Verve Therapeutics Announces Clearance of Investigational New Drug Application by the U.S. FDA for VERVE-101 in Patients with Heterozygous Familial Hypercholesterolemia

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BOSTON, Oct. 23, 2023 (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 lifting of the clinical hold and clearance of its Investigational New Drug (IND) application by the U.S. Food and Drug Administration (FDA) to conduct a clinical trial in the United States evaluating VERVE-101 for the treatment of heterozygous familial hypercholesterolemia (HeFH). VERVE-101 is an investigational, *in vivo* base editing medicine designed to be a single-course treatment that inactivates the *PCSK9* gene in the liver to durably lower blood low-density lipoprotein cholesterol (LDL-C). HeFH is a prevalent and life-threatening inherited disease characterized by lifelong elevations in blood LDL-C and accelerated atherosclerotic cardiovascular disease (ASCVD).

Verve submitted interim clinical data from the dose-escalation portion of the ongoing heart-1 Phase 1b clinical trial and addressed the FDA's preclinical questions in its response to the clinical hold. The heart-1 trial is evaluating the safety, tolerability, pharmacokinetic and pharmacodynamic profile of VERVE-101 in patients with HeFH, and is currently being conducted at sites in the United Kingdom and New Zealand. Verve is scheduled to report interim clinical data from the heart-1 trial in a late-breaking science presentation at the American Heart Association's (AHA) Scientific Sessions 2023 on November 12, 2023 at 3:30pm E.T. in Philadelphia.

"The clearance of our IND application by the FDA is a significant milestone in our effort to offer patients living with HeFH a transformative alternative to the chronic care model of disease management. This clearance, for the first time, enables clinical development of an *in vivo* base editing product candidate in the United States," said Andrew Bellinger, M.D., Ph.D., chief scientific officer of Verve. "Our interactions with the FDA have been valuable, and we plan to incorporate our learnings from this regulatory process to execute a global regulatory strategy across the rest of our pipeline. With the clearance of this IND, we plan to begin the process of activating U.S. clinical trial sites for the heart-1 clinical trial."

About heart-1
heart-1 is an open-label Phase 1b clinical trial in patients with heterozygous familial hypercholesterolemia (HeFH) who have established atherosclerotic cardiovascular disease (ASCVD) to evaluate the safety and tolerability of VERVE-101 administration, with additional analyses for pharmacokinetics and pharmacodynamic reductions in blood PCSK9 protein and low-density lipoprotein cholesterol (LDL-C). Interim clinical data from the dose escalation portion of the heart-1 clinical trial including safety parameters and changes in blood PCSK9 protein and blood LDL-C levels are expected to be presented at the American Heart Association's Scientific Sessions 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 inherited subtype of atherosclerotic cardiovascular disease (ASCVD). VERVE-101 consists of an adenine base editor messenger RNA 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 three programs – VERVE-101, VERVE-102, 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 and VERVE-102 are designed to permanently turn off the *PCSK9* gene in the liver and are being developed initially for heterozygous familial hypercholesterolemia (HeFH) and ultimately to treat atherosclerotic cardiovascular disease (ASCVD) patients 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 for homozygous familial hypercholesterolemia (HoFH) and ultimately to treat patients with refractory hypercholesterolemia. For more information, please visit www.VerveTx.com.

Cautionary Note Regarding 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 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 company's ability to timely submit and receive approvals of regulatory 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, VERVE-102 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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