NEWS RELEASE

Merck’s Enlicitide Decanoate, an Investigational Oral PCSK9 Inhibitor, Demonstrated Significantly Greater LDL-C Reductions at Eight Weeks Compared to Guideline-Recommended Oral Non-Statin Therapies When Added to Background Statins

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The Phase 3 CORALreef AddOn trial compared the efficacy and safety of enlicitide to bempedoic acid, ezetimibe or bempedoic acid with ezetimibe

Enlicitide has the potential to be the first approved oral PCSK9 inhibitor designed to help address critical unmet needs for patients with hypercholesterolemia and help combat the ongoing cardiovascular (CV) epidemic

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced detailed results from CORALreef AddOn, an active comparator study designed to evaluate the efficacy and safety of enlicitide decanoate compared to other oral non-statin therapies (bempedoic acid, ezetimibe or bempedoic acid with ezetimibe) when added to background statins in adults with hypercholesterolemia who have a history of or are at risk for atherosclerotic cardiovascular disease (ASCVD). This is the third positive Phase 3 study of enlicitide decanoate, an investigational, once-daily oral proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor. In the study, treatment with enlicitide resulted in statistically significant and clinically meaningful reductions in low-density lipoprotein cholesterol (LDL-C) compared to bempedoic acid, ezetimibe or bempedoic acid with ezetimibe at eight weeks (day 56) of treatment. The observed LDL-C reduction resulted in greater LDL-C goal attainment with enlicitide than the comparators (secondary endpoint). These late-breaking data were

presented today at the American College of Cardiology's Annual Scientific Session and Expo (ACC.26) (Abstract #336-07) and published simultaneously in JACC.

Results from CORALreef AddOn showed that at eight weeks, enlicitide reduced LDL-C by 64.6% from baseline when added to background treatment with a statin. Additionally, enlicitide reduced LDL-C by 56.7% versus bempedoic acid (95% CI: -64.3, -49.0, p<.0.001), 36.0% versus ezetimibe (95% CI: -41.8, -30.2; p<0.001) and 28.1% versus bempedoic acid with ezetimibe (95% CI: -33.6, -22.6; p<0.001). The overall safety profile was consistent with that observed in the Phase 3 CORALreef **Lipids** and CORALreef **HeFH** clinical trials. High adherence with study intervention (98%) and dosing instructions (≥96%) were observed across treatment groups.

"Results from CORALreef AddOn demonstrate that enlicitide can significantly reduce LDL-C compared to established oral non-statin treatment options, reinforcing the practice-changing potential of an oral PCSK9 inhibitor," said Alberico Catapano, a lead author of the study, professor of pharmacology and director of the center for the study of atherosclerosis at IRCCS Multimedica and University of Milan. "LDL-C is a major modifiable risk factor for ASCVD; ASCVD accounts for the majority of cardiovascular deaths and is a key driver of the ongoing CV epidemic. Nearly 70 percent of people with ASCVD who are treated with lipid-lowering therapies do not reach their target LDL cholesterol levels. Enlicitide, an investigational oral PSCK9 inhibitor, may help close gaps in lipid management by enabling robust LDL-C lowering among at-risk patients not at goal on statin therapy."

"As part of Merck's commitment to help address the CV epidemic, enlicitide was designed to deliver antibody-like LDL-C reduction with a placebo-like safety profile and has the potential to be the first approved oral PCSK9 inhibitor," said Dr. Joerg Koglin, senior vice president, head of general and specialty medicine, global clinical development, Merck Research Laboratories. "The consistency of the results from CORALreef AddOn, together with the data from CORALreef Lipids and CORALreef HeFH, further establish the efficacy and safety profile of enlicitide as a promising potential treatment solution for patients in need of further LDL-C reduction."

Enlicitide also demonstrated statistically significant reductions at eight weeks across key secondary endpoints. Enlicitide significantly reduced apolipoprotein B (ApoB) by 54.6% compared to baseline versus a 5.4% reduction from baseline with bempedoic acid, a 20.2% reduction from baseline with ezetimibe and a 27.7% reduction from baseline with bempedoic acid with ezetimibe (all p<0.001 versus enlicitide). Additionally, treatment with enlicitide significantly reduced non-high-density lipoprotein cholesterol (non-HDL-C) by 58.0% compared to baseline versus a 5.2% reduction from baseline with bempedoic acid, a 25.1% reduction from baseline with ezetimibe and a 31.8% reduction from baseline with bempedoic acid with ezetimibe (all p<0.001 versus enlicitide).

Reduction and goal attainment were also included in the study across a number of measures at eight weeks (non-multiplicity controlled). Treatment with enlicitide resulted in reductions in lipoprotein(a) (Lp(a)) of 26.2% compared to baseline versus an increase of 8.1% from baseline with bempedoic acid, no change from baseline with ezetimibe

and an increase of 10.4% from baseline with bempedoic acid with ezetimibe. The study also showed that 78.2% of patients treated with enlicitide achieved the prespecified goal of at least 50% reduction in LDL-C along with an LDL-C <55 mg/dL (1.42 mmol/L) compared to 2.0% with bempedoic acid, 8.0% with ezetimibe and 20.0% with bempedoic acid with ezetimibe.

The safety profile of enlicitide was consistent with that observed in the Phase 3 CORALreef Lipids and CORALreef HeFH trials, with no clinically meaningful differences in incidences of adverse events (AEs) across the treatment groups. There were no serious AEs (SAEs), discontinuations due to drug-related AEs or discontinuations due to drug-related SAEs for those treated with enlicitide.

In December 2025, the U.S. Food and Drug Administration (FDA) selected enlicitide to receive the Commissioner's National Priority Voucher (CNPV). Merck looks forward to the possibility of bringing enlicitide, which has the potential to be the first approved oral PCSK9 inhibitor, to patients with hypercholesterolemia as quickly as possible.

About CORALreef AddOn

CORALreef AddOn (**NCT06450366**) is a Phase 3, randomized, double-blind, multicenter study designed to evaluate the efficacy and safety of enlicitide versus bempedoic acid, ezetimibe and bempedoic acid with ezetimibe, in adults with hypercholesterolemia and a history of a major ASCVD event or at risk for a first major ASCVD event who are treated with a statin. The primary endpoint is the mean percent change from baseline in LDL-C at week eight. Key secondary endpoints include mean percent change from baseline in non-HDL-C and ApoB. Non-multiplicity-controlled secondary endpoints included mean percent change in Lp(a) and the proportion of patients with at least a 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 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 an investigational novel macrocyclic peptide 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 hypercholesterolemia

Hypercholesterolemia, a type of hyperlipidemia, is a disorder in which there are elevated LDL-C levels in the blood. It affects approximately 86 million adults in the U.S. and is a major risk factor for ASCVD. Nearly 70% of people with ASCVD who are treated with lipid-lowering therapies do not reach target LDL cholesterol levels. High LDL-C, if left untreated, can lead to ASCVD events such as heart attacks and strokes.

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 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**).

Media Contacts:

Julie Cunningham
julie.cunningham@merck.com

Nikki Lupinacci
nicole.lupinacci@merck.com

Investor Contacts:

Peter Dannenbaum
(732) 594-1579

Ayn Wisler
(917) 691-6218

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