NEWS RELEASE

Merck’s Enlicitide Decanoate, an Investigational Oral PCSK9 Inhibitor, Significantly Reduced LDL-C in Adults with Heterozygous Familial Hypercholesterolemia (HeFH) in Phase 3 CORALreef HeFH Trial

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Enlicitide has the potential to be the first approved oral PCSK9 inhibitor designed to deliver antibody-like efficacy and help address critical unmet needs for patients with HeFH to help combat the ongoing CV epidemic

Results were presented today at AHA Scientific Sessions 2025 and simultaneously published in the Journal of the American Medical Association

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced the first presentation of results from the pivotal Phase 3 CORALreef HeFH trial demonstrating that treatment with enlicitide decanoate, an investigational, once-daily oral proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, resulted in a statistically significant and clinically meaningful reduction in low-density lipoprotein cholesterol (LDL-C) of 59.4% compared to placebo at week 24 (95% CI: -65.6, -53.2; p<0.001) in adults with heterozygous familial hypercholesterolemia (HeFH). The effect size and safety profile was comparable to that observed in the pivotal Phase 3 **CORALreef Lipids** study. These late-breaking data will be presented for the first time today at the American Heart Association (AHA) Scientific Sessions 2025 (Abstract #4391641) and published simultaneously in the Journal of the American Medical Association.

In CORALreef HeFH, enlicitide demonstrated statistically significant and clinically meaningful reductions in LDL-C at week 24 (primary endpoint) and statistically significant reductions in secondary endpoints including LDL-C at one

year (week 52), and non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (ApoB), and lipoprotein(a) (Lp(a)) at week 24, in adults with HeFH receiving stable background lipid-lowering therapy including at least moderate or high intensity statin therapy. The overall safety profile was comparable to placebo. High adherence with study intervention (97%) and dosing instructions (96%) were observed across treatment groups.

“Data from CORALreef HeFH demonstrate the potential for enlicitide to help address critical unmet needs for adults with heterozygous familial hypercholesterolemia are at risk for premature atherosclerotic cardiovascular events yet a significant portion of patients do not achieve guideline-recommended LDL-C level despite available lipid-lowering therapies,” said Dr. Christie M. Ballantyne, a lead author of the CORALreef HeFH study and Professor of Medicine at Baylor College of Medicine. “As the potentially first approved oral PCSK9 inhibitor, enlicitide was designed to provide efficacy similar to anti-PCSK9 monoclonal antibodies and may be an important new treatment option to help adults with heterozygous familial hypercholesterolemia reach their guideline-recommended LDL-C goal. Lowering elevated LDL-C levels helps reduce the risk of atherosclerotic cardiovascular disease.”

“Results from the CORALreef HeFH study demonstrated statistically significant and sustained reductions in LDL-C, ApoB, non-HDL-C, and Lp(a) over one year in a diverse population of adults with heterozygous familial hypercholesterolemia receiving stable background lipid-lowering therapies,” said Dr. Dean Y. Li, president, Merck Research Laboratories. “We look forward to sharing the totality of the results from the CORALreef program presented at AHA with regulatory authorities and progressing enlicitide’s ongoing clinical development program to bring forward the potential first approved oral PCSK9 inhibitor to help address the growing CV epidemic.”

In CORALreef HeFH, LDL-C reductions were observed as early as week 4 and maintained through one year. Treatment with enlicitide resulted in a sustained statistically significant reduction in LDL-C of 61.5% compared to placebo (95% CI: -69.4, -53.7, $p<0.001$) at one year. At week 24, enlicitide demonstrated statistically significant reductions in non-HDL-C of 53.0% (95% CI: -58.5, -47.4, $p<0.001$), ApoB of 49.1% (95% CI: -54.0, -44.3, $p<0.001$) and Lp(a) of 27.5% (-95% CI: -34.3, -20.6, $p<0.001$) compared to placebo. The study also showed that 67.3% of patients treated with enlicitide achieved at least a 50% reduction in LDL-C along with an LDL-C <55 mg/dL (1.42 mmol/L) compared to 1.0% in the placebo arm at week 24.

Enlicitide had a safety profile similar to placebo. The incidence of adverse events (AEs), serious AEs and discontinuations due to AEs were similar between groups. Discontinuations due to AEs were low and similar between enlicitide (2.0%) and placebo (3.0%).

Merck plans to share data from this trial, along with data from CORALreef Lipids and CORALreef AddOn with regulatory authorities worldwide.

