NEWS RELEASE

# Merck’s WINREVAIR™ (sotatercept-csrk) Met Primary Endpoint in Phase 2 CADENCE Study in Adults With Combined Post- and Precapillary Pulmonary Hypertension (CpcPH) due to Heart Failure With Preserved Ejection Fraction (HFpEF)

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WINREVAIR demonstrated a statistically significant and clinically meaningful reduction in the primary endpoint of pulmonary vascular resistance (PVR) compared to placebo, improving the ability of blood to transition through the lungs to the heart

These data support proof-of-concept to inform Phase 3 development for WINREVAIR in this population

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced positive topline results from the Phase 2 CADENCE study evaluating WINREVAIR™ (sotatercept-csrk) in adults for the treatment of combined post- and precapillary pulmonary hypertension (CpcPH) due to heart failure with preserved ejection fraction (HFpEF). CADENCE met its primary endpoint, showing a statistically significant and clinically meaningful reduction in pulmonary vascular resistance (PVR) from baseline at 24 weeks compared to placebo. Based on a preliminary assessment, the safety profile observed in the CADENCE study was generally consistent with the known safety profile for WINREVAIR.

“In this study, WINREVAIR improved pulmonary vascular resistance, an important hemodynamic measurement related to cardiac and pulmonary blood vessel function that has the potential to translate into improved outcomes

for patients with combined post- and precapillary pulmonary hypertension due to heart failure with preserved ejection fraction," said Dr. Mahesh Patel, vice president, global clinical development, Merck Research Laboratories. "The CADENCE trial was designed as a proof-of-concept study to evaluate the pharmacological activity of WINREVAIR in a new patient population, with the goal of informing further Phase 3 development."

The company is planning to present these results at a future scientific congress and intends to proceed with Phase 3 development.

WINREVAIR is U.S. Food and Drug Administration (FDA) approved as an activin signaling inhibitor indicated 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 is currently approved in more than 50 countries.

* World Health Organization

## About the CADENCE Study

CADENCE is a randomized, double-blind randomized, placebo-controlled Phase 2 proof-of-concept study (**NCT04945460**) evaluating the efficacy and safety of WINREVAIR versus placebo in adults with CpcPH due to HFpEF. Adult patients in the trial had a diagnosis of CpcPH due to HFpEF with New York Heart Association (NYHA) FC II or III. CADENCE was designed as proof-of-concept study with biomarkers, invasive hemodynamics, non-invasive imaging and exercise capacity. The primary endpoint is change from baseline in PVR. The study further assessed exercise capacity, echocardiographic endpoints, biomarker endpoints and clinical endpoints.

The study enrolled 164 participants, who were randomized in a 1:1:1 ratio to one of the three treatment groups (placebo, 0.3mg/kg WINREVAIR and 0.7mg/kg WINREVAIR) during the placebo-controlled treatment period.

## About Combined Postcapillary and Precapillary Pulmonary Hypertension (CpcPH) due to Heart Failure with Preserved Ejection Fraction (HFpEF)

Combined post- and precapillary pulmonary hypertension (CpcPH) represents a subset of pulmonary hypertension due to left heart disease (PH-LHD), also known as Group 2 pulmonary hypertension. CpcPH is associated with poorer outcomes compared to other types of Group 2 PH. It is harder to treat because it involves both advanced left-sided heart disease and progressive remodeling of the pulmonary vasculature. There are no treatments specifically approved for CpcPH today. CpcPH due to HFpEF is believed to be a rare, though potentially underdiagnosed condition.

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

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