NEWS RELEASE

Merck’s Enlicitide Decanoate, an Investigational Oral PCSK9 Inhibitor, Significantly Reduced LDL-C in Phase 3 CORALreef Lipids Trial

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Enlicitide, designed to deliver antibody-like efficacy, has the potential to be the first approved oral PCSK9 inhibitor to lower LDL-C with a safety profile comparable to placebo

Enlicitide may help address unmet needs in ASCVD, a key driver of 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 the first presentation of results from the pivotal Phase 3 CORALreef Lipids 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 55.8% (primary analysis; 95% CI: -60.9, -50.7; p<0.001) and of 59.7% in a post-hoc reanalysis (95% CI: -62.3, -57.1; p<0.001) compared to placebo at week 24. These late-breaking data will be presented for the first time today at the American Heart Association (AHA) Scientific Sessions 2025 (Abstract #4391578) and were selected for the Late-Breaking Science News Briefing.

In CORALreef Lipids, adults with or at-risk for atherosclerotic cardiovascular disease (ASCVD) on background lipid-lowering therapies or a documented statin intolerance who received once-daily oral enlicitide had statistically significant and clinically meaningful reductions in LDL-C at week 24 (primary endpoint) and statistically significant and sustained reductions in LDL-C through one year (week 52). Enlicitide demonstrated statistically significant reductions in secondary endpoints including non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B

(ApoB) and lipoprotein(a) (Lp(a)) at week 24. The overall safety profile was comparable to placebo. High adherence with study intervention (97%) and dosing instructions (≥97%) were observed across treatment groups.

“Enlicitide demonstrated impressive LDL-C reductions with placebo-like safety in the CORALreef Lipids study, underscoring the practice-changing potential of an oral PCSK9 inhibitor,” said Dr. Ann Marie Navar, a lead author of the study and Associate Professor of Medicine in the Division of Cardiology at UT Southwestern Medical Center. “Despite the availability of lipid-lowering therapies such as statins and injectable PCSK9 inhibitors, the majority of patients with atherosclerotic cardiovascular disease do not reach their LDL-C goal. Enlicitide has the potential to help close gaps in achievement of lipid goals in patients with and at risk for cardiovascular events and ultimately help address the ongoing CV epidemic.”

“Enlicitide was designed to deliver PCSK9 antibody-like efficacy and specificity in an easy-to-use pill,” said Dr. Dean Y. Li, president, Merck Research Laboratories. “Enlicitide, if approved, adds to physicians’ armamentarium to lower LDL-C. This moment is the result of Merck’s legacy and commitment to researching ways to help improve ASCVD outcomes for millions worldwide and our strength in medicinal chemistry using our novel macrocyclic peptide platform. Cardiovascular disease is the leading cause of death globally, and we look forward to bringing a potential new option to help address the CV epidemic.”

At one year, enlicitide showed a sustained statistically significant reduction in LDL-C of 47.6% (primary analysis; 95% CI: -52.7, -42.5; p<0.001) and of 52.4% (post-hoc reanalysis; 95% CI: -55.1, -49.7; p<0.001) compared to placebo. At week 24, enlicitide demonstrated reductions in non-HDL-C of 53.4% (95% CI: -55.5, -51.2; p<0.001), ApoB of 50.3% (95% CI: -52.1, -48.5; p<0.001) and Lp(a) of 28.2% (95% CI: -30.3, -26.0; p<0.001) compared to placebo. The study also showed that 67.5% of patients treated with enlicitide achieved the rigorous prespecified goal of at least 50% reduction in LDL-C along with an LDL-C <55 mg/dL (1.42 mmol/L) compared to 1.2% in the placebo arm at week 24.

Enlicitide had a safety profile similar to placebo. There were no apparent differences between the enlicitide and placebo groups in the incidence of any adverse events (AEs), serious AEs or deaths. Discontinuations due to AEs were low and similar between enlicitide (3.1%) and placebo (4.1%).

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

About CORALreef Lipids

CORALreef Lipids (**NCT05952856**) is a Phase 3 randomized, double-blind, placebo-controlled study designed to evaluate the efficacy, safety and tolerability of enlicitide decanoate in adults with hypercholesterolemia and a history of a major atherosclerotic cardiovascular disease (ASCVD) event or increased risk for a first event.

Participants were required to be treated with stable lipid-lowering therapies including at least a moderate or high intensity statin (or have documented statin intolerance). The study enrolled 2,912 participants who were randomized 2:1 to receive either 20mg of once-daily oral enlicitide (n=1,942) or placebo (n=970). 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. Multiplicity-controlled secondary efficacy endpoints included: mean percent change from baseline in LDL-C at week 52, mean percent change from baseline in other key atherogenic lipids at week 24 (non-HDL-C, ApoB and Lp(a)).

A post-hoc reanalysis was conducted to revise missing data handling rules that resulted in 5 biologically impossible baseline values being included in the primary analysis. The intent of the reanalysis was to provide a more clinically accurate estimate of the treatment effect.

CORALreef Lipids is the largest completed Phase 3 study evaluating enlicitide in a broad range of participants with elevated LDL-C.

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 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 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.

Advancements in the treatment of cardiovascular disease 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 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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