Verve Therapeutics Announces Clearance of First VERVE-101 Clinical Trial Application and Outlines Global Clinical Development Strategy; Reports First Quarter 2022 Financial Results

May 10, 2022

Verve on Track to Begin Dosing HeFH Patients in New Zealand in Mid-2022 in a Phase 1 Clinical Trial with Initial Clinical Data Expected in 2023

Preparing for Submission of United Kingdom and United States Regulatory Filings for VERVE-101 in Second Half of 2022

Cash, Cash Equivalents and Marketable Securities of $323.3 Million with Cash Runway into 2024

CAMBRIDGE, Mass., May 10, 2022 (GLOBE NEWSWIRE) -- Verve Therapeutics, Inc., a biotechnology company pioneering a new approach to the care of cardiovascular disease with single-course gene editing medicines, today outlined its global development strategy for its lead gene editing candidate, VERVE-101, and reported financial results for the first quarter ended March 31, 2022. VERVE-101 is a novel gene editing medicine discovered and developed by Verve that is designed to permanently turn 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 subtype of atherosclerotic cardiovascular disease (ASCVD). The company ultimately plans to expand clinical development of VERVE-101 beyond HeFH for the treatment of patients with established ASCVD not at LDL-C goal on oral therapy.

VERVE-101 Global Clinical Development
Verve has received clearance of its first clinical trial application (CTA) for VERVE-101 in New Zealand and plans to initiate a first-in-human Phase 1 clinical trial in patients with HeFH in mid-2022. This CTA is part of a global regulatory strategy established by Verve for clinical development of VERVE-101, which also includes plans to submit both a CTA in the United Kingdom and an investigational new drug (IND) application in the United States in the second half of 2022. The company anticipates initiating clinical trial sites and patient enrollment in the respective regions shortly following clearance of its applications, should they be accepted. Verve expects to report initial clinical data from the VERVE-101 Phase 1 clinical trial in 2023.

“This CTA clearance represents a tremendous milestone in the evolution of Verve as we start our transition to a clinical-stage gene editing company. To support the global development of VERVE-101, we have worked diligently with both U.S. and international regulatory authorities and key clinical advisors to define clear paths for our regulatory submissions, beginning first in New Zealand and then rapidly expanding to the U.K. and U.S. later this year,” said Sekar Kathiresan, M.D., co-founder and chief executive officer of Verve. “Our global clinical development strategy for VERVE-101 is based on extensive non-human primate (NHP) data that demonstrate the ability of VERVE-101 to potently and durably edit *PCSK9*, leading to LDL-C reductions sustained out to one year. These data form the basis for our CTAs for clinical development in New Zealand and the U.K. The remaining IND-enabling studies are on track to be completed in the third quarter, and we are prepared to rapidly submit our IND upon completion. This is a momentous year as we continue our mission of transforming the treatment of cardiovascular disease from the current chronic care model to that of single-course gene editing medicines.”

ANGPTL3 Program Update
Verve’s ANGPTL3 program is designed to permanently turn off the *ANGPTL3* gene in the liver, a key regulator of cholesterol and triglyceride metabolism, and is being developed for the treatment of homozygous familial hypercholesterolemia (HoFH), a rare genetic subtype of ASCVD characterized by extremely high blood LDL-C, as well as for patients with ASCVD who have not achieved goal LDL-C lowering with oral therapy and a PCSK9 inhibitor. In recently presented data, a 96% reduction in blood ANGPTL3 protein from baseline was observed in NHPs (n=4) treated with a Verve ANGPTL3 base editor, with follow-up out to 616 days. In addition, no long-term impacts were observed on markers of liver toxicity, as measured by alanine aminotransferase (ALT) and bilirubin levels, following treatment administration. Verve expects to identify its base editing development candidate targeting ANGPTL3 and begin IND-enabling studies in the second half of 2022.

