Tenaya Therapeutics Reports Promising Early Data from MyPEAK™-1 Phase 1b/2 Clinical Trial of TN-201 for Treatment of MYBPC3-Associated Hypertrophic Cardiomyopathy

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TN-201 Well Tolerated at 3E13 vg/kg Dose

AAV9 Capsid Demonstrated Robust Delivery of TN-201 Transgene to Heart Muscle Cells Resulting in Increasing RNA Expression and an Increase in Protein Levels Observed at One Year

Circulating Biomarkers and Other Clinical Measures Mostly Remained Stable or Improved from Baseline

Tenaya Management to Host a Webcast Conference Call Today at 8:00 a.m. ET

SOUTH SAN FRANCISCO, Calif., Dec. 17, 2024 (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 reported encouraging early data from the first cohort of patients in the MyPEAK-1 clinical trial of TN-201 gene therapy. TN-201 is being developed for the potential treatment of *MYBPC3*-associated hypertrophic cardiomyopathy (HCM), a condition caused by insufficient levels of myosin-binding protein C (MyBP-C).

Preliminary data from three patients in the first dose cohort of 3E13 vg/kg (Cohort 1) showed that TN-201 was generally well tolerated, with readily detectable vector DNA in the heart, evidence of transgene RNA expression, and increasing TN-201 mRNA and MyBP-C protein levels over time. Circulating biomarkers of cardiac muscle strain and injury remained largely stable, and other clinical markers of disease showed stability or directional improvement in the first two individuals dosed, though longer-term data are needed to characterize TN-201's activity. Tenaya will continue to follow these first three patients with additional data readouts from Cohort 1 and the higher dose Cohort 2 anticipated in 2025.

"The initial patients enrolled in the MyPEAK-1 Phase 1b/2 clinical study are like many we see in our clinic: relatively young adults whose HCM is keeping them from having an adequate quality of life, including being able to perform activities of daily living and whose disease is progressing in spite of treatment interventions, putting them at significant risk of dire complications," said Milind Desai, M.D., M.B.A, Haslam Family Endowed Chair in Cardiovascular Medicine, Vice Chair, Heart Vascular Thoracic Institute, Director of the Hypertrophic Cardiomyopathy Center and at the Cleveland Clinic, and an investigator for the MyPeak-1 Phase 1b/2 clinical trial. "The goal of gene therapy is to halt or even reverse the steady decline in *MYBPC3*-associated HCM by addressing the underlying genetic cause of disease. Initial data from this first-in-human clinical trial of TN-201 demonstrate tolerability and early evidence of protein expression support additional investigation to build on these findings."

"TN-201's emerging safety profile, excellent uptake into cardiomyocytes, and evidence of transgene RNA and protein expression provide important de-risking of the program as we proceed with enrollment of the higher dose cohort," said Whit Tingley, M.D., Ph.D., Tenaya's Chief Medical Officer. "In addition, we have observed encouraging early hints of disease stability and improvement among certain clinical measures of disease, offering further reason to believe in TN-201's promise. Longer-term follow up for all patients in the lower dose cohort and results from the higher dose cohort will further inform our understanding of TN-201 gene therapy's potential in *MYBPC3*-associated HCM."

Interim Phase 1b/2 MyPEAK-1 Results
Data reported today focus on changes over time in the first three patients to receive TN-201 gene therapy. Patients were dosed sequentially with TN-201 via a one-time intravenous infusion of a 3E13 vg/kg dose. Patients enrolled in Cohort 1 were required to be symptomatic adults with *MYBPC3*-associated nonobstructive HCM at sufficiently high risk of sudden cardiac death to warrant an implantable cardiac defibrillator device (ICD). An assessment of Patient 1 at Week 52, Patient 2 at Week 40 and safety data for Patient 3 at 12 weeks are included in this first readout. All three had objectively severe disease at the time of enrollment with mild-to moderate heart failure symptoms that limited the activities of daily living as measured by New York Heart association (NYHA) classification.

TN-201 was generally well tolerated with a manageable safety profile.

- No cardiac toxicities, complement activation-associated adverse effects, or thrombotic microangiopathy (TMA)-related events were observed.
- All three patients experienced isolated elevations in liver enzymes associated with TN-201 treatment. These were not associated with other signs or symptoms of liver damage and were well managed with the administration of corticosteroids, per protocol. Liver enzyme elevations are a known side effect associated with AAV-based gene therapies.
    - One patient experienced asymptomatic and mild (Grade 1) enzyme elevation that was designated as an SAE due to the administration of a corticosteroid bolus in the hospital setting.
- On-study adverse events were primarily mild, transient or reversible. The majority of observed side effects were typical of those observed with use of adeno-associated viral vector (AAV)-based gene therapies or immunosuppressive (IS) regimens.
    - Two serious adverse events (SAEs) occurred that were not related to TN-201.
- Patients 1 and 2 have successfully tapered off immunosuppressives and all three patients remain on study.

TN-201 achieved robust transduction into cardiomyocytes and measurable transgene RNA expression. TN-201 RNA expression and levels of MyBP-C protein increased over time.
Cardiac biopsy samples were collected for analysis at Week 8 for Patients 1 and 2 and Week 52 for Patient 1 to confirm and characterize transduction of TN-201 DNA in the heart, the presence of TN-201 transgene mRNA, and changes in MyBP-C protein. Baseline biopsies have been added to the MyPEAK-1 protocol, beginning with Patient 3 to provide further insights into the changes in MyBP-C protein levels over time.

