Merck Initiates Phase 3 Clinical Program for Oral PCSK9 Inhibitor Candidate MK-0616

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Program plans to enroll approximately 17,000 participants across three global studies

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced the initiation of the company's Phase 3 clinical program, CORALreef, for MK-0616, an investigational, oral proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, being evaluated for the treatment of adults with hypercholesterolemia. This is the first Phase 3 clinical program for an oral PCSK9 inhibitor. The first participants are now enrolling in two registrational Phase 3 studies evaluating low-density lipoprotein (LDL) cholesterol reduction: CORALreef Lipids and CORALreef HeFH. Merck also plans to initiate a Phase 3 cardiovascular outcomes study, CORALreef Outcomes by the end of 2023.

PCSK9 is a validated target for lowering LDL cholesterol. However, there are no oral PCSK9 inhibitors available to physicians and patients. The Phase 3 CORALreef program follows robust Phase 2b results presented at ACC.23/WCC, in which MK-0616 significantly reduced LDL cholesterol compared to placebo at all doses studied in participants with hypercholesterolemia with a broad spectrum of atherosclerotic cardiovascular disease (ASCVD) risk, including participants on high-intensity statin therapy. MK-0616 was generally well-tolerated.

“Elevated LDL cholesterol is a major risk factor for cardiovascular disease, the leading cause of death worldwide. Despite several well-established lipid-lowering therapies, millions of people globally do not achieve and maintain their desired LDL cholesterol treatment goals, leaving them at risk for cardiac events,” said Dr. Marc Sabatine, Chair of the Thrombolysis in Myocardial Infarction (TIMI) Study Group, the Lewis Dexter, MD, Distinguished Chair in Cardiovascular Medicine at Brigham and Women’s Hospital, and a Professor of Medicine at Harvard Medical School.
“MK-0616 showed statistically significant LDL cholesterol lowering activity in the Phase 2 trial and has the unique aspect of being a once daily pill. With its novel modality among PCSK9 inhibitors, MK-0616 could provide an important option for patients for the treatment of hypercholesterolemia.”

“The initiation of a comprehensive Phase 3 program is an important milestone in our goal to offer a highly effective oral medication that could be accessed by a broad population and potentially allow substantially more people to reach their LDL treatment goals,” said Dr. Joerg Koglin, senior vice president, global clinical development, Merck Research Laboratories. “In acknowledgment of the significant racial, ethnic and gender disparities in cardiovascular care, Merck is taking proactive measures to engage potential participants from populations that have historically been underrepresented in clinical trials of this type.”

CORALreef Lipids (NCT05952856) is a randomized, double-blind study enrolling a broad group of participants, including participants with history of at least one major ASCVD event and those at intermediate to high risk for a first event. Participants must be treated with stable lipid lowering therapies, including at least a moderate or high intensity statin, or have documented statin intolerance. The primary objective of this study is to evaluate the efficacy of MK-0616 compared with placebo on the mean percent change from baseline in LDL cholesterol at Week 24. Participants will receive 20 mg of MK-0616 orally once daily for up to 52 weeks or placebo, on top of their background lipid lowering therapies.

CORALreef HeFH (NCT05952869) is a similar study, focused on adult participants with heterozygous familial hypercholesterolemia, who are being treated with stable lipid lowering therapies, including at least a moderate or high intensity statin. The estimated primary completion date for CORALreef Lipids and CORALreef HeFH studies is September 2025.

CORALreef Outcomes (TIMI 77) (NCT06008756) is a randomized, double-blind study in adult participants with high cardiovascular risk, who are being treated with stable lipid lowering therapies, including at least a moderate or high intensity statin. The primary objective is to evaluate the efficacy of MK-0616 compared with placebo, on top of background lipid lowering therapies, in increasing the time to the first occurrence of one of the following events: coronary heart disease death, ischemic stroke, myocardial infarction, acute limb ischemia or major amputation, or urgent arterial revascularization. Merck is collaborating with the TIMI Study Group, a leading academic research organization for cardiovascular clinical trials, on the CORALreef Outcomes study. The estimated primary completion date is November 2029.

Merck’s broad, global Phase 3 program for MK-0616 aims to enroll approximately 17,000 participants across the CORALreef Lipids, CORALreef HeFH and CORALreef Outcomes studies.

About PCSK9 and MK-0616
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 prevents 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.

MK-0616 is an investigational, potentially first oral PCSK9 inhibitor designed to lower LDL cholesterol via the same biological mechanism as currently approved injectable PCSK9 inhibitors but in a daily pill form. MK-0616 is a macrocyclic peptide that binds to PCSK9 and inhibits the interaction of PCSK9 with LDL receptors.

About Hypercholesterolemia

Hypercholesterolemia, a disorder in which there are elevated LDL cholesterol levels in the blood, affects approximately 86 million adults in the U.S., with nearly 25 million having very high total cholesterol above 240 mg/dL. It is a major risk factor associated with ASCVD, which is the leading cause of death in the U.S. and globally. Despite adjusting diet and taking statin therapies, many patients with hypercholesterolemia are still not reaching, or maintaining, their LDL cholesterol lowering goals as recommended by guidelines. High LDL cholesterol, if left untreated, can lead to a high risk of ASCVD events, such as heart attacks and strokes.

Merck's Focus on Cardiovascular Disease

Merck has a long history of developing treatments for cardiovascular disease. More than 60 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. Approximately 18 million people across the globe die every year, and 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 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 the global outbreak of novel coronavirus disease (COVID-19); 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, 2022 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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