Verve Therapeutics Reports Durable and Well-Tolerated Editing of ANGPTL3 Gene Out to More than 20 Months in Non-Human Primates for Potential Treatment of Atherosclerotic Cardiovascular Disease

April 4, 2022

Updated Sequential Dosing Data Show Administration of PCSK9 Base Editor Followed by ANGPTL3 Base Editor is Well-Tolerated in NHPs

Data to be Presented Today at the American College of Cardiology 71st Annual Scientific Session & Expo

CAMBRIDGE, Mass., April 04, 2022 (GLOBE NEWSWIRE) -- Verve Therapeutics, a biotechnology company pioneering a new approach to the care of cardiovascular disease with single-course gene editing medicines, reported updated preclinical data in non-human primates (NHPs) showing durable and well-tolerated editing of the *ANGPTL3* gene following administration of the company's ANGPTL3 base editor, supporting its potential as a treatment for atherosclerotic cardiovascular disease (ASCVD). In addition, the company provided an update on its sequential dosing research efforts, demonstrating that administration of a PCSK9 base editor followed by an ANGPTL3 base editor was durable and well-tolerated in NHPs. The data are being presented today during an oral session at the American College of Cardiology 71st Annual Scientific Session & Expo (ACC 2022).

"We know that the best way to treat ASCVD is to lower disease-causing low-density lipoprotein cholesterol (LDL-C) as much as possible for as long as possible. Given the complexities of ASCVD and the challenges with current chronic care treatments, it's clear that certain patient populations will require different solutions," said Andrew Bellinger, M.D., Ph.D., chief medical and scientific officer of Verve. "We are pleased to see durable editing now out to nearly two years in NHPs following a single administration of an ANGPTL3 base editor, which we believe could offer a gene editing treatment solution for multiple patient populations. Further, we believe that sequential dosing targeting two different lipid pathways could offer a long-term solution for patients who do not achieve LDL-C lowering goals with just one treatment. Most important to our success with our treatments is ensuring that they are safe and well-tolerated, and in today's findings, we further highlight the tolerability of our base editors with no long-term impact observed on markers of liver toxicity."

ANGPTL3 Long-Term Durability and Tolerability Data
ANGPTL3 is a well-validated gene known to regulate blood LDL-C and triglycerides. Verve expects to advance an *in vivo* ANGPTL3 base editing program for two indications with substantial unmet need: (1) treatment of homozygous familial hypercholesterolemia (HoFH), a rare genetic subtype of ASCVD characterized by extremely high blood LDL-C; and (2) patients with ASCVD who have not achieved goal LDL-C lowering with oral therapy and a PCSK9 inhibitor. In the data reported today, a 96% reduction in blood ANGPTL3 protein from baseline was observed in NHPs (N=4) treated with an ANGPTL3 base editor, with follow-up now out to 616 days. In addition, no long-term impacts were observed on markers of liver toxicity, as measured by alanine aminotransferase (ALT) and bilirubin levels following treatment administration.

Sequential Dosing Update
As previously reported, Verve assessed sequential dosing of its PCSK9 base editor followed 30 days later by its ANGPTL3 base editor in NHPs, a dosing strategy that could benefit patients with ASCVD who have not achieved goal LDL-C lowering following oral options. In a 90-day study, a 91% reduction of blood PCSK9 protein was observed after dosing with the PCSK9 base editor and an 89% reduction of blood ANGPTL3 protein was observed after the second dose – the ANGPTL3 base editor. Both reductions remained durable to the conclusion of the study. Importantly, sequential dosing was well-tolerated in treated NHPs, with transient and fully reversible ALT elevations observed and no impact on bilirubin.

ACC 2022 Presentation Details:
Title: Sequential In Vivo Crispr Base Editing of the PCSK9 and ANGPTL3 Genes in Non-Human Primates
Track: Highlighted Original Research: Ischemic Heart Disease and the Year in Review
Session: 913
Time: Monday, April 4, 2022, 9:06 a.m. – 9:16 a.m. ET

About Verve Therapeutics
Verve Therapeutics, Inc. (Nasdaq: VERV) is a genetic medicines company pioneering a new approach to the care of cardiovascular disease, 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, currently in IND-enabling studies, 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 initiation, and timing, of the 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.

Investor Contact
Jen Robinson
Verve Therapeutics, Inc.
jrobinson@vervetx.com

Media Contact
Gina Nugent
Ten Bridge Communications
gina@tenbridgecommunications.com