NEWS RELEASE

U.S. FDA Approves Updated Indication for WINREVAIR™ (sotatercept-csrk) in Adults with Pulmonary Arterial Hypertension (PAH, WHO* Group 1 Pulmonary Hypertension) Based on Phase 3 ZENITH Study

2025-10-27

Adding WINREVAIR to background PAH therapy improved exercise capacity and WHO functional class (FC), and reduced the risk of clinical worsening events, including hospitalization for PAH, lung transplantation and death

ZENITH data add to growing body of evidence supporting a positive benefit risk profile of WINREVAIR in a broad range of adult patients with PAH

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved an update to the U.S. product label based on the Phase 3 ZENITH trial for WINREVAIR™ (sotatercept-csrk) for injection, 45mg, 60mg. WINREVAIR, an activin signaling inhibitor, is now FDA-approved for the treatment of adults with pulmonary arterial hypertension (PAH, WHO Group 1 pulmonary hypertension) to improve exercise capacity and WHO functional class (FC), and reduce the risk of clinical worsening events, including hospitalization for PAH, lung transplantation and death. WINREVAIR was initially approved based on the pivotal STELLAR study in March 2024. Today's approval expanded the indication of WINREVAIR to include components of the clinical worsening events: hospitalization for PAH, lung transplantation and death.

In ZENITH (N=172; 86 WINREVAIR, 86 placebo), adding WINREVAIR to background therapy demonstrated a statistically significant and clinically meaningful 76% reduction in the risk of major morbidity and mortality outcomes in adults with PAH WHO functional class III or IV compared to placebo (HR: 0.24; 95% CI: 0.13, 0.43; p<0.0001). The trial's composite primary efficacy endpoint events — time to first occurrence of all-cause death, lung transplantation or PAH-worsening hospitalization of ≥24 hours — occurred in 15 WINREVAIR-treated participants (17%) versus 47 placebo-treated participants (55%). Due to overwhelming efficacy based on the primary endpoint result, the ZENITH trial was stopped early at the interim analysis and patients were offered the opportunity to receive WINREVAIR through an open-label long-term follow-up study.

"For patients with PAH, the risk of serious events such as hospitalization, transplantation or death remains unacceptably high despite being maximally treated with traditional therapies," said Dr. Vallerie McLaughlin**, Kim A Eagle MD Endowed Professor of Cardiovascular Medicine and Director, Pulmonary Hypertension Program, University of Michigan in Ann Arbor. "Results from the pivotal ZENITH trial add to the growing body of data and support the potential for WINREVAIR as standard of care."

Healthcare providers should monitor hemoglobin and platelets before each dose of WINREVAIR for the first 5 doses, or longer if values are unstable, and periodically thereafter to determine if dose adjustments are required. WINREVAIR may increase hemoglobin and may lead to erythrocytosis, which if severe may increase the risk of thromboembolic events or hyperviscosity syndrome. WINREVAIR also may decrease platelet count and lead to severe thrombocytopenia, which may increase the risk of bleeding; thrombocytopenia occurred more frequently in patients also receiving prostacyclin infusion. Treatment should not be initiated if platelet count is <50,000/mm3. See additional Selected Safety Information below.

The most common adverse reactions (≥10% for WINREVAIR and at least 5% more than placebo) in ZENITH were infections (67.4% vs 44.2%), epistaxis (45.3% vs 9.3%), diarrhea (25.6% vs 17.4%), telangiectasia (25.6% vs 3.5%), increased hemoglobin (15.1% vs 1.2%), rash (10.5% vs 4.7%), erythema (10.5% vs 3.5%) and gingival bleeding (10.5% vs 2.3%).The median duration of exposure was longer in the WINREVAIR group (435 days) than in the placebo group (268 days). In the WINREVAIR group, 1 patient (1%) discontinued study intervention due to an adverse event, compared with 4 patients (5%) in the placebo group.

"Merck's leadership in PAH research is anchored in a comprehensive clinical program that continues to advance science and deliver meaningful evidence for physicians and patients," said Dr. Joerg Koglin, senior vice president, global clinical development, Merck Research Laboratories. "This approval represents another step forward in our mission to deliver on the promise of WINREVAIR, an activin signaling inhibitor with an indication recognizing its impact to adult patients with PAH on the risk of clinical worsening events, including death, lung transplantation and PAH hospitalization."

*World Health Organization

**Dr. McLaughlin is a member of the adult sotatercept steering committee, an investigator in the ZENITH study and a paid consultant to Merck.

About ZENITH

The ZENITH study (NCT04896008) was a global, double-blind, placebo-controlled, multicenter, parallel-group clinical trial in which 172 adult participants with PAH (WHO FC III or IV) at high risk of mortality were randomized in a 1:1 ratio to either WINREVAIR (target dose 0.7 mg/kg) (n=86) plus background PAH therapy or placebo (n=86) plus background PAH therapy administered subcutaneously once every 3 weeks.

The most common PAH etiologies were idiopathic PAH (50%), PAH associated with connective tissue diseases (CTD) (28%), and heritable PAH (11%). The mean time since PAH diagnosis to screening was 8 years. The study excluded patients diagnosed with human immunodeficiency virus (HIV)-associated PAH, PAH associated with portal hypertension, pulmonary veno-occlusive disease, or pulmonary capillary hemangiomatosis or overt signs of capillary and/or venous involvement. Participants were on background PAH treatment, 72% on triple therapy, 28% on double therapy and 59% on prostacyclin infusion therapy. There were more participants in WHO FC III (74%) compared to WHO FC IV (26%). The REVEAL Lite 2 risk score was <9 for 2% of participants, 9 to 10 for 67% of participants and ≥11% for 30% of participants. The primary efficacy endpoint 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 endpoints included overall survival and several additional measures.

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 pulmonary hypertension) to improve exercise capacity and World Health Organization (WHO) functional class (FC), and reduce the risk of clinical worsening events, including hospitalization for PAH, lung transplantation and death. 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

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 (e.g., gastrointestinal, intracranial hemorrhage) was reported in 4% vs 1% (STELLAR) and 7% vs 5% (ZENITH) of patients taking WINREVAIR vs placebo, respectively. 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. Evaluate and treat bleeding accordingly. 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 (≥10% for WINREVAIR and at least 5% more than placebo) occurring in the STELLAR Phase 3 clinical trial 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 6.3%) and erythema (13.5% vs 3.1%). The most common adverse reactions in the ZENITH trial were infections (67.4% vs 44.2%), epistaxis (45.3% vs 9.3%), diarrhea (25.6 % vs 17.4%), telangiectasia (25.6 % vs 3.5%), increased hemoglobin (15.1% vs 1.2%), rash (10.5% vs 4.7%), erythema (10.5% vs 3.5%) and gingival bleeding (10.5% vs 2.3%).

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 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 **http://www.merck.com/product/usa/pi_circulars/w/winrevair/winrevair_ifu_1-vial_2-vial_kits.pdf**.

Media Contacts:

Olivia Finucane
+44 7881 262476

Nikki Lupinacci
(718) 644-0730

Investor Contacts:

Peter Dannenbaum
(732) 594-1579

Ayn Wisler
(917) 691-6218

Source: Merck & Co., Inc.