Verve Therapeutics Announces Development of Proprietary GalNAc-LNP Delivery Technology Enabling Efficient In Vivo Liver Delivery of Base Editors

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CAMBRIDGE, Mass., Sept. 23, 2021 (GLOBE NEWSWIRE) -- Verve Therapeutics, a biotech company pioneering a new approach to the care of cardiovascular disease with single-course gene editing medicines, today announced new *in vivo* data from the company's proprietary lipid nanoparticle (LNP) delivery technology leveraging an internally discovered GalNAc-targeting ligand for delivery of base editors to the liver. Findings highlight the ability of Verve's novel GalNAc-LNP to achieve high efficiency liver delivery and base editing in mouse models of homozygous familial hypercholesterolemia (HoFH), a form of atherosclerotic cardiovascular disease (ASCVD). The data will be presented today at the TIDES USA Oligonucleotide & Peptide Therapeutics Conference.

Verve is advancing a pipeline of single-course *in vivo* gene editing programs for the treatment of ASCVD indications, including HoFH. Verve's gene editing programs consist of LNPs that encapsulate mRNA encoding for a gene or base editor, as well as a guide RNA targeting the gene of interest expressed in the liver. For patients with HoFH, LNP-mediated liver delivery is challenging because complete deficiency in the low-density lipoprotein receptor (LDLR) gene in this patient population often drives HoFH pathophysiology, and uptake of LNPs into the liver is generally thought to be through a LDLR-dependent pathway. To overcome this, Verve has developed a novel approach that bypasses the LDLR and delivers LNPs to the liver through a different receptor. Asialoglycoprotein receptors (ASGPRs) are highly expressed in the liver with a high capacity to mediate uptake into the liver, independent of LDLR. As such, by incorporating an internally discovered GalNAc molecule, the targeting ligand for ASGPR, into an LNP, Verve was able to efficiently and safely deliver a base editor to the liver in a mouse model of HoFH.

"Our goal at Verve is to transform the future treatment of cardiovascular disease by creating single-course gene editing treatments, with lead programs that leverage base editors to turn off disease-driving genes in the liver," said Andrew Bellinger, M.D., Ph.D., chief scientific officer of Verve. "In some patient populations, such as HoFH, using LNPs for delivery of base editors is not possible, requiring the need for an alternative delivery approach to treat these patients. To address this, we have designed and developed a proprietary GalNAc-LNP to enable efficient and potent liver editing regardless of LDLR expression. We are very excited to share findings leveraging this delivery approach, which may allow us to reach patients who lack LDLR and may be applicable in other populations where liver-targeted delivery is advantageous."

Verve's proprietary GalNAc-LNP was designed using novel chemical ligand compositions and a potent low ligand surface density, which is designed to optimize recognition and binding to ASGPRs. In addition, the formulation has been developed using a scalable process with favorable manufacturing properties similar to standard LNPs. Data presented today demonstrate:

- High efficiency liver delivery of an adenine base editor targeting ANGPTL3 in both LDLR heterozygous and homozygous deficient mouse models;
- Low GalNAc-lipid content with 0.05 mol% leading to maximal liver editing in an LDLR knockout model;
- A scalable process of incorporating the GalNAc ligand into the LNP with near-homogenous distribution of GalNAc ligand; and
- Potent editing *in vivo* regardless of the LDLR status of the mouse.

Verve is advancing a gene editing program that targets ANGPTL3, a gene known to regulate blood LDL-C and triglycerides. Such a program would have potential indications in both HoFH and in heterozygous familial hypercholesterolemia. Verve is designing this program to utilize a GalNAc-modified LNP encapsulating an mRNA encoding a base editor and a gRNA targeting the ANGPTL3 gene. The company's program is currently in the lead optimization stage, and the company expects to name its development candidate and initiate IND-enabling studies in 2022.

Presentation Details
Title: Targeted Delivery of Base Editors to Hepatocytes *In Vivo*
Track: Oligonucleotide CMC and Targeted Delivery TRACK: Targeted Delivery of Therapeutic Oligonucleotides
Date/Time: Thursday, September 23, 2021, 8:30 a.m. - 9:00 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 turn off the PCSK9 gene in the liver in order to disrupt blood PCSK9 protein production and thereby 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 Company's planned IND submissions and future clinical trials and its research and development plans. 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, and obtain and maintain regulatory approvals for, its product candidates;

continue to 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.

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