Verve Therapeutics Announces Pipeline Progress and Reports Third Quarter 2024 Financial Results

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Seven participants across two cohorts dosed in the Heart-2 Phase 1b clinical trial of VERVE-102 targeting PCSK9; Initial data planned for the first half of 2025

First participant dosed in the Pulse-1 Phase 1b clinical trial of VERVE-201 targeting ANGPTL3; Regulatory clearances in Australia, Canada, and the U.K.

Cash, cash equivalents, and marketable securities of $539.9 million; cash runway through 2026

BOSTON, Nov. 05, 2024 (GLOBE NEWSWIRE) -- Verve Therapeutics, a clinical-stage company developing a new class of genetic medicines for cardiovascular disease, today reported pipeline updates and financial results for the quarter ended September 30, 2024.

“In the third quarter, we made considerable progress towards our mission to develop a new class of genetic medicines where a one-time treatment leads to lifelong lowering of blood cholesterol,” said Sekar Kathiresan, M.D., co-founder and chief executive officer of Verve Therapeutics. “We continue to execute on the Heart-2 clinical trial and are pleased to share that as of October 29, 2024, seven participants have been dosed. VERVE-102 has been well-tolerated, with no serious adverse events and no clinically significant laboratory abnormalities observed. We look forward to providing initial data from the Heart-2 clinical trial and an update on the PCSK9 program in the first half of 2025.”

Dr. Kathiresan continued, “In addition, we are excited to announce that the first participant in the Pulse-1 Phase 1b clinical trial for our ANGPTL3 product candidate, VERVE-201, was recently dosed. With cash runway through 2026, we are well-positioned to execute additional important milestones across our pipeline and advance our early-stage programs, including our program targeting LPA. With two product candidates being tested in the clinic, we expect 2025 to be an eventful year for Verve as we develop a new approach for the treatment of cardiovascular disease.”

PCSK9 Program
Enrollment Ongoing in Heart-2 Phase 1b Clinical Trial Evaluating VERVE-102

- VERVE-102 is a novel, investigational gene editing medicine designed to be a single course treatment that permanently turns off the *PCSK9* gene in the liver and durably reduces disease-driving low-density lipoprotein cholesterol (LDL-C). VERVE-102 consists of messenger RNA expressing an adenine base editor and an optimized guide RNA targeting the *PCSK9* gene identical to VERVE-101, the company’s initial PCSK9 product candidate that showed proof-of concept for this mechanism. However, compared to VERVE-101, VERVE-102 uses a different lipid nanoparticle (LNP) delivery system, which includes a different ionizable lipid and Verve’s proprietary GalNAc liver-targeting ligand, designed to allow the LNP to access liver cells using either the low-density lipoprotein receptor (LDLR) or the asialoglycoprotein receptor (ASGPR).

- VERVE-102 is being evaluated in the Heart-2 open-label Phase 1b clinical trial in two patient populations who require deep and durable reductions of LDL-C levels in the blood: adults living with heterozygous familial hypercholesterolemia (HeFH) and adults living with premature coronary artery disease (CAD). The Heart-2 clinical trial is expected to include four dose cohorts, each comprised of three to nine patients with either HeFH or premature CAD.

- As of October 29, 2024, dosing has been completed in seven participants in the first two dose cohorts, 0.3 mg/kg and 0.45 mg/kg, in the Heart-2 clinical trial. VERVE-102 has been well-tolerated. No serious adverse events and no clinically significant laboratory abnormalities have been observed. Following the standard review from the independent data and safety monitoring board (DSMB), the company expects to continue the dose escalation portion of the clinical trial.

- Verve recently received clearance of its Clinical Trial Applications (CTAs) for the Heart-2 clinical trial in Israel and New Zealand. Enrollment remains ongoing in Australia, Canada, and the U.K.

- In November 2024, Verve plans to present a moderated digital poster at the American Heart Association (AHA) Scientific Sessions describing the design of the Heart-2 Phase 1b clinical trial.