About CORALreef HeFH

CORALreef HeFH (**NCT05952869**) is a Phase 3, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of enlicitide compared to placebo in adults with HeFH who had a history of or were at risk for a major ASCVD event and received stable background lipid-lowering therapy including at least moderate or high intensity statins. The study enrolled 303 participants who were randomized 2:1 to receive either 20 mg of enlicitide orally once daily or placebo. The primary endpoints were mean percent change in LDL-C from baseline at week 24 versus placebo, number of participants with one or more AEs, and number of participants who discontinued study drug due to an AE. Key secondary multiplicity-controlled efficacy endpoints included change in LDL-C at one year (week 52) and changes in non-HDL-C, ApoB and Lp(a) at week 24. Non-multiplicity-controlled secondary endpoints included LDL-C goal attainment of at least a 50% reduction in LDL-C and an LDL-C <70 mg/dL (1.81 mmol/L) and at least 50% reduction in LDL-C and an LDL-C <55 mg/dL (1.42 mmol/L).

About enlicitide and PCSK9

Enlicitide has the potential to be the first FDA approved oral PCSK9 inhibitor. It is designed to lower LDL-C via the same biological mechanism as currently approved monoclonal antibody, injectable PCSK9 inhibitors but in a daily pill form. Enlicitide is a novel small molecule macrocyclic peptide candidate that binds to PCSK9 and inhibits the interaction of PCSK9 with LDL receptors.

PCSK9 plays a key role in cholesterol homeostasis by regulating levels of the LDL receptor, which is responsible for the uptake of cholesterol into cells. Inhibition of PCSK9 is designed to prevent the interaction of PCSK9 with LDL receptors. This results in greater numbers of LDL receptors available on the cell surface to remove LDL cholesterol from the blood.

About CORALreef Clinical Trial Program

The efficacy and safety profile of enlicitide is being evaluated through the comprehensive CORALreef Clinical Trial program evaluating over 19,000 participants who have hypercholesterolemia. As previously announced, enlicitide demonstrated statistically significant and clinically meaningful reductions in LDL-C in three pivotal Phase 3 studies: CORALreef Lipids (**NCT05952856**), CORALreef HeFH (**NCT05952869**) and CORALreef AddOn (**NCT06450366**). Enlicitide is continuing to be evaluated in the large cardiovascular outcomes trial, CORALreef Outcomes (**NCT06008756**), which has completed enrollment with over 14,500 participants. Additional CORALreef clinical trials include CORALreef Extension (**NCT06492291**), CORALreef Pediatric (**NCT07058077**) and CORALreef Combination (**NCT07216482**).

About heterozygous familial hypercholesterolemia (HeFH)

Heterozygous familial hypercholesterolemia (HeFH) is a common genetic disorder that affects approximately 1 in 250 individuals and is characterized by elevated levels of LDL-C. Patients with HeFH typically present with substantially elevated LDL-C levels and face an increased risk of premature atherosclerotic cardiovascular disease (ASCVD) due to cumulative lifetime exposure to LDL-C. HeFH cannot be managed through lifestyle and diet changes alone, and cholesterol-lowering medication is typically needed for patients to manage this condition. A large proportion of patients with HeFH fail to achieve guideline-recommended LDL-C goals despite available therapies and have a 13-fold higher risk for coronary artery disease compared with the general population.

About the CV epidemic and atherosclerotic cardiovascular disease

The silent CV epidemic is the leading cause of deaths globally, contributing to the majority of heart attacks and strokes, and deaths related to CV continue to rise. ASCVD accounts for 85% of CV deaths. It is caused by the buildup of plaque within the arteries, leading to narrowed or blocked blood vessels that can result in serious CV events such as heart attacks and strokes as well as coronary artery disease, peripheral artery disease and cerebrovascular disease.

Merck's focus on cardiovascular disease

Merck has a long history of developing treatments for cardiovascular disease. Nearly 70 years ago, we introduced our first cardiovascular therapy—and our scientific efforts to understand and treat cardiovascular-related disorders have continued. Cardiovascular disease continues to be one of the most serious health challenges of the 21st century and is the leading cause of death worldwide. Approximately 18 million people across the globe die from cardiovascular disease every year; in the United States, one person dies every 36 seconds from cardiovascular disease.

At Merck, we strive for scientific excellence and innovation in all stages of research, from discovery through approval and life cycle management. We work with experts throughout the cardiovascular and pulmonary community to advance research that can help improve the lives of patients globally.

Information for other currently enrolling cardiovascular studies can be found by visiting: **https://www.merckclinicaltrials.com/cardiovascular**.

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**).

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