Verve Therapeutics Announces Publication of VERVE-101 Preclinical Data in Circulation and Presentations at the American Heart Association Annual Meeting

October 31, 2022

Verve Researchers Awarded Paul Dudley White International Scholar Award from the American Heart Association for Highest Ranked Abstract Submitted from the United States to Scientific Sessions 2022

BOSTON, Oct. 31, 2022 (GLOBE NEWSWIRE) -- Verve Therapeutics, Inc., a clinical-stage biotechnology company pioneering a new approach to the care of cardiovascular disease with single-course gene editing medicines, today announced that preclinical data supporting VERVE-101 as a treatment for heterozygous familial hypercholesterolemia (HeFH), a genetic form of atherosclerotic cardiovascular disease (ASCVD), has been published in the American Heart Association's peer-reviewed journal *Circulation*. VERVE-101 is an investigational *in vivo* base editing medicine designed to permanently turn off the *PCSK9* gene in the liver to durably lower low density lipoprotein cholesterol (LDL-C), a key causal driver of ASCVD.

The published findings are from a study in non-human primates (NHPs), in which animals received a one-time infusion of a control (n=10) or VERVE-101 at a dose of 0.75 mg/kg (n=4) or 1.5 mg/kg (n=22). The animals in the 0.75 mg/kg arm were evaluated 365 days post-treatment and demonstrated a mean reduction in blood PCSK9 protein of 67% and LDL-C reduction of 49% from baseline. The animals that received the 1.5 mg/kg dose were evaluated at up to 476 days post-treatment and demonstrated a mean reduction in PCSK9 protein of 83% and LDL-C reduction of 69% from baseline. Liver safety measurements assessed one year after dosing were normal in all treated animals and liver microscopic examinations in a subset of NHPs who underwent scheduled necropsy were normal. There was no detected impact on markers of glucose homeostasis, including fasting glucose and hemoglobin A1c, in treated NHPs.

In addition, a second set of experiments evaluated the potential for VERVE-101 to edit germline cells or be passed on to offspring. In six sexually mature male NHPs, sequencing of sperm samples before and after treatment with VERVE-101 showed no evidence of *PCSK9* gene editing. Genotyping of 436 offspring of female mice treated with the murine surrogate of VERVE-101 observed that the *PCSK9* edit was not transmitted to any of the offspring.

"The totality of data generated for our VERVE-101 program support our ongoing heart-1 global clinical program and the potential of VERVE-101 as a single-course treatment for HeFH," said Andrew Bellinger, M.D., Ph.D., chief medical and scientific officer of Verve. "The consistency of preclinical data showing durable editing of the *PCSK9* gene and lowering of LDL-C, combined with these new findings showing no evidence of germline transmission, bolster our confidence in the potential for VERVE-101 to offer a long-term, well-tolerated treatment for patients with HeFH and for patients with established ASCVD not at LDL-C goal on oral therapy. We look forward to participating in the upcoming AHA meeting to share these findings with the scientific community."

These data will also be presented in an oral presentation at the American Heart Association (AHA) Scientific Sessions 2022. The abstract for the presentation was selected as the U.S. winner of the 2022 Paul Dudley White International Scholar Award, which recognizes authors that contributed to the highest ranked accepted abstract from each submitting country for the annual Scientific Sessions.

In addition to this presentation, Verve's chief executive officer, Sekar Kathiresan, M.D., will speak on the potential for gene editing as a lipid management strategy in an education session on the evolving landscape of lipid management. AHA 2022 is being held November 5-7, 2022, in Chicago, US.

AHA Presentation Details:
Main session: The Evolving Landscape of Lipid Management
Title: The Potential for Gene Editing as a Lipid Management Strategy
Date: Saturday, November 5, 2022, from 9:50 – 10:00 a.m. CT
Location: Main Event II

Session: George Lyman Duff Memorial Lecture (AT.AOS.439)
Title: VERVE-101—An Investigational Single-Course Gene Editing Medicine Targeting PCSK9—Durably and Potently Lowers PCSK9 and LDL-C Concentrations in Non-Human Primates
Date: Sunday, November 6, 2022, from 5:24 – 5:34 p.m. CT
Location: S401ABC

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 genetic 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 LDL receptor expression, which leads to lower LDL-C levels, thereby reducing the risk for ASCVD.

About Verve Therapeutics
Verve Therapeutics, Inc. (Nasdaq: VERV) is a clinical-stage 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 – VERVE-101 and VERVE-201 – target genes that have been extensively validated as targets for lowering low-density lipoprotein cholesterol (LDL-C), a root cause of cardiovascular disease, in order to durably reduce blood LDL-C levels. VERVE-101 is designed to permanently turn off the *PCSK9* gene in the liver and is being developed initially for heterozygous familial hypercholesterolemia (HeFH) and ultimately to treat atherosclerotic cardiovascular disease (ASCVD) not at LDL-C goal on oral therapy. VERVE-201 is designed to permanently turn off the *ANGPTL3* gene in the liver and is initially being developed in homozygous familial hypercholesterolemia (HoFH) and ultimately in patients with ASCVD who have not achieved goal LDL-C with oral therapy and a PCSK9 inhibitor. 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 research and development plans and the potential advantages and therapeutic potential of the company's programs, including VERVE-101. 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, enroll and complete its ongoing and future 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 VERVE-201; 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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