Verve Therapeutics Announces Pipeline Progress and Anticipated 2025 Milestones

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Initial data for the Heart-2 Phase 1b clinical trial of VERVE-102 targeting PCSK9 expected in second quarter of 2025

Dosing in the Heart-2 trial has moved to the 0.6 mg/kg cohort

VERVE-301 nominated as development candidate targeting the LPA gene; Verve to receive an associated milestone payment from Eli Lilly

Well-capitalized with cash runway extending into mid-2027

Company to present at 43rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025, at 2:15 p.m. ET/11:15 a.m. PT

BOSTON, Jan. 13, 2025 (GLOBE NEWSWIRE) -- Verve Therapeutics, a clinical-stage company developing a new class of genetic medicines for cardiovascular disease, today highlighted its recent pipeline progress and anticipated 2025 milestones.

"Our mission is to advance a new class of *in vivo* gene editing medicines for cardiovascular disease that target three key drivers of high cholesterol - LDL-C, remnant cholesterol, and Lp(a). Verve's medicines are designed to lead to lifelong cholesterol lowering after a single treatment. 2024 marked a year of crucial progress, with ongoing proof-of-concept data in humans demonstrating that we can use base editing to turn off the *PCSK9* gene in the liver and durably lower blood cholesterol after a single intravenous infusion," said Sekar Kathiresan, M.D., co-founder and chief executive officer of Verve Therapeutics. "Building on this momentum, we are developing three lipid-lowering medicines each utilizing our proprietary GalNAc-LNP liver delivery technology. 2025 is anticipated to bring important milestones across our pipeline, including an initial Phase 1b data readout for VERVE-102 in the second quarter, a final Phase 1b data readout for the dose escalation portion of the VERVE-102 trial in the second half of 2025, the opportunity for Eli Lilly to opt-in to the PCSK9 program in the second half of 2025, a program update for VERVE-201 targeting *ANGPTL3* in the second half of 2025, and continued advancement of our collaboration with Eli Lilly to develop VERVE-301 targeting the *LPA* gene."

Pipeline Updates and 2025 Anticipated Milestones

PCSK9 Program

Initial Data for the Heart-2 Phase 1b Clinical Trial Evaluating VERVE-102 Expected in the Second Quarter of 2025

- VERVE-102, a novel, investigational base editing medicine targeting *PCSK9*, is being evaluated in the Heart-2 open-label Phase 1b clinical trial in two patient populations who require deep and durable reductions of low-density lipoprotein cholesterol (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 the data cut-off date 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. In these seven participants, VERVE-102 has been well-tolerated and 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) in November, dosing in the Heart-2 clinical trial has now moved to the third dose cohort, 0.6 mg/kg.
- Verve expects to announce initial data from the Heart-2 clinical trial as well as an update on the PCSK9 program in the second quarter of 2025. This initial data set is expected to include ten to twelve participants across the first three dose cohorts (0.3 mg/kg, 0.45 mg/kg, and 0.6 mg/kg) with at least 28 days of follow-up for each participant. Verve expects to report demographic and initial safety and efficacy data.
- Verve expects to report the final data for the dose escalation portion of the Heart-2 clinical trial in the second half of 2025.
- Under the PCSK9 program collaboration agreement with Verve, Eli Lilly and Company (Lilly) holds the right to opt-in to share worldwide development expenses (33% contributed by Lilly)

and to jointly commercialize and share profits and expenses related to commercialization in the United States on a 50/50 basis. Verve retains control of the development and commercialization of all collaboration products in the United States, and Verve holds all product rights outside the United States. Verve expects to deliver the opt-in data package for the PCSK9 program and receive a decision from Lilly in the second half of 2025.
- Verve plans to initiate the Phase 2 clinical trial for the PCSK9 program in the second half of 2025.

ANGPTL3 Program

Pulse-1 Phase 1b Clinical Trial for VERVE-201 Continues to Progress

- In November 2024, Verve announced that the first participant has been dosed with VERVE-201, a novel, investigational base editing medicine targeting *ANGPTL3*, 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 refractory hypercholesterolemia (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.
- Verve expects to provide an update on the ANGPTL3 program in the second half of 2025.

LPA Program

Nomination of VERVE-301 as a Development Candidate Targeting the *LPA* gene

- Verve today announced the nomination of VERVE-301 as the company's development candidate targeting the LPA gene. VERVE-301 uses a novel, *in vivo* gene editing approach designed to permanently turn off the LPA gene in the liver to reduce blood lipoprotein(a) [Lp(a)] levels. Lp(a) is a genetically validated, independent risk factor for atherosclerotic cardiovascular disease (ASCVD), ischemic stroke, thrombosis, and aortic stenosis. This increased risk is most pronounced in individuals with very high Lp(a) concentrations (e.g., ≥ 125 nmol/L). An estimated 1.4 billion people worldwide have an Lp(a) concentration above this threshold. Lp(a) concentrations are determined at birth. Unfortunately, lifestyle changes - such as diet and exercise - as well as currently approved lipid-lowering therapies, have minimal to no impact on reducing Lp(a) levels.
- Verve has an exclusive research collaboration with Lilly to advance its *in vivo* gene editing program to lower Lp(a) for the treatment of ASCVD. As part of this collaboration agreement, Verve will receive a milestone payment in conjunction with the development candidate nomination. Verve will advance the research and development of its Lp(a) program through the completion of Phase 1 clinical development, which will be funded by Lilly. Lilly will then be responsible for subsequent development, and the potential manufacturing and commercialization of VERVE-301. Verve is eligible to receive up to a total of $465 million in research, development, and commercial milestones, as well as tiered royalties on global net sales. In addition, following the completion of Phase 1 clinical trials and subject to an opt-in fee, Verve has the right to opt-in to co-fund and share margins globally on the Lp(a) program (in lieu of receipt of milestones and royalties).

Updated Cash Runway
With Verve's existing cash, cash equivalents and marketable securities, including the milestone payment to be received from Lilly under the Lp(a) program, Verve expects its capital position to be sufficient to fund its operations into mid-2027.

Upcoming J.P. Morgan Healthcare Conference Presentation and Webcast
Sek Kathiresan, M.D., co-founder and chief executive officer of Verve, will present a company overview at the 43rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025, at 2:15 p.m. ET/11:15 a.m. PT. A live webcast of this event will be available on the Investors Events section of Verve's website at www.vervetx.com. An archived replay will be available for approximately 30 days following the event.

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 therapies to single-course gene editing medicines. The company's lead programs –VERVE-102, VERVE-201, and VERVE-301 – target the three cholesterol drivers of atherosclerosis: LDL-C, remnant cholesterol, and Lp(a). VERVE-102 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 patients with established atherosclerotic cardiovascular disease (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). VERVE-301 is designed to permanently turn off the *LPA* gene to reduce Lp(a) levels. Lp(a) is a genetically validated, independent risk factor for ASCVD, ischemic stroke, thrombosis, and aortic stenosis. 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 and timing for initiation of the Phase 2 clinical trial for the PCSK9 program; the timing of updates for the PCSK9 and ANGPTL3 programs; the development of VERVE-301; the receipt of a milestone payment from Lilly under the LPA program and timing of Lilly's opt-in decision for the PCSK9 program; the potential future milestone payments and potential royalties under the collaboration agreement with Lilly; the company's 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 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 preclinical studies and 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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