Verve Therapeutics Announces Clearance of Clinical Trial Authorisation Application by the United Kingdom Medicines and Healthcare Products Regulatory Agency for VERVE-101 in Patients with Heterozygous Familial Hypercholesterolemia

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CAMBRIDGE, Mass., Sept. 21, 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 the clearance of its Clinical Trial Authorisation (CTA) application by the United Kingdom (U.K.) Medicines and Healthcare products Regulatory Agency (MHRA) for VERVE-101 as a potential treatment for patients with heterozygous familial hypercholesterolemia (HeFH). HeFH is a prevalent and potentially life-threatening genetic subtype of atherosclerotic cardiovascular disease (ASCVD) characterized by extremely high blood levels of disease-driving low-density lipoprotein cholesterol (LDL-C).

This U.K. CTA is part of a global regulatory strategy established by Verve for clinical development of VERVE-101, which also includes a cleared CTA in New Zealand and an anticipated regulatory clearance for an investigational new drug (IND) application in the United States in the second half of 2022. Verve is currently enrolling patients in its heart-1 clinical trial of VERVE-101 for HeFH in New Zealand and expects to begin enrolling patients in the U.K. imminently.

“This CTA marks the second regulatory clearance for VERVE-101 as we execute our global strategy focused on bringing a potential single-course gene editing treatment to patients with ASCVD around the world, beginning with HeFH,” said Andrew Bellinger, M.D., Ph.D., chief medical and scientific officer of Verve. “We believe that VERVE-101 has the potential to transform the care and treatment of cardiovascular disease, and we are dedicated to ensuring efficient advancement of heart-1 in order to build a better understanding of its impact in humans. Enrollment in New Zealand is progressing well and, with this latest clearance, we’re working diligently with our investigators in the U.K. to begin patient enrollment and dosing as quickly as possible. We continue to anticipate an interim clinical data readout in 2023.”

About heart-1
The heart-1 clinical trial is designed to enroll approximately 40 adult heterozygous familial hypercholesterolemia (HeFH) patients with established atherosclerotic cardiovascular disease (ASCVD) and evaluate the safety and tolerability of VERVE-101 administration, with additional analyses for pharmacokinetics and reductions in blood PCSK9 protein and low-density lipoprotein cholesterol (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 from 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 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 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 enrollment of patients in the ongoing heart-1 clinical trial, the timing and availability of clinical trial data from the heart-1 clinical trial and the status and timing of the company’s regulatory submissions, its 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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