NEWS RELEASE

Merck Announces Phase 3 HYPERION Study of WINREVAIR™ (sotatercept-csrk) Met Primary Endpoint in Recently Diagnosed Adults with Pulmonary Arterial Hypertension (PAH)

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WINREVAIR significantly reduced the risk of clinical worsening events in recently diagnosed PAH patients over 70 percent of whom were on double background therapy

HYPERION, third Phase 3 study to demonstrate significant efficacy in adults with PAH, was previously stopped early based on review of available data from clinical program

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 3 HYPERION study evaluating WINREVAIR™ (sotatercept-csrk) versus placebo (both in combination with background therapy) in recently diagnosed adults with pulmonary arterial hypertension (PAH, WHO* Group 1) functional class (FC) II or III at intermediate or high risk of disease progression. HYPERION met its primary endpoint of time to clinical worsening (TTCW) as measured by a composite endpoint of all-cause death, the need for non-planned PAH-related hospitalization ≥ 24 hours, atrial septostomy, lung transplantation, or PAH deterioration.

In HYPERION, WINREVAIR added on top of background therapy (72.2% of patients on double therapy) within 12 months after initial diagnosis of PAH demonstrated a statistically significant and clinically meaningful reduction in the risk of clinical worsening events when compared to placebo. HYPERION is the third Phase 3 study of WINREVAIR to demonstrate significant efficacy in adults with PAH. The first was the STELLAR study previously **presented** at ACC.23, followed by the ZENITH study **presented** at ACC.25. In contrast to HYPERION, these previous studies

included a patient population where a majority of participants were on triple therapy. The safety profile of WINREVAIR was generally consistent with that observed in previous studies.

As **announced** in January, HYPERION was stopped early and moved to final analysis based on the positive results from the interim analysis of the Phase 3 ZENITH trial and a review of the totality of data from the WINREVAIR clinical program to date, and all patients were offered the opportunity to receive WINREVAIR through the SOTERIA open-label extension study.

“PAH is a progressive and debilitating disease with a poor prognosis that can be difficult to diagnose and treat. Patients often struggle for years to find a treatment plan that helps manage the disease, so it’s critical to provide new options earlier in the treatment journey,” said Dr. Vallerie McLaughlin**, Kim A Eagle MD Endowed Professor of Cardiovascular Medicine and Director, Pulmonary Hypertension Program, University of Michigan in Ann Arbor. “The HYPERION study demonstrated that WINREVAIR on top of background therapy met its primary outcome measure of reduction in the time to clinical worsening events in adults who have been recently diagnosed with PAH. WINREVAIR has brought significant optimism to patients, their families and investigators and we thank all study participants for being part of this important study.”

“To date, the strong clinical profile of WINREVAIR, a first-in-class activin signaling inhibitor, had been primarily established through previous studies in a prevalent patient population comprised of patients that were several years into their treatment journey. These positive results from HYPERION expand on the body of clinical evidence now including recently diagnosed adults, supporting the practice-changing potential of WINREVAIR in a broad spectrum of PAH patients, including those earlier in their treatment journey," said Dr. Joerg Koglin, senior vice president, head of general and specialty medicine, global clinical development, Merck Research Laboratories. “We look forward to presenting these data to the scientific community at a future medical meeting.”

Results from HYPERION will be presented at an upcoming medical meeting later this year and will be submitted to regulatory authorities. WINREVAIR is currently approved in more than 45 countries based on the results from the STELLAR study.

*World Health Organization

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

About HYPERION

The HYPERION study (**NCT04811092**) is a global, double-blind, placebo-controlled clinical trial to evaluate

WINREVAIR when added to background PAH therapy in newly diagnosed intermediate or high-risk PAH patients. Participants who enrolled in the study had a diagnosis of symptomatic PAH (WHO Group 1, classified as FC II [21.3%; 68/320 participants] or III [78.8%; 252/320 participants] within 12 months of study screening. Eligible participants had a confirmed diagnosis of PAH in any of the following subtypes: idiopathic PAH (59.4%; 190/320), heritable PAH (5.9%; 19/320), PAH associated with connective tissue diseases (CTD) (30.3%; 97/320), drug- or toxin-induced PAH (2.5%; 8/320), or PAH associated with simple, congenital systemic-to-pulmonary shunts at least 1 year following repair (1.9%; 6/320). The study excluded patients with PAH Group 1 subtypes: human immunodeficiency virus (HIV)-associated PAH and PAH associated with portal hypertension, schistosomiasis-associated PAH, pulmonary veno occlusive disease, and pulmonary capillary hemangiomatosis.

The study enrolled 320 study participants over the age of 18, who were randomized in a 1:1 ratio to receive either WINREVAIR or placebo both on top of background therapy. Participants were at an intermediate to high risk of disease progression and on stable doses of double (72.2%; 231/320 participants) or triple (27.8%; 89/320 participants) background PAH therapies for at least 90 days prior to screening. A majority (83.4%; 267/320 participants) were not on prostacyclin-infusion therapy.

The primary composite outcome measure is TTCW as measured by first confirmed morbidity or mortality event. Clinical worsening events are defined as all-cause death, non-planned PAH worsening-related hospitalization of ≥ 24 hours, atrial septostomy, lung transplantation, and deterioration in six-minute walk test from baseline combined with at least one of the following changes including worsening of WHO FC from baseline, signs/symptoms of increased right heart failure, addition of a background PAH therapy or change in the background PAH therapy delivery route to parenteral.

Secondary outcome measures were assessed relative to baseline at Week 24: proportion of participants achieving multicomponent improvement (consisting of improvement in 6MWD, improvement in N-terminal pro-B-type natriuretic peptide (NT-proBNP) level and improvement in WHO FC or maintenance of WHO FC II) as well as 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) 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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