Verve Therapeutics Provides Regulatory Update on VERVE-101 Investigational New Drug Application and Reports Third Quarter 2022 Financial Results

November 7, 2022

VERVE-101 Investigational New Drug Application Placed on Hold by U.S. Food and Drug Administration

Dosing Completed in First Dose Cohort of the heart-1 Clinical Trial of VERVE-101 in Patients with HeFH; Independent Data Safety Monitoring Board Recommended Proceeding to Second Dose Level in New Zealand and U.K.

Well-capitalized with $550.7 Million Supporting Runway into Second Half of 2025

BOSTON, Nov. 07, 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 reported corporate updates and financial results for the third quarter ended September 30, 2022.

Update on VERVE-101 Investigational New Drug (IND) Application to U.S. FDA: Verve announced today that the U.S. Food and Drug Administration (FDA) has placed a hold on its IND application to conduct a clinical trial evaluating VERVE-101 in patients with heterozygous familial hypercholesterolemia (HeFH), a prevalent and potentially life-threatening subtype of atherosclerotic cardiovascular disease (ASCVD), in the United States. VERVE-101 is a novel, investigational gene editing medicine designed to be a single-course treatment to permanently turn off the *PCSK9* gene in the liver to reduce disease-driving low-density lipoprotein cholesterol (LDL-C). VERVE-101 is currently being evaluated in the heart-1 Phase 1 clinical trial in New Zealand and the United Kingdom (U.K.). Verve submitted its IND application for VERVE-101 to the FDA in October and received notification of a hold from the FDA on Friday, November 4, 2022. The company expects to receive an official letter with the FDA's questions within 30 days. Verve plans to provide updates pending engagement with the FDA and intends to work closely with the FDA to resolve the hold as promptly as possible in order to initiate dosing in the U.S.

heart-1 Trial Update
Clinical data from the ongoing heart-1 study in New Zealand and the U.K. were not included in the IND package submitted to the FDA. Verve has completed dosing of VERVE-101 in the first dose cohort of the dose-escalation portion of the heart-1 trial, which was well tolerated in all three patients. There have been no treatment-related adverse events reported to date, and all adverse events observed have been Grade 1 in nature. The independent Data Safety Monitoring Board (DSMB) has reviewed safety data from the first cohort and recommended dose escalation to the planned second dose level, which is expected to begin soon. Enrollment efforts are ongoing in New Zealand and the U.K. The company plans to report initial safety and pharmacodynamic data for all dose cohorts of the dose-escalation portion of the heart-1 study at a medical meeting in the second half of 2023.

"We founded Verve with a vision of providing patients with ASCVD a transformative alternative to the current chronic care management system," said Sekar Kathiresan, M.D., co-founder and chief executive officer of Verve. "We prepared a comprehensive regulatory package for VERVE-101, a first-in-class *in vivo* liver base editing program, that we submitted to the FDA in October. We anticipate receiving details from the FDA in the next month, and are committed to working closely with the Agency to address their questions, so that we may open enrollment for patients with HeFH in the U.S."

"We are pleased to have completed dosing in the first dose cohort of the heart-1 trial and to have received a recommendation by an independent DSMB to move to the second dose level," said Andrew Bellinger, M.D., Ph.D., chief medical and scientific officer of Verve. "The safety profile observed in the first dose cohort with VERVE-101 is encouraging, and in-line with safety data generated with VERVE-101 in our preclinical studies. Enrollment efforts for the second dose cohort continue in New Zealand and the U.K."

Additional Pipeline Updates

- **VERVE-201 IND-Enabling Studies Underway:** Verve has initiated IND-enabling studies for its ANGPTL3 program, VERVE-201, which is designed to permanently turn off the *ANGPTL3* gene in the liver, a key regulator of cholesterol and triglyceride metabolism. The company is initially advancing VERVE-201 as a treatment for homozygous familial hypercholesterolemia (HoFH), a rare and often fatal genetic subtype of premature ASCVD characterized by extremely high blood LDL-C. In August, Verve presented data highlighting the extensive work conducted to identify VERVE-201 as a development candidate.

