



## Verve Therapeutics Doses First Human with an Investigational In Vivo Base Editing Medicine, VERVE-101, as a Potential Treatment for Heterozygous Familial Hypercholesterolemia

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*Phase 1b Clinical Trial, heart-1, Now Underway and Enrolling Patients with Heterozygous Familial Hypercholesterolemia in New Zealand*

*Company Executing VERVE-101 Global Regulatory Strategy with Potential Clearances for a UK Clinical Trial Application and US Investigational New Drug Application in Second Half of 2022*

CAMBRIDGE, Mass., July 12, 2022 (GLOBE NEWSWIRE) -- [Verve Therapeutics](#), a biotechnology company pioneering a new approach to the care of cardiovascular disease with single-course gene editing medicines, today announced that the first patient has been dosed with VERVE-101, in its heart-1 clinical trial. VERVE-101 is a novel, investigational gene editing medicine developed by Verve and designed to be a single-course treatment that permanently turns off the *PCSK9* gene in the liver to reduce disease-driving low-density lipoprotein cholesterol (LDL-C). heart-1 is a global Phase 1b clinical trial that will evaluate VERVE-101 as a treatment for patients with heterozygous familial hypercholesterolemia (HeFH), a prevalent and potentially life-threatening subtype of atherosclerotic cardiovascular disease (ASCVD).

"VERVE-101 is a first-in-class gene editing medicine that we have designed to make a single spelling change in liver DNA to permanently turn off a disease-causing gene. The dosing of the first human with such an investigational base editing medicine represents a significant achievement by our team and for the field of gene editing," said Sekar Kathiresan, M.D., co-founder and chief executive officer of Verve. "Preclinical data suggest that VERVE-101 has the potential to offer people with HeFH a game-changing treatment option, transforming the traditional chronic care model to a single-course, life-long treatment solution."

"Our ultimate goal with VERVE-101 is to bring a new option to the millions of people with ASCVD around the world, and dosing participants in the Phase 1 study for this first indication, HeFH, is a key inflection point to achieving that goal," said Andrew Bellinger, M.D., Ph.D., chief scientific and medical officer of Verve. "With the current standard of care treatment for HeFH, less than 20% of patients achieve LDL-C goal levels due to the limitations of the chronic model which requires rigorous patient adherence, regular health care access, and extensive health care infrastructure. VERVE-101 has the potential to change the way cardiovascular disease is cared for by lowering LDL-C as low as possible for as long as possible after a single treatment."

The heart-1 clinical trial is designed to enroll approximately 40 adult HeFH patients with established ASCVD and evaluate the safety and tolerability of VERVE-101 administration, with additional analyses for pharmacokinetics and reductions in blood PCSK9 protein and LDL-C. The trial includes three parts – (A) a single ascending dose portion, followed by (B) an expansion single-dose cohort, in which additional participants will receive the selected potentially therapeutic dose and (C) an optional second-dose cohort, in which eligible participants in lower dose cohorts in Part A have the option to receive a second treatment to reach the selected potentially therapeutic dose. Interim clinical data for the heart-1 clinical trial including safety parameters, blood PCSK9 level and blood LDL-C level are expected in 2023. For more information, please visit [clinicaltrials.gov](#).

### About VERVE-101

VERVE-101 is a novel, investigational gene editing medicine designed to be a single course treatment that permanently turns off the *PCSK9* gene in the liver to reduce disease-driving low-density lipoprotein cholesterol (LDL-C). VERVE-101 is being developed initially as a treatment for patients with heterozygous familial hypercholesterolemia (HeFH), a prevalent and potentially life-threatening subtype of atherosclerotic cardiovascular disease (ASCVD). VERVE-101 consists of an adenine base editor messenger RNA (licensed from Beam Therapeutics Inc.) and an optimized guide RNA targeting the *PCSK9* gene packaged in an engineered lipid nanoparticle. By making a single A-to-G change in the DNA genetic sequence of *PCSK9*, VERVE-101 aims to inactivate the target gene. Inactivation of the *PCSK9* gene has been shown to up-regulate LDLR expression, which leads to lower LDL-C levels, thereby reducing the risk for ASCVD.

### About Verve Therapeutics

Verve Therapeutics, Inc. (Nasdaq: VERV) is a genetic medicines company pioneering a new approach to the care of cardiovascular disease, potentially transforming treatment from chronic management to single-course gene editing medicines. The company's initial two programs target *PCSK9* and *ANGPTL3*, genes that have been extensively validated as targets for lowering blood lipids such as low-density lipoprotein cholesterol (LDL-C), a root cause of cardiovascular disease. Verve's lead product candidate, VERVE-101, is designed to permanently turn off the *PCSK9* gene in the liver in order to disrupt blood PCSK9 protein production and thereby durably reduce blood LDL-C levels, with the goal of reducing a patient's risk for cardiovascular disease. VERVE-101 is being developed initially for the treatment of patients with heterozygous familial hypercholesterolemia, a potentially fatal genetic heart disease. For more information, please visit [www.VerveTx.com](#).

### Forward Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the company's regulatory submissions and clinical trials, including the heart-1 trial and expected timing of interim data, its research and development plans and the potential advantages and therapeutic potential of the company's programs. All statements, other than statements of historical facts, contained in this press release, including statements regarding the company's strategy, future operations, future financial position, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and

uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with the company's limited operating history; the timing of and the company's ability to submit applications for, its product candidates; advance its product candidates in clinical trials; initiate and enroll clinical trials on the timeline expected or at all; correctly estimate the potential patient population and/or market for the company's product candidates; replicate in clinical trials positive results found in preclinical studies and/or earlier-stage clinical trials of VERVE-101 and its other product candidates; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; obtain, maintain or protect intellectual property rights related to its product candidates; manage expenses; and raise the substantial additional capital needed to achieve its business objectives. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the company's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, as well as discussions of potential risks, uncertainties and other important factors, in the company's most recent filings with the Securities and Exchange Commission and in other filings that the company makes with the Securities and Exchange Commission in the future. In addition, the forward-looking statements included in this press release represent the company's views as of the date hereof and should not be relied upon as representing the company's views as of any date subsequent to the date hereof. The company anticipates that subsequent events and developments will cause the company's views to change. However, while the company may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so.

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