NEWS RELEASE

FDA Grants Priority Review for WINREVAIR™ (sotatercept-csrk) to Update Label Based on Results From ZENITH Trial

2025-07-02

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has accepted and granted priority review for a new supplemental Biologics License Application (sBLA) seeking approval to update the U.S. product label based on the Phase 3 ZENITH trial for WINREVAIR™ (sotatercept-csrk). In 2024, WINREVAIR was approved for the treatment of adults with pulmonary arterial hypertension (PAH, Group 1 PH) to increase exercise capacity, improve WHO* functional class (FC), and reduce the risk of clinical worsening events. The FDA has set a Prescription Drug User Fee Act (PDUFA), or target action date, of Oct. 25, 2025.

The sBLA is based on data from the Phase 3 ZENITH trial. The ZENITH trial was the first PAH Phase 3 outcome study to use a primary endpoint comprised entirely of major morbidity and mortality events. It was also the first PAH Phase 3 study stopped early by an independent data monitoring committee for overwhelming efficacy. In ZENITH, WINREVAIR demonstrated a 76% reduction in the risk of a composite of all-cause death, lung transplantation, and hospitalization for PAH ≥24 hours compared to placebo. Improvement was observed early in treatment with increasing benefit throughout the study. The safety profile of WINREVAIR in ZENITH was generally consistent with that observed in previous studies. These results were published in the **New England Journal of Medicine**.

“We are pleased that the FDA has accepted our sBLA for WINREVAIR and granted a priority review to consider an update to labeling for WINREVAIR to include the impressive results of ZENITH. There remains a significant unmet medical need for patients living with PAH who, despite being on background therapy, remain at higher risk of morbidity and mortality,” said Dr. Joerg Koglin, senior vice president, global clinical development, Merck Research

Laboratories. “The FDA’s Priority Review designation acceptance of our sBLA reinforces our confidence in WINREVAIR for a broad range of patients and represents a critical step toward advancing the treatment of PAH.”

WINREVAIR is currently approved in more than 45 countries based on the results from the STELLAR trial.

*World Health Organization

About ZENITH

The ZENITH study (**NCT04896008**) is a global, double-blind, placebo-controlled clinical trial to evaluate WINREVAIR when added to maximum tolerated background PAH therapy on time to first event of all-cause death, lung transplantation, or PAH worsening related hospitalization of ≥ 24 hours, in adult participants with WHO functional class III or IV PAH at high risk of mortality. ZENITH study inclusion criteria required Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL) Lite 2.0 risk score of ≥9.

The study enrolled 172 participants, who were randomized in a 1:1 ratio to either WINREVAIR plus background PAH therapy or placebo plus background PAH therapy. The primary composite outcome measure was time to first confirmed major morbidity or mortality event. Events were defined as all-cause death, lung transplantation, or PAH worsening-related hospitalization of ≥ 24 hours. Secondary outcome measures included overall survival, transplant-free survival and several additional measures. The study excluded patients with PAH Group 1 subtypes: human immunodeficiency virus (HIV)-associated PAH and PAH associated with portal hypertension as well as diagnosis of pulmonary veno-occlusive diseases, pulmonary capillary hemangiomatosis or overt signs of capillary and/or venous involvement.

Participants who completed the ZENITH trial were offered the opportunity to receive WINREVAIR as part of the open-label, long-term extension study, SOTERIA (**NCT04796337**), consistent with that study’s eligibility criteria.

About WINREVAIR™ (sotatercept-csrk) for injection, for subcutaneous use, 45 mg, 60 mg

WINREVAIR is FDA-approved for the treatment of adults with pulmonary arterial hypertension (PAH, WHO Group 1) to increase exercise capacity, improve WHO functional class (FC) and reduce the risk of clinical worsening events. WINREVAIR is the first activin signaling inhibitor therapy approved to treat PAH. WINREVAIR improves the balance between pro-proliferative and anti-proliferative signaling to modulate vascular proliferation. In preclinical models, WINREVAIR induced cellular changes that were associated with thinner vessel walls, partial reversal of right ventricular remodeling, and improved hemodynamics.