Recent Data Presentation

- **Preclinical Data for VERVE-101 Published in *Circulation* and Presented at the American Heart Association (AHA) 2022 Annual Meeting:** Verve recently announced that preclinical data supporting VERVE-101 as a treatment for HeFH has been published in the American Heart Association's peer-reviewed journal *Circulation*. The published data showed a durable reduction in blood PCSK9 protein and LDL-C reduction. In addition, Verve presented preclinical data from experiments demonstrating the absence of evidence of editing of the *PCSK9* gene in germline tissue (i.e., sperm cells or egg cells) when VERVE-101 was administered to male non-human primates and female mice, respectively. These data

were also presented in an oral presentation at the American Heart Association (AHA) Scientific Sessions 2022.

Third Quarter 2022 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $550.7 million as of September 30, 2022, as compared to $360.4 million as of December 31, 2021. The company's cash, cash equivalents and marketable securities as of September 30, 2022, include $60 million received from Vertex and $247.5 million in net proceeds from the company's issuance of common stock during the third quarter. The company's cash, cash equivalents and marketable securities are expected to be sufficient to fund the company's current operating plan into the second half of 2025.
- **Research & Development (R&D) Expenses:** R&D expenses were $35.2 million for the third quarter of 2022, compared to $17.5 million for the third quarter of 2021.
- **General & Administrative (G&A) Expenses:** G&A expenses were $9.6 million for the third quarter of 2022, compared to $6.0 million for the third quarter of 2021.
- **Net Loss:** Net loss was $45.2 million, or $0.79 basic and diluted net loss per share, for the third quarter of 2022, compared to $22.7 million, or $0.47 basic and diluted net loss per share, for the third quarter of 2021.

About heart-1
heart-1 is an open-label Phase1b clinical trial designed to enroll approximately 40 adult 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 reductions in blood PCSK9 protein and low-density lipoprotein cholesterol (LDL-C). Initial clinical data from the dose escalation portion of the heart-1 clinical trial including safety parameters, blood PCSK9 level, and blood LDL-C level are expected in the second half of 2023. For more information, please visit clinicaltrials.gov.

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) 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 in homozygous familial hypercholesterolemia (HoFH) and ultimately to treat 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 company's expectations regarding communications related to the clinical hold on the IND for VERVE-101; the company's plans and expectations regarding discussions with the FDA with respect to the IND and the outcomes from the discussions, the company's ability to enroll patients in its ongoing heart-1 trial, the timing and availability of clinical data from its heart-1 clinical trial, its research and development plans, the potential advantages and therapeutic potential of the company's programs, including VERVE-101 and VERVE-201, 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, 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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Verve Therapeutics, Inc.
Selected Condensed Financial Information
(in thousands, except share and per share amounts)
(unaudited)

Condensed consolidated statements of operations	Three months ended September 30, 2022	Three months ended September 30, 2021	Nine months ended September 30, 2022	Nine months ended September 30, 2021
Collaboration revenue	$ 929	$ —	$ 929	$ —
Operating expenses:				
Research and development	$ 35,197	$ 17,495	$ 92,811	$ 42,263
General and administrative	9,592	6,007	26,095	12,264
Total operating expenses	44,789	23,502	118,906	54,527
Loss from operations	(43,860)	(23,502)	(117,977)	(54,527)
Other (expense) income:				
Change in fair value of antidilution rights liability	-	-	-	(25,574)
Change in fair value of success payment liability	(3,306)	700	(691)	(8,954)
Interest and other income, net	1,976	53	2,366	78
Total other (expense) income, net	(1,330)	753	1,675	(34,450)
Net loss	$ (45,190)	$ (22,749)	$ (116,302)	$ (88,977)
Net loss per common share attributable to common stockholders, basic and diluted	$ (0.79)	$ (0.47)	$ (2.26)	$ (4.52)
Weighted-average common shares used in net loss per share attributable to common stockholders, basic and diluted	57,207,125	47,992,773	51,516,037	19,698,450

Condensed consolidated balance sheet data	September 30, 2022	December 31, 2021
Assets		
Cash, cash equivalents and marketable securities	$ 550,710	$ 360,442
Total assets	$ 673,355	$ 384,124
Total liabilities	$ 125,412	$ 26,772
Total stockholders' equity	$ 547,943	$ 357,352