- Verve expects to provide initial data from the Heart-2 clinical trial and an update on the PCSK9 program in the first half of 2025. The company also plans to initiate the Phase 2 clinical trial for the PCSK9 program in the second half of 2025.

Analyses of Heart-1 Phase 1b Clinical Trial of VERVE-101

- Verve recently reported updated durability data from the Heart-1 clinical trial of VERVE-101 at the European Society of Gene and Cell Therapy (ESGCT) 2024 Congress and the American Society of Nephrology Kidney Week 2024 Meeting. Mean, time-averaged PCSK9 protein reductions of greater than 60% were observed in each of the two higher dose cohorts (0.45 mg/kg and 0.6 mg/kg), and mean, time-averaged LDL-C reductions of 42% at 0.45 mg/kg (n=6) and time-averaged LDL-C reduction of 57% at 0.6 mg/kg (n=1) were observed. In the single participant in the highest dose cohort, LDL-C reduction has now been sustained out to 18 months after the single dose. No new treatment related adverse events have been reported since March 2024. Verve believes that these new durability data further support the potential of once-and-done gene editing medicines for the treatment of cardiovascular disease.

- Verve has completed a series of nonclinical studies as part of its investigation into the previously disclosed laboratory abnormalities observed with VERVE-101. In order to isolate the role of the LNP and determine whether the laboratory abnormalities observed in the Heart-1 clinical trial were due to the LNP delivery system, these studies used a version of VERVE-101 with a non-targeting guide RNA designed to preclude base editing. Data from these studies continue to support Verve's understanding that the LNP in VERVE-101 is likely the primary driver of the laboratory abnormalities observed in the Heart-1 clinical trial. The Heart-1 clinical trial will remain paused during the dose escalation portion of the Heart-2 clinical trial evaluating VERVE-102.

ANGPTL3 Program
First Participant Dosed with VERVE-201 in the Pulse-1 Phase 1b Clinical Trial

- VERVE-201 is a novel, investigational gene editing medicine designed to be a single course treatment that permanently turns off the *ANGPTL3* gene in the liver to reduce disease-driving LDL-C as well as remnant cholesterol and utilizes Verve's proprietary GalNAc-LNP delivery technology. VERVE-201 is being developed in two patient populations: patients with refractory hypercholesterolemia (RH), defined as those who are unable to achieve adequate LDL-C reduction with maximally tolerated standard of care therapies, potentially including PCSK9 inhibitors, and patients living with homozygous familial hypercholesterolemia (HoFH), a rare and often fatal inherited cause of premature ASCVD characterized by extremely high blood LDL-C. The aim of this medicine is to reduce the heavy treatment burden associated with available therapies, including the requirement for multiple oral, injectable, and intravenous infusions, often administered over decades.

- Verve announced today that the first participant has been dosed with VERVE-201 in its Pulse-1 Phase 1b clinical trial.

  The Pulse-1 clinical trial is designed to evaluate the safety and tolerability of VERVE-201 administration in adult patients with RH who require additional lowering of LDL-C despite treatment with maximally tolerated standard of care therapies, potentially including PCSK9 inhibitors. Endpoints also include pharmacokinetics and changes in blood ANGPTL3 protein and LDL-C levels. The Pulse-1 clinical trial is a single-ascending dose study that has an adaptive design. The Pulse-1 clinical trial is expected to include four dose cohorts each comprised of three to nine patients with RH.

- Verve recently received regulatory clearances to initiate the Pulse-1 clinical trial in Australia, Canada, and the U.K.

Upcoming Investor Events
Verve plans to participate in fireside chats during the following upcoming investor events:

- Guggenheim's Inaugural Healthcare Innovation Conference, November 11 at 4:00 PM ET, Boston, MA
- Stifel 2024 Healthcare Conference, November 18 at 3:00 PM ET, New York, NY
- Jefferies London Healthcare Conference, November 20 at 4:00 PM GMT, London, UK

Upcoming Medical Meeting Presentations
Verve plans to present a moderated digital poster at the American Heart Association (AHA) Scientific Sessions in Chicago, IL. Details of the poster session are as follows:

Title: Design of Heart-2: a phase 1b clinical trial of VERVE-102, an *in vivo* base editing medicine delivered by a GalNAc-LNP and targeting *PCSK9* to durably lower LDL cholesterol
Session: Genomic Therapies for Cardiovascular Disease
Date and Time: November 16 at 10:35 AM CT

Third Quarter 2024 Financial Results

Cash Position: Verve ended the third quarter of 2024 with $539.9 million in cash, cash equivalents, and marketable securities. Verve expects its capital position to be sufficient to fund its operations through 2026.

