Tenaya Therapeutics Announces 2025 Strategic Priorities and Anticipated Milestones

January 13, 2025

Continued Focus on Driving Advancement of TN-201 and TN-401 Gene Therapies for Cardiomyopathies

Dosing Initiated in Cohort 2 of the MyPEAK™-1 Phase 1b/2 Clinical Trial of TN-201 for Treatment of MYBPC3-Associated Hypertrophic Cardiomyopathy

Additional Cohort 1 Data to be Reported in 1H25 Building on Promising Initial Data

Initial Data from RIDGE™-1 Phase 1b Clinical Trial of TN-401 for PKP2-Associated Arrhythmogenic Right Ventricular Cardiomyopathy Expected in 2H25

SOUTH SAN FRANCISCO, Calif., Jan. 13, 2025 (GLOBE NEWSWIRE) -- Tenaya Therapeutics, Inc. (NASDAQ: TNYA), a clinical-stage biotechnology company with a mission to discover, develop and deliver potentially curative therapies that address the underlying causes of heart disease, today provided an update on its clinical development programs and outlined its strategic priorities for 2025.

“2024 was a pivotal year for Tenaya, marked by important operational execution across our clinical-stage pipeline of gene therapy candidates with the potential to target and address the underlying drivers of heart disease,” said Faraz Ali, Chief Executive Officer of Tenaya. “As we enter 2025, we are eager to build on this momentum to accelerate enrollment and report on safety, biopsy and initial clinical endpoints from both our TN-201 and TN-401 programs throughout the year.”

Program Updates and Anticipated 2025 Milestones:

TN-201 – Gene Therapy for *MYBPC3*-Associated Hypertrophic Cardiomyopathy (HCM)

- Tenaya anticipates reporting additional data from Cohort 1 from the ongoing MyPEAK-1 Phase 1b/2 clinical trial of TN-201 for the potential treatment of *MYBPC3*-associated HCM in the first half of 2025. These data are expected to include safety and available assessments from the first three patients dosed, 52-week biopsy data for Patient 2, and baseline and post-dose biopsy data for Patient 3.
    - In December 2024, Tenaya announced initial interim data from Cohort 1, which showed TN-201 administered at the starting dose of 3E13 vg/kg was generally well-tolerated among the first three patients enrolled in the study. Among the first two patients, TN-201 achieved readily detectable vector DNA in the heart and evidence of transgene RNA expression. Serial biopsies at Week 8 and Week 52 for Patient 1 demonstrated increasing TN-201 mRNA and MyBP-C protein levels over time. Circulating biomarkers of cardiac muscle strain and injury remained largely stable, and certain clinical markers of disease showed stability or directional improvement in the first two individuals dosed, while other measures were not yet available, interpretable or mixed.
- The first patient received TN-201 at the 6E13 vg/kg dose in 2024 and enrollment in Cohort 2 of the MyPEAK-1 clinical trial is ongoing. Tenaya anticipates completing Cohort 2 enrollment in the first half of 2025 and providing initial Cohort 2 data and an update on Cohort 1 in the second half of 2025.
    - Cohort 2 of MyPEAK-1 expanded participant eligibility to include *MYBPC3*-associated HCM adults with the obstructive form of disease and patients without implantable cardioverter defibrillators (ICDs). All patients in Cohort 2 will receive a baseline biopsy, one post-dose and one at 52-weeks.
- Tenaya plans to present data from its pediatric non-interventional natural history study, known as MyClimb, in the second half of 2025.
    - The MyClimb study was initiated in 2021 to characterize the disease burden and progression of *MYBPC3*-associated HCM in patients under eighteen and has enrolled more than 200 participants.

TN-401 –Gene Therapy for *PKP2*-Associated Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

- Tenaya expects to complete enrollment of Cohort 1 of the RIDGE-1 Phase 1b clinical trial in the first half of 2025.
- Initial clinical data from the first cohort of patients receiving TN-401 at the 3E13 vg/kg dose, including safety and post-dose biopsy results, is expected in the second half of 2025.
    - TN-401 is Tenaya’s potential first-in-class AAV9-based gene therapy designed to deliver a functional *PKP2* gene to heart muscle cells. The working *PKP2* gene is intended to increase levels of *PKP2*, which are needed to maintain the structural integrity and cell-to-cell signaling of heart muscle cells.
    - In November 2024, Tenaya announced the dosing of the first patient in the RIDGE-1 trial.

- Tenaya anticipates activating its first ex-U.S. RIDGE-1 clinical site in the first half of 2025.
- Tenaya plans to present data from the non-interventional natural history and seroprevalence study (known as RIDGE) in the first half of 2025. To date, RIDGE has enrolled more than 100 *PKP2*-associated ARVC participants across 18 clinical sites.
    - Initial seroprevalence data from RIDGE presented in July 2024 indicated that antibodies to AAV9 were below the eligibility threshold for participation RIDGE-1.

Tenaya has established a rich portfolio of proprietary capabilities for targeted drug discovery and validation, and the design, production and targeted delivery of genetic medicines. In 2025, the company plans to continue research on promising targets for potential therapeutic utility and pursue platform enhancements that may further Tenaya's ability to deliver on its mission of discovering and developing disease-modifying medicines for heart disease.