- At Week 8, Patients 1 and 2 achieved evidence of robust cardiac transduction at levels that were above those that were effective in preclinical knockout mouse models of disease and perform favorably to published levels for other clinical-stage AAV gene therapy agents for genetic cardiomyopathies.
- At Week 8, Patients 1 and 2 achieved TN-201-derived mRNA at levels similar to those of other clinical-stage cardiac gene therapies, though lower than those observed in preclinical studies. TN-201 mRNA expression increased by 50% at the Week 52 biopsy for Patient 1, offering early evidence of anticipated durability of expression.
- Total levels of MyBP-C protein were quantified and demonstrated a 3% increase from Weeks 8 to 52 in Patient 1. This increase, combined with the increase observed in TN-201 mRNA expression suggest that TN-201 gene therapy is successfully being transcribed and expressed after reaching target cells. As TN-201 generated MyBP-C and endogenous MyBP-C are indistinguishable via assay, baseline biopsies will further elucidate protein level changes.

Clinical measures of HCM mostly remained stable or improved from baseline.

- Circulating biomarkers of heart muscle strain (measured via NT-proBNP) remained stable overall. Cardiac troponin I, a biomarker of heart muscle injury, normalized in Patient 2.
- Improvement or stabilization from baseline was observed in some clinical endpoints, including improvements in NYHA classification for Patients 1 and 2, while other measures were not yet available, interpretable or were mixed.
- The overall clinical picture is anticipated to become clearer with time, more follow-up, and more patients.

“Taken together, the TN-201 data reported today are in line with our overall expectations at this early juncture in the study. The high levels of cardiac transduction and early evidence of increasing transgene expression support our confidence in TN-201’s potential at this early stage. We look forward to building on these results over time,” said Faraz Ali, Tenaya’s Chief Executive Officer. “We deeply appreciate the support we are receiving from the larger community of HCM clinicians and affected families, and we are especially grateful to our study investigators and to the first three patients in Cohort 1 without whom the promise and potential of TN-201 could not be explored.”

Investor and Analyst Conference Call and Live Webcast
Tenaya management will host a conference call and webcast today beginning at 8:00 am. ET/5:00 AM PT to discuss the initial MyPEAK-1 results. Investors and analysts may access the call here. A live webcast of the conference call, including an accompanying slide presentation, will be available on the Investors section of Tenaya’s website. A replay of the webcast, and accompanying slides, will be available on the Tenaya website for approximately 90 days following the call.

About the MyPEAK-1 Phase 1b/2 Clinical Trial
The MyPEAK-1 Phase 1b/2 clinical trial (Clinicaltrials.gov ID: NCT05836259) is an ongoing, multi-center, open-label, dose-escalating study designed to assess the safety, tolerability and clinical efficacy of a one-time intravenous infusion of TN-201 gene replacement therapy. The trial is enrolling symptomatic (New York Heart Association Class II or III) adults who have been diagnosed with *MYBPC3*-associated HCM. MyPEAK-1 is testing doses of 3E13 vg/kg and 6E13 vg/kg in two cohorts of three patients each. MyPEAK-1 may enroll up to 24 *MYBPC3*-associated HCM adults with either nonobstructive or obstructive forms of HCM in planned dose expansion cohorts.

To learn more about gene therapy for HCM and participation in the MyPEAK-1 study, please visit HCMStudies.com.

About *MYBPC3*-Associated Hypertrophic Cardiomyopathy 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) *MYBPC3*-associated HCM is a severe and progressive condition affecting adults, teens, children and infants. Mutations of the *MYBPC3* gene result in insufficient expression of a protein, called MyBP-C, needed to regulate heart contraction. The heart becomes hypercontractile and the left ventricle thickens, resulting in symptoms such as chest pain, shortness of breath, palpitations and fainting. Patients whose disease is caused by *MYBPC3* mutations are more likely than those with non-genetic forms of HCM to experience earlier disease onset and have high rates of serious outcomes, including heart failure symptoms, arrhythmias, stroke and sudden cardiac arrest or death.(2) There are currently no approved therapeutics that address the underlying genetic cause of HCM.

About TN-201
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 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) Ho, et al., *Circulation* 2018

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 “will,” “anticipated,” “believe,” “look forward,” “potential,” and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, the planned timing to report additional data from MyPEAK-1; the clinical, therapeutic and commercial potential of, and expectations regarding TN-201; the value of additional MyPEAK-1 data to inform the potential of TN-201; the inferences regarding MyBP-C protein and mRNA expression; statements regarding the continued development TN-201 and TN-201 clinical outcomes, which may materially change as patient enrollment continues or more patient data become available; and statements made by Tenaya’s Chief Medical Officer and Chief Executive Officer and investigator for MyPEAK-1. 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 data at the referenced time; the timing and progress of MyPEAK-1; the potential failure of TN-201 to demonstrate safety and/or efficacy in clinical testing; the potential for any MyPEAK-1 clinical trial results to differ from preclinical, interim, preliminary or expected results; Tenaya’s ability to enroll and maintain patients in clinical trials, including MyPEAK-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; 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.

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