Approval Announcement

Merck's LIPFENDRA® (enlicitide) is the First and Only Once-Daily Oral PCSK9 Inhibitor Approved by the U.S. FDA to Reduce LDL-C in Adults with Hypercholesterolemia

At week 24 in the CORALreef Lipids and CORALreef HeFH trials, LIPFENDRA significantly reduced LDL-C by a placebo-adjusted 56% and 59%, respectively

LIPFENDRA is a novel macrocyclic peptide that binds to PCSK9 and inhibits the interaction of PCSK9 with LDL receptors

RAHWAY, N.J., July 16, 2026 – Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced the U.S. Food and Drug Administration (FDA) has approved LIPFENDRA® (enlicitide) tablets 20 mg. LIPFENDRA is indicated as an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in adults with hypercholesterolemia, including heterozygous familial hypercholesterolemia (HeFH). Cardiovascular outcomes trials have demonstrated that reducing LDL-C lowers the risk for major adverse cardiovascular events (MACE) in adults at increased risk when treated with statins or monoclonal antibody proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors as an add-on to statin therapy. LIPFENDRA is a novel macrocyclic peptide and is the first FDA-approved oral PCSK9 inhibitor shown to lower LDL-C, also known as bad cholesterol.

"By harnessing the innovative science of PCSK9 inhibitors and novel macrocyclic peptide technology, LIPFENDRA was designed to significantly lower LDL-C in the form of a convenient once-daily pill," said Dr. Dean Y. Li, president, Merck Research Laboratories. "This is a pivotal moment as we bring the first U.S. FDA-approved oral PCSK9 inhibitor to adults with high LDL-C, offering patients an important new option. We're proud of our work with regulators on this rigorous and efficient review process."

The approval is based on two Phase 3 trials from the CORALreef clinical program: CORALreef Lipids and CORALreef HeFH. In CORALreef Lipids, LIPFENDRA reduced LDL-C by 56% compared to placebo at week 24 (primary endpoint: 57% reduction from baseline). A 60% decrease from baseline in LDL-C was observed with LIPFENDRA when biologically impossible baseline LDL-C values were removed according to revised data handling rules (post-hoc). In CORALreef HeFH, LIPFENDRA reduced LDL-C by 59% at week 24 compared to

placebo (primary endpoint: 58% reduction from baseline). Results from these Phase 3 trials showed treatment with LIPFENDRA resulted in reductions across other atherogenic lipoproteins associated with atherosclerotic cardiovascular disease (ASCVD) risk including non-high-density lipoprotein cholesterol (non-HDL-C) and apolipoprotein B (ApoB). The safety profile of LIPFENDRA in CORALreef Lipids was similar to placebo. In CORALreef HeFH, the most common adverse reactions in adults with HeFH treated with LIPFENDRA that occurred at higher frequencies compared to placebo were diarrhea (LIPFENDRA 7%, placebo 2%) and dizziness (LIPFENDRA 9%, placebo 4%). In both trials, similar proportions of LIPFENDRA-treated patients and placebo-treated patients discontinued treatment because of an adverse reaction. For additional information on results from the CORALreef trials, see "Clinical data supporting FDA approval" below.

"High LDL-C is a major risk factor for atherosclerotic cardiovascular disease, which is the leading cause of death globally," said Dr. Ann Marie Navar, a lead author of the CORALreef Lipids study and associate professor of medicine in the Division of Cardiology at UT Southwestern Medical Center. "In two Phase 3 trials, LIPFENDRA led to impressive reductions in LDL-C. Now, for the first time, patients have an oral PCSK9 inhibitor for LDL lowering."

An ongoing clinical trial is studying the effect of LIPFENDRA on cardiovascular morbidity and mortality. It is not yet known if LIPFENDRA can reduce the risk of cardiovascular morbidity and mortality.

"One of the greatest opportunities to help manage the risk of ASCVD lies in the timely identification and appropriate treatment of risk factors, such as LDL-C," said Katherine Wilemon, CEO of the Family Heart Foundation. "We are encouraged by the approval of a new oral PCSK9 inhibitor option for adults who need additional LDL-C lowering."

Clinical data supporting FDA approval

LIPFENDRA was approved based on results from two pivotal Phase 3 trials from the CORALreef clinical trial program:

- At week 24, in the CORALreef Lipids trial, treatment with LIPFENDRA resulted in:
  - A statistically significant and clinically meaningful reduction in LDL-C of 56% compared to placebo at week 24 (95% CI: -61, -51; $p<0.001$), with a reduction from baseline (primary endpoint) in LDL-C of 57% for LIPFENDRA compared to an increase of 3% for placebo;
  - When LDL-C values ≤0 were removed according to revised data handling rules (post-hoc), a statistically significant and clinically meaningful reduction in LDL-C of 60% for LIPFENDRA compared to an increase of 3% for placebo at week 24 (95% CI: -62, -57%).
  - Statistically significant reductions in secondary endpoints from baseline to week 24 compared to an increase of 3% for placebo:
    - 54% mean reduction in non-HDL-C for LIPFENDRA;
    - 50% mean reduction in ApoB for LIPFENDRA.

