NEWS RELEASE

Positive Data from Phase 2 CADENCE Trial Provides Definitive Proof-of-Concept for WINREVAIR™ (sotatercept-csrk) in Adults With the Syndrome of Combined Post- and Precapillary Pulmonary Hypertension and Heart Failure With Preserved Ejection Fraction

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Merck's WINREVAIR met primary endpoint of change in pulmonary vascular resistance (PVR), significantly improving the ability of blood to flow through the lungs to the heart

Totality of evidence across hemodynamic, functional, echocardiographic and clinical endpoints supports advancing development of WINREVAIR for this distinct patient population into a registrational Phase 3 study

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced detailed results from the Phase 2 CADENCE study, which was designed to evaluate the efficacy, safety and tolerability of two doses (0.3 mg/kg and 0.7 mg/kg) of WINREVAIR™ (sotatercept-csrk) for the treatment of adults with the syndrome of combined post- and precapillary pulmonary hypertension and heart failure with preserved ejection fraction (CpcPH-HFpEF). In this distinct patient population, WINREVAIR showed a statistically significant and clinically meaningful reduction from baseline in pulmonary vascular resistance (PVR) versus placebo (n=55) at week 24, with a 1.02 Wood units reduction for the 0.3 mg/kg dose (n=54, [95% CI, -1.81, -0.23], p=0.004) and a 0.75 Wood units reduction for the 0.7 mg/kg dose (n=55, [95% CI -1.52, 0.03], p=0.024). As noted below, important secondary endpoints explored include six-minute walk distance (6MWD), echocardiographic measures,

N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and time to clinical worsening (TTCW). These late-breaking data were presented today in a late-breaking clinical trial presentation at the American College of Cardiology's Annual Scientific Session and Expo (ACC.26), simultaneously published in Circulation and featured as part of an ACC.26 press conference.

"CpcPH-HFpEF is a distinct, identifiable and well-characterized condition that develops in people with advanced heart failure and typically impacts people who are older and have other comorbid conditions. While it is an uncommon condition and underdiagnosed, it is associated with a high morbidity and mortality rate and there are no approved treatment options specifically for CpcPH-HFpEF," said Dr. Mardi Gomberg-Maitland, MSc, Walter G. Ross professor of clinical research, director of Pulmonary Hypertension Program, George Washington University School of Medicine and Health Sciences. "The Phase 2 CADENCE study results suggest that WINREVAIR has direct pulmonary vascular and cardiac effects in this distinct population, which may translate to clinically meaningful improvements. These proof-of-concept data provide strong rationale for further evaluation in a Phase 3 study."

In this Phase 2 study designed to assess proof-of-concept and different doses, patients in the WINREVAIR 0.7 mg/kg arm showed an increase of 5.8 meters in 6MWD that did not reach statistical significance (95% CI, -17.3, 28.9). While subsequent secondary endpoints were not formally tested due to the prespecified hierarchical testing strategy, there was a 20.3-meter increase from baseline in 6MWD in patients treated with WINREVAIR 0.3 mg/kg (95% CI, 1.5, 39.1). Additional findings from the week 24 analysis of these secondary endpoints compared to placebo include:

- the reduction in mean pulmonary arterial pressure (mPAP) from baseline was -9.19 for WINREVAIR 0.3 mg/kg (95% CI, -13.00, -5.38) and was -9.22 for WINREVAIR 0.7 mg/kg (95% CI, -12.97, -5.46);
- the reduction in pulmonary arterial wedge pressure (PAWP) from baseline was -3.04 for WINREVAIR 0.3 mg/kg (95% CI, -5.77, -0.32) and -2.53 for WINREVAIR 0.7 mg/kg (95% CI, -5.33, 0.28);
- the reduction in NT-proBNP levels from baseline was -344 pg/mL for WINREVAIR 0.3 mg/kg (95% CI, -656, -31); and -402 pg/mL for WINREVAIR 0.7 mg/kg (95% CI, -846, 42);
- the time to first occurrence of a clinical worsening event was prolonged with WINREVAIR 0.3 mg/kg (HR: 0.18 [95% CI, 0.05, 0.62]) and WINREVAIR 0.7 mg/kg (HR: 0.59 [95% CI, 0.25, 1.36]).

The safety profile observed in CpcPH-HFpEF was generally consistent with the known safety profile for WINREVAIR in pulmonary arterial hypertension (PAH).

"The totality of evidence and consistency in trends across multiple endpoints from the CADENCE study support advancement of WINREVAIR into a registrational Phase 3 program in CpcPH-HFpEF. While both doses suggest efficacy, CADENCE results support that the 0.3 mg/kg dose may optimize the benefit-risk profile of WINREVAIR in the distinct population of CpcPH-HFpEF," said Dr. Mahesh Patel, vice president, global clinical development, Merck Research Laboratories. "We are working with regulatory agencies to design a Phase 3 registrational study with

endpoints that focus on clinical outcomes most relevant to the needs of this population, with the ultimate goal of providing the first treatment option for CpcPH-HFpEF."

