A single dose of Lilly's PCSK9 base editor, VERVE-102, reduced PCSK9 by up to 88% and LDL-C by up to 62%, with durable effects supporting its potential as a one-time treatment for hypercholesterolemia

May 25, 2026

In the Phase 1b Heart-2 trial, a single intravenous infusion of VERVE-102 produced dose-dependent lowering of PCSK9 and LDL-C, with both reductions sustained over follow-up of up to 18 months in participants at high risk for cardiovascular disease

VERVE-102 is designed to mimic the protective effect of naturally occurring loss-of-function variants in PCSK9, which are associated with markedly lower lifetime risk of coronary heart disease

Lilly plans to begin enrolling the Phase 2 clinical study of VERVE-102 by the end of this year

INDIANAPOLIS, May 25, 2026 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive Phase 1b Heart-2 study results for VERVE-102, an investigational *in vivo* base editing medicine designed to durably turn off the *PCSK9* gene in the liver and lower blood low-density lipoprotein cholesterol (LDL-C) following a single infusion. The Heart-2 trial is evaluating VERVE-102 in adults with heterozygous familial hypercholesterolemia (HeFH) or premature coronary artery disease (CAD). These data were presented as a late-breaking oral presentation at the European Atherosclerosis Society (EAS) Congress and simultaneously published in *The New England Journal of Medicine*.

In the Heart-2 study, a single intravenous infusion of VERVE-102 resulted in meaningful lowering of circulating PCSK9 protein and corresponding reductions in LDL-C across all evaluated dose levels. In this interim analysis of 35 participants, a single dose of VERVE-102 resulted in dose-dependent mean reductions in PCSK9 ranging from 51% to 88%, at the lowest 0.3 mg/kg dose to the highest 1.0 mg/kg dose, respectively. Corresponding mean reductions in LDL-C were 9% (0.3 mg/kg), 44% (0.45 mg/kg), 45% (0.6 mg/kg), 33% (0.7 mg/kg), 51% (0.8 mg/kg), and 62% (1.0 mg/kg). These reductions were sustained over time, with durability observed for up to 18 months following treatment.

"These early data give us encouraging evidence that *in vivo* base editing of *PCSK9* may offer a novel approach to achieving substantial and durable LDL-C reduction with a one-time treatment," said Riyaz S. Patel, M.D., cardiologist at Barts Health NHS Trust and professor of cardiology at University College London. "Many patients with elevated LDL-C struggle to achieve sustained control despite ongoing efforts with the medicines available today, putting them at significant risk for cardiovascular events. With coronary artery disease still one of the leading causes of death worldwide, the need for new approaches is real."

VERVE-102 was well tolerated across all dose levels with no treatment-related serious adverse events (AEs) and no dose-limiting toxicities reported. AEs related to VERVE-102 included low-grade infusion-related reactions and fatigue. All participants received the full planned dose, and no participant withdrew from the study.

"Twenty years ago, genetics showed us that people born with *PCSK9* naturally turned off have low LDL-C for life and are remarkably protected from heart attack, yet today's chronic therapies struggle to deliver this lifelong lowering," said Sekar Kathiresan, M.D., Lilly senior vice president, and co-founder of Verve Therapeutics. "The Heart-2 results provide early clinical evidence that a single dose of VERVE-102 may mimic the LDL-C lowering effects of *PCSK9* cardioprotective variants, potentially transforming cardiovascular care from chronic management to a one-time treatment."

The U.S. Food and Drug Administration (FDA) has granted Fast Track designation for VERVE-102 to reduce LDL-C in participants with hyperlipidemia and high lifetime cardiovascular risk. HeFH affects approximately 1 in 200 to 250 people and is characterized by lifelong elevations in LDL-C, leading to premature cardiovascular disease, including CAD.[1,2] Worldwide, CAD remains a leading cause of death, affecting more than 300 million people.[3]

Lilly plans to initiate the Phase 2 clinical study of VERVE-102 by the end of this year.

About VERVE-102 and VERVE trial programs
VERVE-102, an investigational *in vivo* base editing medicine, is designed to be a single-course treatment that turns off the *PCSK9* gene in the liver and durably reduces disease-driving LDL-C. VERVE-102 consists of a messenger RNA encoding an adenine base editor and a guide RNA (gRNA) targeting the *PCSK9* gene. Both are encapsulated in a lipid nanoparticle (LNP) and administered as a single intravenous infusion over approximately four hours. VERVE-102 uses Verve's proprietary GalNAc-LNP delivery technology, which is designed to allow the LNP to access liver cells using either the low-density lipoprotein receptor (LDLR) or the asialoglycoprotein receptor (ASGPR).

In addition to the PCSK9 program, the Pulse-1 Phase 1b trial for VERVE-201, an investigational *in vivo* gene editing medicine targeting the *ANGPTL3* gene, is ongoing.

About Heart-2
Heart-2 is an ongoing open-label, single-ascending dose Phase 1b study designed to evaluate the safety, tolerability and pharmacodynamic effects of VERVE-102 in adults with HeFH or premature CAD who require additional lowering of LDL-C, despite maximally tolerated oral lipid lowering therapy. This interim analysis included 35 participants who received a single intravenous infusion of VERVE-102 across six dose cohorts (0.3 mg/kg, 0.45 mg/kg, 0.6 mg/kg, 0.7 mg/kg, 0.8 mg/kg and 1.0 mg/kg). All participants received the full planned dose and were followed for at least 28 days, with a subset now followed for up to 18 months. HeFH is diagnosed based on high LDL-C levels, a personal or family history of atherosclerotic cardiovascular disease, physical exam features and/or mutations identified in certain genes. Premature CAD is defined as evidence of CAD (heart attack, coronary revascularization procedure, or coronary atherosclerosis on imaging) occurring in men 55 years old or younger or women 65 years old or younger. Participants are expected to enroll in a long-term follow-up study for up to 15 years. As of the February 27, 2026, data cut-off, the

median follow-up duration was approximately nine months, with 15 participants followed for at least one year.

References

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About Lilly

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Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about VERVE-102 as a potential treatment for people with heterozygous familial hypercholesterolemia (HeFH) or premature coronary artery disease (CAD) and the timeline for future readouts, presentations, and other milestones relating to VERVE-102 and its clinical trials, and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that VERVE-102 will prove to be a safe and effective treatment for people with HeFH or premature CAD, that VERVE-102 will receive regulatory approval, or that Lilly will execute its strategy as expected. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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