start taking VELSIPITY:** VELSIPITY may cause your heart rate to temporarily slow down especially after you take your first dose. You will have a test called an electrocardiogram (ECG) to check the electrical activity of your heart before you take your first dose of VELSIPITY. Call your healthcare provider if you experience these symptoms of slow heart rate: feeling dizzy, feeling lightheaded, feeling like your heart is beating slowly or skipping beats, feeling short of breath, feeling confused, feeling tired, or chest pain.

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

- have a serious infection or an infection that does not go away or that keeps coming back (chronic).
- are unable to fight infections due to a disease.
- have received a vaccine in the past 4 weeks or are scheduled to receive a vaccine. You should be brought up to date with all age-required vaccines before starting treatment with VELSIPITY. VELSIPITY may affect how well a vaccine works. Tell your healthcare provider that you are receiving treatment with VELSIPITY before receiving a vaccine.

- have chickenpox or received the vaccine for chickenpox. Your healthcare provider may do a blood test for the chickenpox virus. You may need to get the full course of the chickenpox vaccine and then wait 4 weeks before you start taking VELSIPITY.
- have a slow heart rate.
- have an irregular or abnormal heartbeat (arrhythmia).
- have heart disease, Class I or II heart failure, history of a heart attack, high blood pressure or uncontrolled high blood pressure.
- have cerebrovascular disease or history of a stroke or ministroke.
- history of repeated fainting.
- have or have had liver problems.
- have or have had skin cancer.
- have breathing problems, including untreated sleep apnea.
- are pregnant or plan to become pregnant. VELSIPITY may harm your unborn baby. Talk with your healthcare provider if you are pregnant or plan to become pregnant. If you are a female who can become pregnant, talk with your healthcare provider and use effective birth control during your treatment with VELSIPITY and for 7 days after you stop taking VELSIPITY. If you become pregnant while taking VELSIPITY or within 7 days after you stop taking VELSIPITY, talk with your healthcare provider and enroll in the VELSIPITY Pregnancy Registry by calling 1-800-616-3791.
- are breastfeeding or plan to breastfeed. It is not known if VELSIPITY passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take VELSIPITY.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Using VELSIPITY with other medicines can cause serious side effects. Especially tell your healthcare provider if you take or have taken:

- medicines to control your heart rhythm (antiarrhythmics), heartbeat, or blood pressure. These may be called beta blockers or calcium channel blockers.
- medicines that affect your immune system.
- certain medicines known as moderate to strong inhibitors of both CYP2C9 and CYP3A4, medicines such as fluconazole. If you are taking fluconazole, you should not take VELSIPITY.
- Rifampin. If you are taking rifampin, you should not take VELSIPITY.
- You should not receive **live** vaccines at least 4 weeks before starting VELSIPITY, during treatment with VELSIPITY and for 5 weeks after you stop taking VELSIPITY. Talk to your healthcare provider before you receive a vaccine during treatment and for 5 weeks after treatment with VELSIPITY. If you receive a live vaccine, you may get the infection the vaccine was meant to prevent. Vaccines may not work as well when given during treatment with VELSIPITY.

VELSIPITY can cause serious side effects, including:

- **Liver problems.** VELSIPITY may cause liver problems. Your healthcare provider will do blood tests to check your liver before you start taking VELSIPITY. Call your healthcare provider right away if you have any of the following symptoms: unexplained nausea, vomiting, stomach area (abdominal pain), tiredness, loss of appetite, yellowing of the whites of your eyes or skin, or dark-colored urine.
- **Increased blood pressure.** Your healthcare provider should check your blood pressure during treatment with VELSIPITY and treat you as needed.
- **A problem with your vision called macular edema.** Your healthcare provider should test your vision around the time you start taking VELSIPITY or at any time you notice vision changes during your treatment with VELSIPITY. Call your healthcare provider right away if you have any of the following symptoms: blurriness or shadows in the center of your vision, sensitivity to light, a blind spot in the center

of your vision, or unusually colored vision.

- **Types of skin cancer.** Certain types of skin cancer have happened with medicines in the same class as VELSIPITY. Limit the amount of time you spend in sunlight and ultraviolet (UV) light while taking VELSIPITY. Wear protective clothing and use a sunscreen with a high sun protection factor. Tell your healthcare provider if you have any changes in the appearance of your skin.
- **Swelling and narrowing of the blood vessels in your brain.** A condition called Posterior Reversible Encephalopathy Syndrome (PRES) has happened with drugs in the same class. Symptoms of PRES usually get better when you discontinue treatment. If not treated, PRES may cause a stroke. Call your healthcare provider right away if you have any of the following symptoms: sudden severe headache, sudden confusion, sudden loss of vision or other changes in your vision, or seizure. If you develop any of these symptoms, your healthcare provider will stop treatment with VELSIPITY.
- **Breathing problems.** Some people who take medicines in the same class as VELSIPITY may experience shortness of breath. Your healthcare provider may do tests to check your breathing during treatment with VELSIPITY. Call your healthcare provider right away if you have new or worsening breathing problems.

The most common side effects of VELSIPITY include headache, elevated liver tests, and dizziness. These are not all of the possible side effects of VELSIPITY. For more information, ask your healthcare provider or pharmacist. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Pfizer at 1-800-438-1985.

INDICATION

VELSIPITY is a prescription medicine used to treat adults with moderately to severely active ulcerative colitis. It is not known if VELSIPITY is safe and effective in children.

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 October 13, 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 VELSIPITY (etrasimod), including its potential benefits, an approval in the U.S. for adults with moderately to severely active ulcerative colitis and applications pending for VELSIPITY (etrasimod) in other jurisdictions, 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 VELSIPITY

(etrasimod); 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 VELSIPITY (etrasimod); whether and when any applications that may be pending or filed for VELSIPITY (etrasimod) 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 VELSIPITY (etrasimod) 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 VELSIPITY (etrasimod); 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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