About the CADENCE study and additional results

CADENCE is a double-blind, randomized, placebo-controlled Phase 2 proof-of-concept study (**NCT04945460**) evaluating the efficacy, safety and tolerability of WINREVAIR versus placebo in adults with CpcPH-HFpEF. Adult patients in the trial had a diagnosis of CpcPH-HFpEF with New York Heart Association (NYHA) FC II or III. The study enrolled 164 participants, and the demographics and clinical characteristics at baseline were generally balanced. The median age was 75 years old (69-79) and 69.5% of the patients were female (n=114). 65.9% of patients had a NYHA FC III diagnosis and 34.1% had a NYHA FC II diagnosis. At baseline, 34.8% had atrial fibrillation and 46.3% had diabetes.

A total of 164 participants were randomized in a 1:1:1 ratio to one of the three treatment groups: placebo once every three weeks (Q3W) (n=55), 0.3 mg/kg WINREVAIR Q3W (n=54) and 0.7 mg/kg WINREVAIR Q3W (n=55) during the placebo-controlled treatment period. For those randomized to the 0.7 mg/kg dose of WINREVAIR, participants received a starting dose level of WINREVAIR 0.3 mg/kg for the initial three dosing visits, then escalated to the 0.7 mg/kg dose Q3W.

The CADENCE trial was designed as a 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 also evaluated exercise capacity, as well as echocardiographic, biomarker and clinical endpoints. Time to clinical worsening was defined by a composite endpoint of death, ≥1 hospitalization due to cardiopulmonary indication; ≥1 administration of intravenous diuretics or subcutaneous furosemide or ≥15 percent decrease from baseline in 6MWD confirmed by two tests. At baseline, the median PVR was 5.2 Wood units (4.0, 6.9), mPAP was 43 mmHg (38.0, 50.0), PAWP was 21.0 mmHg (18.0, 25.0), the median 6MWD was 273.8 meters (199.5, 343.8), and the median NT-proBNP level was 1119 pg/mL (554-2383).

Serious adverse events (SAEs) were reported in 20% of participants receiving WINREVAIR 0.3 mg/kg, 33% of participants receiving WINREVAIR 0.7 mg/kg and 22% receiving placebo. Adverse events leading to treatment discontinuation were comparable between WINREVAIR 0.3 mg/kg and placebo, with no discontinuations in either group. There were three discontinuations due to an AE and one discontinuation due to a drug-related AE in the WINREVAIR 0.7 mg/kg group. Bleeding events occurred in 26% of patients in the WINREVAIR 0.3 mg/kg group, 27% in the WINREVAIR 0.7 mg/kg group and 24% of patients in the placebo group. Adverse events leading to death occurred in one patient in the WINREVAIR 0.7 mg/kg group and two patients in the placebo group. Adverse events with an incidence of ≥10% in any group included diarrhea, fatigue, peripheral edema, influenza, nasopharyngitis, urinary tract infection, dizziness, headache and dyspnea.

About the syndrome of combined post- and precapillary pulmonary hypertension and heart failure with preserved ejection fraction (CpcPH-HFpEF)

Combined post- and precapillary pulmonary hypertension and heart failure with preserved ejection fraction (CpcPH-HFpEF) is a distinct, identifiable and well-characterized condition that develops in people with long-term or advanced heart failure. Different from Group 1 pulmonary arterial hypertension (PAH), CpcPH-HFpEF is caused by two interrelated components: pulmonary vascular disease and cardiac disease. CpcPH-HFpEF is thought to be uncommon and underdiagnosed, typically impacting people who are older and have other comorbid conditions. It is associated with a worse prognosis and higher mortality rate compared to HFpEF alone. There are no treatments specifically approved for CpcPH-HFpEF.

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 for WINREVAIR

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.

Merck’s focus on cardiometabolic and respiratory diseases

Merck has a long history of developing treatments for cardiometabolic and respiratory diseases. Building on a legacy that began nearly 70 years ago with the introduction of our first cardiovascular therapy, we are committed to advancing research for patients impacted by cardiometabolic and respiratory diseases. Our focus spans a range of diseases, including atherosclerotic cardiovascular disease, heart failure, pulmonary hypertension and chronic obstructive pulmonary disease (COPD).

Advancements in the treatment of cardiometabolic and respiratory diseases can make a critical difference for patients and health systems around the world. At Merck, we strive for scientific excellence and innovation in all stages of research, from discovery through approval and life cycle management. We partner with experts in the community to advance research that can help improve the lives of patients.

For more information, visit **https://www.merck.com/research/cardiometabolic-and-respiratory-diseases/**.

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, 2025 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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