Verve Therapeutics Reports Additional VERVE-101 and GalNAc-Lipid Nanoparticle Delivery Data in Non-Human Primates at TIDES USA 2022

May 9, 2022

VERVE-101 Preclinical Data Package Supports Company's Global Development Strategy and Regulatory Submissions for Clinical Trials in Patients with HeFH

Single Intravenous Infusion of VERVE-101 Clinical Formulation Led to Mean 68% Reduction in Plasma LDL-C in NHPs Out to One-Year with Good Tolerability; VERVE-101 Precursor Formulation Led to Durability of LDL-C Reduction Observed Out to More Than 20 Months

In Vivo *Delivery of Base Editors with Proprietary GalNAc-Lipid Nanoparticle Demonstrates Improved Potency Compared with Standard Lipid Nanoparticles, Including 98% Reduction in Blood ANGPTL3 in NHPs at Day 15*

CAMBRIDGE, Mass., May 09, 2022 (GLOBE NEWSWIRE) -- Verve Therapeutics, a biotechnology company pioneering a new approach to the care of cardiovascular disease with single-course gene editing medicines, announced that new preclinical data from its VERVE-101 program and GalNAc-lipid nanoparticle (GalNAc-LNP) delivery technology will be presented this week during an oral session at the TIDES USA 2022 Oligonucleotide & Peptide Therapeutics Conference. The full presentation can be found online here.

Verve is advancing VERVE-101 initially as a treatment for heterozygous familial hypercholesterolemia (HeFH), a genetic form of atherosclerotic cardiovascular disease (ASCVD). Updated data with the clinical formulation of VERVE-101 demonstrated potent and durable editing of the *PCSK9* gene and reductions of LDL-C in non-human primates (NHPs), with follow up now out to one year. Importantly, administration of VERVE-101 was well-tolerated in the study. In addition, data evaluating the company's proprietary GalNAc-LNPs to deliver base editors to the liver resulted in improved editing potency in wild-type NHPs, when compared to delivery of the editor with standard LNPs.

"We are highly encouraged by the updated VERVE-101 program data to be presented this week, which we believe demonstrate the remarkable editing capabilities of our technology with a well-tolerated safety profile in preclinical models. The durability data now out to one-year in NHPs, coupled with our extensive GLP toxicology work, form the basis of our planned global regulatory submissions this year and support VERVE-101 advancement into the clinic," said Andrew Bellinger, M.D., Ph.D., chief scientific and medical officer of Verve. "We're also excited to share new data highlighting the ability of our internally developed GalNAc-LNP to efficiently, and with higher potency than standard LNPs, deliver our ANGPTL3 base editor to the livers of healthy animals. With an observed 98% reduction of plasma ANGPTL3 after 15 days, we believe that this delivery technology has the potential to be a best-in-class method for *in vivo* delivery of gene editing medicines. Our focus at Verve remains centered around bringing forward single-course gene editing medicines that transform the future of cardiovascular disease treatment, and these exciting data bring us closer to our vision of reaching millions of patients around the globe."

Updated VERVE-101 Data
Verve's lead program, VERVE-101, is designed to permanently turn off the *PCSK9* gene in the liver to reduce disease-driving LDL-C. VERVE-101 is being developed initially for the treatment of patients with HeFH, a potentially fatal genetic heart disease. Updated data to be presented at TIDES showed:

- An 89% mean reduction in blood PCSK9 protein and a 68% mean reduction in LDL-C in NHPs administered a one-time 1.5mg/kg infusion of VERVE-101 (n=22) after one year of follow-up
- A 69% mean reduction in blood PCSK9 protein and a 50% mean reduction in LDL-C in NHPs administered a one-time 0.75mg/kg infusion of VERVE-101 (n=4) after one year of follow-up
- No observed adverse events with only transient impacts on alanine aminotransferase (ALT) that resolved by day 14 and no observed impacts on glucose or total bilirubin levels in NHPs treated with the 1.5mg/kg or 0.75mg/kg doses of VERVE-101
- In both HeFH and wild type mice, the mouse surrogate of VERVE-101 led to similar reduction in blood PCSK9 and was well-tolerated across three dose levels – 0.05mg/kg, 0.5 mg/kg and 5.0mg/kg – in a six-month GLP toxicity study
- In addition, Verve shared long-term durability data using a VERVE-101 precursor in NHPs, in which an 88% mean reduction in blood PCSK9 protein and a greater than 60% mean reduction in LDL-C has now been observed out to more than 20 months following a single administration of the therapy

Updated GalNAc-LNP Delivery Data
Verve is advancing its proprietary GalNAc-LNP to enable enhanced delivery of base editors to the liver *in vivo,* potentially leading to more potent editing. Verve has previously shown the ability of its GalNAc-LNP to deliver its ANGPTL3 base editor in NHP models of homozygous familial hypercholesterolemia. Today's data build on that and include findings from an evaluation in wild-type NHPs comparing the ability of GalNAc-LNP to deliver its ANGPTL3 base editor versus delivery with standard LNPs. Three doses were evaluated – 0.75mg/kg, 1.5mg/mg and 3.0mg/kg and showed:

- When compared with a standard LNP (without GalNAc), delivery with a GalNAc-LNP led to an improvement in editing potency across all dose levels
- Improved potency and consistency of ANGPTL3 blood protein reductions with 51%, 83% and 98% mean reductions

observed across the 0.75mg/kg, 1.5mg/kg and 3.0 mg/kg dose groups, respectively
- GalNAc-LNPs were well-tolerated without adverse event observations and with only transient increases in ALT observed across dose levels which resolved by day 14 and were identical with and without GalNAc
- Biodistribution primarily to the liver, consistent with what has been observed using standard LNPs

Presentation Information
Title: In Vivo CRISPR Base Editing to Treat ASCVD
Track: Genome Editing and mRNA
Date/Time: Wednesday, May 11, 2022, 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 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 implications of preclinical data, 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.

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