Verve Therapeutics Highlights Preclinical Data Supporting Nomination of VERVE-201 ANGPTL3 Product Candidate at the European Society of Cardiology 2022 Congress

August 22, 2022

CAMBRIDGE, Mass., Aug. 22, 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 new preclinical data supporting the nomination of the company's second product candidate, VERVE-201. VERVE-201 is designed to permanently turn off the *ANGPTL3* gene in the liver, a key regulator of cholesterol and triglyceride metabolism, with a precise A-to-G base pair DNA change. Verve is initially developing VERVE-201 for the treatment of homozygous familial hypercholesterolemia (HoFH), a rare genetic subtype of atherosclerotic cardiovascular disease (ASCVD) characterized by extremely high blood low-density lipoprotein cholesterol (LDL-C), as well as for patients with ASCVD who have not achieved goal LDL-C with oral therapy and a PCSK9 inhibitor. The preclinical data will be highlighted on August 29, 2022 in a poster session during the European Society of Cardiology 2022 Congress in Barcelona.

"*ANGPTL3* is a well-validated target for lowering LDL-C. Through turning off this gene in the liver, we believe we have a significant opportunity to help patients with HoFH or ASCVD reach LDL-C goals and improve clinical outcomes," said Andrew Bellinger, M.D., Ph.D., chief scientific and medical officer of Verve. "Our research and development team has now generated two cardiovascular gene editing clinical candidates, as well as novel delivery technology, which is a testament to the ingenuity and dedication of an incredible team. Today we share some of this extensive research to identify a product candidate that we believe can provide potent and durable inactivation of *ANGPTL3* with limited to no off-target editing. The selection of VERVE-201 is an exciting step forward, and we look forward to initiating studies this year to enable an investigational new drug application and potentially bring VERVE-201 into the clinic in 2024."

Prior to nominating VERVE-201, Verve used a rigorous process to optimize preclinical safety and efficacy. Verve screened more than 200 engineered and chemically modified adenine base editor (ABE) and guide RNA (gRNA) configurations targeting *ANGPTL3* to assess their potency and on-target/off-target profiles. An optimized configuration was selected and evaluated in primary human liver cells, which showed potent, on-target editing of the *ANGPTL3* gene with no detectable off-target and no detectable structural variants as assessed using high-coverage whole genome optical mapping. Verve also conducted a non-human primate (NHP) study (n=9), which showed that the optimized configuration, an NHP surrogate version of VERVE-201, demonstrated potent liver *ANGPTL3* editing ranging from 54-57% and reductions in blood ANGPTL3 protein ranging from 95-98% across three dose levels. To enable efficient delivery of VERVE-201 in HoFH patients with the highest unmet need, VERVE-201 is using Verve's proprietary GalNAc-lipid nanoparticle (GalNAc-LNP) delivery technology.

In addition to the VERVE-201 work, Verve shared an update on previously reported data with an ANGPTL3 precursor formulation targeting the same base editing outcome in NHPs. These data demonstrated durable editing in the liver of treated NHPs (n=4) of 61% at over two years following dosing, which was identical to editing levels measured via liver biopsy on day 15.

Presentation Details

- **Title:** An *in vivo* CRISPR base editing therapy to inactivate the *ANGPTL3* gene: nomination of a development candidate for VERVE-201
- **Session:** RNA and gene therapy of vascular diseases
- **Date & Time:** August 29, 2022, between 3:15 – 4:00 p.m. CEST

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 initially being developed for heterozygous familial hypercholesterolemia. VERVE-201 is designed to permanently turn off the *ANGPTL3* gene in the liver and is initially being developed for homozygous familial hypercholesterolemia and those with atherosclerotic cardiovascular disease 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 initiation, and timing, of the company's regulatory submissions and future clinical trials, its research and development plans, and the potential advantages and therapeutic potential of the company's programs, including VERVE-201. 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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