Tenaya Therapeutics Announces Late Breaker Presentation of New Data from MyPEAK™-1 Phase 1b/2 Clinical Trial of TN-201 at American College of Cardiology Annual Meeting

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

New Biopsy Data Reaffirm Robust Transduction and RNA Expression with TN-201; RNA and Protein Levels Increase Over Time

All Cohort 1 Patients with Severe Disease at Baseline Achieved NYHA Class I

Two of Three Patients Experienced Improvements in One or More Measures of Hypertrophy

Expects to Complete Enrollment of Cohort 2 in 1H25 and to Report Initial Data in 2H25

SOUTH SAN FRANCISCO, Calif., March 31, 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, announced that interim data from the first three patients enrolled in the company's MyPEAK-1 Phase 1b/2 clinical trial of TN-201 were highlighted in a Late-Breaker presentation at the 2025 American College of Cardiology Scientific Sessions (ACC.25). TN-201 is being developed for the potential treatment of Myosin Binding Protein C3 *MYBPC3*-associated hypertrophic cardiomyopathy (HCM), a condition caused by insufficient levels of myosin-binding protein C (MyBP-C).

"TN-201 is the first gene therapy to be tested in HCM patients whose disease is caused by mutations to the *MYBPC3* gene. For patients with this mutation, their disease is often more aggressive in its progression and they are at higher risk of serious – sometimes fatal – complications," said Milind Desai, M.D., M.B.A, Haslam Family Endowed Chair in Cardiovascular Medicine, Vice Chair of Education in the Heart Vascular Thoracic Institute, Director of the Hypertrophic Cardiomyopathy Center at Cleveland Clinic, and an investigator for the MyPEAK-1 Phase 1b/2 clinical trial. "I look forward to continuing to study and evaluate this to see if this patient population is one that could be treated with gene therapy, as we have seen with other diseases."

"TN-201's emerging safety profile at the 3E13 vg/kg dose, combined with biopsy results showing robust transduction, encouraging expression in the heart and suggestions of clinical improvement or stability are positive early signals of TN-201's clinical impact," said Whit Tingley, M.D., PhD., Tenaya's Chief Medical Officer. "These data reinforce our optimism about TN-201's potential to transform the treatment landscape for *MYBPC3*-associated HCM patients by addressing the underlying cause of their disease. We look forward to reporting additional data from Cohort 1 and getting our first look at the higher dose cohort later this year. We are profoundly grateful to the HCM community for their support of this work, and particularly to all those participating in the MyPEAK-1 clinical trial."

- Interim data presented at ACC.25 include results from serial biopsies and assessments of Patient 1 and 2 at Week 52 and Patient 3 at Week 26, analyzing changes over time in the first three patients to receive a one-time infusion of TN-201 gene therapy (Cohort 1). TN-201 was generally well tolerated at 3E13 vg/kg, and treatment-emergent adverse events (AEs) were primarily mild, manageable and/or reversible.
- Serial biopsies taken at two timepoints for all three patients demonstrated sustained presence of TN-201 DNA in the heart (0.8 to 1.4 vg/dg) and robust TN-201 RNA expression (>1.25x10^5 copies per microgram of RNA) that increased as much as 13-fold from Week 8 to Week 52 post-dose.
- MyBP-C protein levels increased from 56 to 59% and from 62 to 64% of normal between Week 8 and Week 52 for Patients 1 and 2, respectively. 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.
    - Patient 3 was the first patient on study to receive a baseline biopsy, which is expected to offer insight into the total change in protein levels following TN-201 treatment. The post-dose biopsy sample from Patient 3 was not evaluable; a second post dose biopsy is planned later this year and will be reported in a future data readout.
- Cardiac troponin, a biomarker of myocardial injury, was elevated in Cohort 1 patients at baseline and decreased by more than 60% in two patients, whose levels are now normal or near normal. NT-proBNP, a biomarker of cardiac strain, increased and remained elevated while patients were on immunosuppression, but returned to baseline as immunosuppressive drugs were discontinued.
- Key measures of hypertrophy, or enlargement of the heart, improved in two patients while other assessments remained stable. Left ventricular posterior wall thickness, which was elevated at baseline, decreased in two patients by up to 40% into the normal range for healthy individuals. In one patient, left ventricular mass (LVMI) improved by 10%. Additional measures of hypertrophy and diastolic function remained stable.
- All three patients in Cohort 1 had objectively severe disease at the time of enrollment with mild-to moderate heart failure symptoms (New York Heart Association (NYHA) classification II or III) that interfered in activities of daily living. All three