About *MYBPC3*-Associated Hypertrophic Cardiomyopathy and TN-201 Gene Therapy
Variants in the Myosin Binding Protein C3 (*MYBPC3)* gene are the most common genetic cause of hypertrophic cardiomyopathy (HCM), accounting for approximately 20% of the overall HCM population, or 120,000 patients, in the United States alone.(1) TN-201 is an adeno-associated virus serotype 9 (AAV9)-based gene therapy designed to deliver a working *MYBPC3* gene to heart muscle cells via a single intravenous infusion, increasing MyBP-C protein levels to address the underlying cause of *MYBPC3*-associated HCM with the aim of halting or even reversing disease after a single dose. The U.S. Food and Drug Administration has granted TN-201 Fast Track, Orphan Drug and Rare Pediatric Drug Designations. TN-201 has also received orphan medicinal product designation from the European Commission.

About PKP2-associated ARVC and TN-401 Gene Therapy
TN-401 is being developed for the treatment of arrhythmogenic right ventricular cardiomyopathy (ARVC, also known as arrhythmogenic cardiomyopathy or ACM) caused by mutations in the *plakophilin-2* (*PKP2)* gene. *PKP2* gene mutations result in insufficient levels of critical proteins needed to maintain the structural integrity and cell-to-cell signaling of heart muscle cells. TN-401 gene replacement therapy is designed to deliver a functional *PKP2* gene into heart muscle cells using an adeno associated virus serotype 9 (AAV9) capsid. In preclinical studies, the new, healthy *PKP2* gene was successfully integrated into heart cells where it produced the missing protein to slow or even reverse the course of disease. TN-401 normalized heart rhythms, reversed disease progression and extended survival following a single dose in a knock-out genetic model of disease. The prevalence of *PKP2*-associated ARVC is estimated at more than 70,000 people in the U.S. alone.(2) TN-401 has received Orphan Drug and Fast Track Designations from the FDA. TN-401 has also received orphan medicinal product designation from the European Commission.

About Tenaya Therapeutics
Tenaya Therapeutics is a clinical-stage biotechnology company committed to a bold mission: to discover, develop and deliver potentially curative therapies that address the underlying drivers of heart disease. Tenaya employs a suite of integrated internal capabilities, including modality agnostic target validation, capsid engineering and manufacturing, to generate a portfolio of genetic medicines aimed at the treatment of both rare genetic disorders and more prevalent heart conditions. Tenaya's pipeline includes TN-201, a gene therapy for MYBPC3-associated hypertrophic cardiomyopathy (HCM), TN-401, a gene therapy for PKP2-associated arrhythmogenic right ventricular cardiomyopathy (ARVC), TN-301, a small molecule HDAC6 inhibitor intended for heart failure with preserved ejection fraction (HFpEF), and multiple early-stage programs in preclinical development. For more information, visit www.tenayatherapeutics.com.

(1) Sedaghat-Hemedani, et al., *Clinical Research Cardiology*, 2017
(2) Peters, et a, Int J Cardiol 2004; McKenna, Nat Rev Card, 2021

Forward Looking Statements
This press release contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Statements in this press release that are not purely historical are forward-looking statements. Words such as "continued," "to be," "anticipates," "expected," "plans," "potential," and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, statements regarding the advancement TN-201 and TN-401; planned timing to report additional Cohort 1 and Cohort 2 data from MyPEAK-1 and related focus of the data readouts; TN-201 clinical outcomes, which may materially change as patient enrollment continues or more patient data become available; the clinical, therapeutic and commercial potential of, and expectations regarding TN-201 and TN-401; expectations regarding completion of Cohort 1 enrollment for RIDGE-1 and ex-U.S. clinical site activation; planned timing for initial data from RIDGE-1 and related focus of the data readout; anticipated timing for completion of Cohort 2 enrollment for MyPEAK-1; planned timing to present data from MyClimb and RIDGE; statements regarding Tenaya's research related activities; and statements made by Tenaya's Chief Executive Officer. The forward-looking statements contained herein are based upon Tenaya's current expectations and involve assumptions that may never materialize or may prove to be incorrect. These forward-looking statements are neither promises nor guarantees and are subject to a variety of risks and uncertainties, including but not limited to: availability of MyPEAK-1 and RIDGE-1 data at the referenced times; the timing and progress of MyPEAK-1 and RIDGE-1; the potential failure of TN-201 and TN-401 to demonstrate safety and/or efficacy in clinical testing; the potential for any MyPEAK-1 and/or RIDGE-1 clinical trial results to differ from preclinical, initial, interim, preliminary or expected results; Tenaya's ability to enroll and maintain patients in clinical trials, including MyPEAK-1 and RIDGE-1; risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as an early stage company; availability of MyClimb and RIDGE data at the referenced time; Tenaya's continuing compliance with applicable legal and regulatory requirements; Tenaya's ability to raise any additional funding it will need to continue to pursue its product development plans; Tenaya's reliance on third parties; Tenaya's manufacturing, commercialization and marketing capabilities and strategy; the loss of key scientific or management personnel; competition in the industry in which Tenaya operates; Tenaya's ability to obtain and maintain intellectual property protection for its product candidates; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section titled "Risk Factors" in Tenaya's Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2024, and other documents that Tenaya files from time to time with the Securities and Exchange Commission. These forward-looking statements are made as of the date of this press release, and Tenaya assumes no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Contact
Michelle Corral
VP, Corporate Communications and Investor Relations

IR@tenayathera.com

Investors
Anne-Marie Fields
Precision AQ (formerly Stern Investor Relations)
annemarie.fields@precisionaq.com

Media
Wendy Ryan
Ten Bridge Communications
wendy@tenbridgecommunications.com