- At week 24, in the CORALreef HeFH trial, treatment with LIPFENDRA resulted in:
  - A statistically significant and clinically meaningful reduction in LDL-C of 59% compared to placebo (95% CI: -66, -53; p<0.001), with a reduction from baseline (primary endpoint) in LDL-C of 58% for LIPFENDRA compared to an increase of 3% for placebo;
  - Statistically significant reductions in secondary endpoints from baseline to week 24 compared to an increase of 2% for placebo:
    - 52% mean reduction in non-HDL-C for LIPFENDRA;
    - 48% mean reduction in ApoB for LIPFENDRA.

In CORALreef Lipids, the frequencies of adverse reactions in adults with hypercholesterolemia were similar between those treated with LIPFENDRA and those receiving placebo. Similar proportions of LIPFENDRA-treated patients and placebo-treated patients discontinued treatment because of an adverse reaction. In CORALreef HeFH, the most common adverse reactions in adults with HeFH treated with LIPFENDRA that occurred at higher frequencies compared to placebo were diarrhea (LIPFENDRA 7%, placebo 2%) and dizziness (LIPFENDRA 9%, placebo 4%). Similar proportions of LIPFENDRA-treated patients and placebo-treated patients discontinued treatment because of an adverse reaction. The safety profile observed in adults with HeFH in CORALreef HeFH was otherwise generally consistent with that observed in adults with hypercholesterolemia in CORALreef Lipids.

About CORALreef Lipids and HeFH

CORALreef Lipids (NCT05952856) was a Phase 3, multicenter, double-blind, randomized, placebo-controlled study in which 2,904 patients with hypercholesterolemia (including those with and without HeFH) and a history of a major ASCVD event or increased risk for development of a first major ASCVD event were randomized in a 2:1 ratio to receive LIPFENDRA 20 mg orally once daily (n=1,935) or placebo (n=969) for 52 weeks. Patients required additional LDL-C reduction despite stable lipid-lowering treatment with moderate- or high-intensity statins (unless statin intolerance was documented) with or without other lipid-modifying therapy. Patients taking PCSK9 inhibitors were excluded from the trial. The primary efficacy outcome measure was the mean percent change from baseline to week 24 in LDL-C.

CORALreef HeFH (NCT05952869) was a Phase 3, multicenter, double-blind, randomized, placebo-controlled study in which 303 patients with HeFH were randomized in a 2:1 ratio to receive LIPFENDRA 20 mg orally once daily (n=202) or placebo (n=101) for 52 weeks. Patients required additional LDL-C reduction despite stable lipid-lowering treatment with moderate- or high-intensity statins, with or without other lipid-modifying therapy. The diagnosis of HeFH was made by clinical criteria or genotyping. The primary efficacy outcome measure was the mean percent change from baseline to week 24 in LDL-C.

About LIPFENDRA® (enlicitide) tablets 20 mg

LIPFENDRA is an oral proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor FDA-approved as an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in adults with hypercholesterolemia, including heterozygous familial hypercholesterolemia (HeFH). Cardiovascular outcomes trials have demonstrated that reducing

LIPFENDRA® (enlicitide) tablets 20 mg

LDL-C lowers the risk for major adverse cardiovascular events (MACE) in adults at increased risk, when treated with statins or monoclonal antibody PCSK9 inhibitors as an add-on to statin therapy. LIPFENDRA is the first oral PCSK9 inhibitor approved to reduce LDL-C and is a novel macrocyclic peptide that inhibits the binding of PCSK9 to LDL receptors.

Selected Safety Information

In the CORALreef Lipids trial the frequencies of adverse reactions were similar between adults treated with LIPFENDRA and those receiving placebo. Similar proportions of LIPFENDRA-treated patients and placebo-treated patients discontinued treatment because of an adverse reaction.

In the CORALreef HeFH trial the most common adverse reactions in adults with HeFH that occurred at higher frequencies compared to placebo were diarrhea (LIPFENDRA 7%, placebo 2%) and dizziness (LIPFENDRA 9%, placebo 4%). Similar proportions of LIPFENDRA-treated patients and placebo-treated patients discontinued treatment because of an adverse reaction. The safety profile was otherwise generally consistent with that observed in adults with hypercholesterolemia in the CORALreef Lipids trial.

LIPFENDRA Dosage and Administration

The recommended dosage of LIPFENDRA is one 20 mg tablet taken orally once daily. Assess LDL-C when clinically appropriate. The LDL-C-lowering effect of LIPFENDRA may be measured as early as 4 weeks after initiation.

Take LIPFENDRA on an empty stomach in the morning with water, black coffee, or plain tea. Swallow the tablet whole. Do not split, crush, or chew the tablet. After taking LIPFENDRA, wait at least 30 minutes before eating food or drinking beverages other than water, black coffee or plain tea.

LIPFENDRA can be taken with other medications.

If a dose is missed, take the missed dose as soon as possible, at least 30 minutes before the next food or drink (other than water, black coffee, or plain tea). Do not take 2 doses on the same day.

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.

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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).

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Please see Prescribing Information for LIPFENDRA® (enlicitide) at https://www.merck.com/product/usa/pi_circulars/l/lipfendra/lipfendra_pi.pdf and Patient

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