



NEWS RELEASE

Merck Scientists Publish Landmark Paper on Novel Method for Large-Scale Biocatalytic Synthesis of Investigational Oral PCSK9 Inhibitor, Enlicitide Decanoate

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Publication in Science magazine outlines blueprint for the scalable synthesis of complex orally available macrocyclic peptides

Enlicitide, a novel macrocyclic peptide, has the potential to be the first approved oral PCSK9 inhibitor

RAHWAY, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside the United States and Canada, announced today the publication of work describing the large-scale synthesis of enlicitide decanoate, the company's investigational oral PCSK9 inhibitor, using a tailored suite of enzymes in the latest issue of the peer reviewed journal Science.

"Macrocyclic peptides have the potential to unlock new opportunities to develop oral treatment options for challenging therapeutic targets and broaden patient access," said Dr. Dean Y. Li, president, Merck Research Laboratories. "The scalable production process for enlicitide described in this publication showcases Merck's scientific capabilities and underscores our sustained commitment to helping address the global cardiovascular epidemic."

In this publication, Merck scientists detail the biocatalytic assembly of enlicitide using a suite of enzymes that catalyze selective peptide fragment formation, coupling, and macrocyclization. Together with efficient purifications



using crystallization, this strategy enabled the manufacture of a product that would not be possible with traditional synthetic methods. The method described offers a sustainable blueprint for the scalable development of complex macrocyclic peptide therapeutics, environmental advantages and manufacturing efficiencies that support efforts to expand patient access.

About biocatalysis

Biocatalysis describes the process of using enzymes to conduct chemical synthesis. Biocatalysis offers environmental sustainability advantages over chemical catalyst methods. For more than 25 years Merck has invested in the development of biocatalysis including the generation of novel enzymes for the synthesis and novel manufacturing of pharmaceutical products at scale.

About macrocyclic peptides

Over a decade ago, an interdisciplinary team of Merck scientists were challenged to create a type of medicine that may provide the potency and selectivity of a biologic therapy but in the form of a pill. Macrocyclic peptides are intricate ring-shaped molecules with the ability to target and disrupt protein-protein interactions while retaining oral bioavailability. For more information regarding our approach to macrocyclic peptides, visit [merck.com](https://www.merck.com)

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 a novel 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 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.

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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