have now achieved NYHA Class I, defined as having no limitations on physical activity.

"We are excited by these promising early data from Dose Cohort 1 and the prospects for initial data from Dose Cohort 2 later this year where two of three patients have already been dosed," said Faraz Ali, Chief Executive Officer of Tenaya. "We are also pleased that with our recent financing, plus adjustments to our spend, we have updated our cash guidance into the second half of 2026 and are well-positioned to achieve important clinical data milestones on both the TN-201 and TN-401 gene therapy programs over the next 12 months."

The interim MyPEAK-1 data were presented today by Dr. Desai during the Clinical and Investigative Horizons session in a Late-breaker presentation talk titled, "First Report of Phase 1b/2a Study Evaluating Safety and Early Efficacy of TN-201, an Adeno-Associated Virus Serotype 9 Gene Replacement Therapy, in Adults with *MYBPC3*-Associated Hypertrophic Cardiomyopathy".

Tenaya researchers also presented data at ACC.25 offering new insights into the disease burden of patents with *MYBPC3*-associated HCM compared to other HCM populations. Results from this study, "Differences in Patient Characteristics and Burden of Disease in Adults with *MYBPC3*-Associated HCM (#129)", conducted in collaboration with the Sarcomeric Human Cardiomyopathy Registry (SHaRE), analyzed outcomes for 1,637 *MYBPC3*-associated HCM adults by age of diagnosis.

- Patients with pathogenic/likely pathogenic *MYBPC3* mutations were found to be at risk for serious clinical manifestations including heart failure, arrhythmias, and sudden cardiac death.
- Younger patients progressed more rapidly and were more likely to experience serious outcomes.
- Approximately 50% of adult patients diagnosed before the age of 40 experience a serious cardiac event by the age of 50.

Both presentations are available on the Tenaya website.

Cohorts 1 and 2 in the Ongoing MyPEAK-1 Phase 1b/2 Clinical Trial
Data reported today focus on changes over time in the first three patients to receive TN-201 gene therapy. All three participants presented with nonobstructive HCM having previously undergone myectomy and remained at sufficiently high risk of sudden cardiac death to warrant an implantable cardiac defibrillator device (ICD).

Per protocol, all patients received immunosuppressives consisting of sirolimus and prednisone before and after dosing, which was tapered over time based on monitoring of liver and inflammatory markers. All three patients have successfully tapered off immunosuppressives and remain on study.

Following dosing of the first three patients in MyPEAK-1, an independent data and safety monitoring board (DSMB) evaluated available safety data. The DSMB endorsed the broadening of eligibility criteria and enrollment of the planned high dose cohort. Accordingly, patients are now being enrolled in Cohort 2 to receive TN-201 at a dose of 6E13 vg/kg. Tenaya anticipates completion of enrollment of the first three patients in Cohort 2 in the first half of the year and plans to share initial safety and biopsy data from Cohort 2, along with additional follow-up data from Cohort 1, in the second half of this year.

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 "expects," "potential," "look forward," "optimism," "could," "encouraging," "planned," "guidance" and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, the planned timing to complete enrollment and report additional data from MyPEAK-1; the clinical, therapeutic and commercial potential of, and expectations regarding TN-201 as a treatment for *MYBPC3*-associated HCM; 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; Tenaya's cash guidance commitment to focusing its resources on generating clinical data for its gene therapy pipeline 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 Annual Report on Form 10-K for the fiscal year ended December 31, 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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