Collaboration Revenue: Collaboration revenue was $6.9 million for the third quarter of 2024, compared to $3.1 million for the third quarter of 2023. The increase was primarily due to an increase in research services performed under the company's collaboration agreements.

Research & Development (R&D) Expenses: R&D expenses were $49.9 million for the third quarter of 2024, compared to $43.8 million for the third quarter of 2023. Stock-based compensation expense included in R&D expenses was $5.4 million and $4.9 million for the third quarter of 2024 and 2023, respectively.

General & Administrative (G&A) Expenses: G&A expenses were $13.8 million for the third quarter of 2024, compared to $11.7 million for the third quarter of 2023. Stock-based compensation expense included in G&A expenses was $5.4 million and $3.9 million for the third quarter of 2024 and 2023, respectively.

Net Loss: Net loss was $50.1 million, or $0.59 basic and diluted net loss per share, for the third quarter of 2024, compared to $45.8 million, or $0.72 basic and diluted net loss per share, for the third quarter of 2023.

About Verve Therapeutics
Verve Therapeutics, Inc. (Nasdaq: VERV) is a clinical-stage company developing a new class of genetic medicines for cardiovascular disease with the potential to transform treatment from chronic management to single-course gene editing medicines. The company's lead 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 atherosclerotic cardiovascular disease (ASCVD). 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 patients with established ASCVD who continue to be impacted by high LDL-C levels. VERVE-201 is designed to permanently turn off the *ANGPTL3* gene in the liver and is initially being developed for refractory hypercholesterolemia, where patients still have high LDL-C despite treatment with maximally tolerated standard of care therapies, and homozygous familial hypercholesterolemia (HoFH). 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 company's ongoing Heart-2 clinical trial and Pulse-1 clinical trial; the timing and availability of data for the Heart-2 trial, PCSK9 program and Pulse-1 trial; expectations for the company's Heart-1 clinical trial; 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 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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Verve Therapeutics, Inc.
Selected Condensed Consolidated Financial Information
(in thousands, except share and per share amounts)
(unaudited)

	Three months ended September 30,		Nine months ended September 30,	
Condensed consolidated statements of operations	**2024**	**2023**	**2024**	**2023**
Collaboration revenue	$ 6,865	$ 3,117	$ 19,252	$ 6,614
Operating expenses:				
Research and development	49,938	43,765	149,299	138,135
General and administrative	13,837	11,686	42,546	37,655
Total operating expenses	63,775	55,451	191,845	175,790
Loss from operations	(56,910)	(52,334)	(172,593)	(169,176)
Other income (expense):				
Change in fair value of success payment liability	(6)	802	1,743	878
Interest and other income, net	6,887	5,841	22,452	16,825
Total other income, net	6,881	6,643	24,195	17,703
Loss before provision for income taxes	(50,029)	(45,691)	(148,398)	(151,473)
Provision for income taxes	(104)	(67)	(276)	(243)
Net loss	$ (50,133)	$ (45,758)	$ (148,674)	$ (151,716)
Net loss per common share, basic and diluted	$ (0.59)	$ (0.72)	$ (1.77)	$ (2.43)
Weighted-average common shares used in net loss per share, basic and diluted	84,632,952	63,211,849	83,999,797	62,322,965

Condensed consolidated balance sheet data	**September 30, 2024**	**December 31, 2023**
Cash, cash equivalents and marketable securities	$ 539,920	$ 623,950
Total assets	$ 663,906	$ 752,688
Total liabilities	$ 155,355	$ 153,186
Total stockholders' equity	$ 508,551	$ 599,502