“Beyond VERVE-101, we continue to advance our product-focused pipeline, leveraging our approach of going after validated disease targets and determining the best technology to address them,” said Andrew Bellinger, M.D., Ph.D., chief scientific and medical officer of Verve. “Recent data from our ANGPTL3 program support its continued development toward IND-enabling studies. 2022 represents a significant year of progress, and in addition to advancing our lead programs, we are also actively conducting research to identify new targets we may be able to address, as we work toward our goal of providing better treatments for the millions of people living with cardiovascular disease around the globe.”

Upcoming Medical Meeting Presentations

- **TIDES 2022:** Verve will present updated VERVE-101 preclinical data in NHPs demonstrating durable and potent editing of the *PCSK9* gene with follow up now out to one year. In addition, the company will present data highlighting the potential of its proprietary GalNAc-LNP to deliver base editors to the livers of wild-type NHPs more efficiently than the same LNP without GalNAc targeting. Details of the full data can be seen here.
  - **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
- **ASGCT 2022:** Verve will provide a company overview and outline findings from robust off-target editing analyses during a poster and oral session at the American Society of Gene and Cell Therapy (ASGCT) 25th Annual Meeting.

- **Poster Session Title:** Comprehensive Evaluation for Off-Target Editing of *In Vivo* Base Editing Medicines Targeting the PCSK9 Gene
  - **Track:** Gene Targeting and Gene Correction
  - **Date/Time:** Monday, May 16, 2022, 5:30 p.m. – 6:30 p.m. ET
- **Oral Session Title:** *In Vivo* CRISPR Base Editing of PCSK9 Durably Lowers Cholesterol in Primates
  - **Track:** CRISPR/CAS9 Gene Editing - Concepts to *In Vivo* Editing
  - **Date/Time:** Tuesday, May 17, 2022, 8:00 a.m. – 9:45 a.m. ET

First Quarter 2022 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $323.3 million as of March 31, 2022, as compared to $360.4 million as of December 31, 2021. Based on current operating plans, Verve expects its existing cash, cash equivalents and marketable securities will enable the company to fund its operating expenses and capital expenditure requirements into 2024.
- **Research & Development (R&D) Expenses:** R&D expenses were $24.5 million for the first quarter of 2022, compared to $11.3 million for the first quarter of 2021.
- **General & Administrative (G&A) Expenses:** G&A expenses were $7.4 million for the first quarter of 2022, compared to $2.7 million for the first quarter of 2021.
- **Net Loss:** Net loss was $30.2 million, or $0.62 basic and diluted net loss per share, for the first quarter of 2022, compared to $13.3 million, or $4.99 basic and diluted net loss per share, for the first quarter of 2021.

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 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 regulatory submissions and future clinical trials, its research and development plans, the potential advantages and therapeutic potential of the company's programs, and the period over which the company believes that its existing, cash, cash equivalents and marketable securities will be sufficient to fund its operating expenses. 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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Selected Condensed Financial Information
(in thousands, except share and per share amounts)
(unaudited)

Condensed consolidated statements of operations	**Three months ended March 31,**	
	2022	**2021**
Operating expenses:		
Research and development	$ 24,490	$ 11,345
General and administrative	7,435	2,716
Total operating expenses	31,925	14,061
Loss from operations	(31,925)	(14,061)
Other income:		
Change in fair value of antidilution rights liability	-	396
Change in fair value of success payment liability	1,677	382
Interest and other income, net	82	20
Total other income, net	1,759	798
Net loss	$ (30,166)	$ (13,263)
Net loss per common share, attributable to common stockholders, basic and diluted	$ (0.62)	$ (4.99)
Weighted-average common shares used in net loss per share attributable to common stockholders, basic and diluted	48,571,214	2,656,278

Condensed consolidated balance sheet data	**March 31, 2022**	**December 31, 2021**
Cash, cash equivalents and marketable securities	$ 323,299	$ 360,442
Total assets	349,241	384,124
Total liabilities	17,851	26,772
Total stockholders' equity	331,390	357,352