WINREVAIR is the subject of a licensing agreement with Bristol Myers Squibb.

Selected Safety Information for WINREVAIR in the U.S.

WINREVAIR may increase hemoglobin (Hgb). Severe erythrocytosis may increase the risk of thromboembolic events or hyperviscosity syndrome. Monitor Hgb before each dose for the first 5 doses, or longer if values are unstable, and periodically thereafter, to determine if dose adjustments are required.

WINREVAIR may decrease platelet count. Severe thrombocytopenia may increase the risk of bleeding. Thrombocytopenia occurred more frequently in patients also receiving prostacyclin infusion. Do not initiate treatment if platelet count is <50,000/mm3. Monitor platelets before each dose for the first 5 doses, or longer if values are unstable, and periodically thereafter to determine whether dose adjustments are required.

In clinical studies, serious bleeding (eg, gastrointestinal, intracranial hemorrhage) was reported in 4% of patients taking WINREVAIR and 1% of patients taking placebo. Patients with serious bleeding were more likely to be on prostacyclin background therapy and/or antithrombotic agents, or have low platelet counts. Advise patients about signs and symptoms of blood loss. Do not administer WINREVAIR if the patient is experiencing serious bleeding.

WINREVAIR may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use an effective method of contraception during treatment with WINREVAIR and for at least 4 months after the final dose. Pregnancy testing is recommended for females of reproductive potential before starting WINREVAIR treatment.

Based on findings in animals, WINREVAIR may impair female and male fertility. Advise patients on the potential effects on fertility.

The most common adverse reactions occurring in the phase 3 clinical trial (≥10% for WINREVAIR and at least 5% more than placebo) were headache (24.5% vs 17.5%), epistaxis (22.1% vs 1.9%), rash (20.2% vs 8.1%), telangiectasia (16.6% vs 4.4%), diarrhea (15.3% vs 10.0%), dizziness (14.7% vs 6.2%), and erythema (13.5% vs 3.1%).

Because of the potential for serious adverse reactions in the breastfed child, advise patients that breastfeeding is not recommended during treatment with WINREVAIR, and for 4 months after the final dose.

About PAH

Pulmonary arterial hypertension (PAH) is a rare, progressive and life-threatening blood vessel disorder characterized by the constriction of small pulmonary arteries and elevated blood pressure in the pulmonary circulation. Approximately 40,000 people in the U.S. are living with PAH. The disease progresses rapidly for many patients. PAH results in significant strain on the heart, leading to limited physical activity, heart failure and reduced life expectancy. The five-year mortality rate for patients with PAH is approximately 43%.

About Merck

At Merck, known as MSD outside of the United States and Canada, we are unified around our purpose: We use the power of leading-edge science to save and improve lives around the world. For more than 130 years, we have brought hope to humanity through the development of important medicines and vaccines. We aspire to be the premier research-intensive biopharmaceutical company in the world – and today, we are at the forefront of research to deliver innovative health solutions that advance the prevention and treatment of diseases in people and animals. We foster a diverse and inclusive global workforce and operate responsibly every day to enable a safe, sustainable and healthy future for all people and communities. For more information, visit **www.merck.com** and connect with us on **X (formerly Twitter)**, **Facebook**, **Instagram**, **YouTube** and **LinkedIn**.

Forward-Looking Statement of Merck & Co., Inc., Rahway, N.J., USA

This news release of Merck & Co., Inc., Rahway, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline candidates that the candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's Annual Report on Form 10-K for the year ended December 31, 2024 and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (**www.sec.gov**).

Please see Prescribing Information for WINREVAIR (sotatercept-csrk) at **http://www.merck.com/product/usa/pi_circulars/w/winrevair/winrevair_pi.pdf**, Patient Information for WINREVAIR at

http://www.merck.com/product/usa/pi_circulars/w/winrevair/winrevair_ppi.pdf, and Instructions for Use for WINREVAIR (1-vial kit, 2-vial kit) at **https://www.merck.com/product/usa/pi_circulars/w/winrevair/winrevair_ifu_1-vial_2-vial_kits.pdf**.

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Source: Merck & Co., Inc.