Tenaya Therapeutics Presents Promising Interim Clinical Data from MYPEAK™-1 Phase 1b/2a Clinical Trial of TN-201 Gene Therapy for the Treatment of MYBPC3-Associated Hypertrophic Cardiomyopathy

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MyPEAK-1 Data Presented During Late-Breaking Session at AHA Scientific Sessions 2025 with Simultaneous Publication in Cardiovascular Research

TN-201 Has Been Generally Well Tolerated at Both Doses

Longer-term Follow Up of Cohort 1 Patients Showed Consistent, Deeper, and Durable Improvement in Measures of Hypertrophy

Initial Cohort 2 Data Demonstrated Early Dose Responsive Increases in TN-201 Transduction and MyBP-C Protein Expression

Tenaya Management to Host Webcast Call for Analysts and Investors on Monday, November 10 at 8:00 a.m. EST

NEW ORLEANS and SOUTH SAN FRANCISCO, Calif., Nov. 08, 2025 (GLOBE NEWSWIRE) -- Tenaya Therapeutics, Inc. (NASDAQ: TNYA) announced that new interim safety and efficacy data from the company's MyPEAK™-1 Phase 1b/2a clinical trial of TN-201 were presented today during the Late-Breaking Science: Main Event session at the American Heart Association's (AHA) Scientific Sessions 2025 by Milind Desai, M.D., MBA, director of the Hypertrophic Cardiomyopathy Center at Cleveland Clinic and vice chair of Cleveland Clinic's Heart, Vascular & Thoracic Institute. These data, which included longer-term follow-up results for three patients dosed with TN-201 gene therapy at a dose of 3E13vg/kg (Cohort 1) and initial results for three patients who received TN-201 at a dose of 6E13 vg/kg (Cohort 2) were simultaneously published in *Cardiovascular Research*.

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). Single administration of TN-201 gene therapy was generally well-tolerated at both the 3E13 vg/kg and 6E13 vg/kg dose levels and immunogenicity was well managed through monitoring and individualized tapering of immunosuppressives. TN-201 achieved robust transduction and durable expression with early dose-dependent increase in both transduction and MyBP-C protein expression. Among Cohort 1 patients for whom there was greater than one year of follow up, decreases in circulating biomarkers and reductions in measures of left ventricular hypertrophy deepened over time.

"These initial results are promising for a patient population that too often live with difficult, even dangerous, symptoms," said Dr. Desai, an investigator for the MyPeak-1 Phase 1b/2a clinical trial. "In the past decade, we've made great progress in understanding and treating hypertrophic cardiomyopathy, and as our understanding of the genetic underpinnings of HCM increases, research into gene therapies such as TN-201 offer the opportunity to further advance and improve patient care."

"Results of TN-201 treatment are in line with our expectations for this stage of trial, with a manageable safety profile and dose-dependent MyBP-C protein level increases over time. In particular, the durable changes in multiple parameters of disease – biomarkers, hypertrophy and heart failure symptoms – all moving with directional consistency toward normalization after a single dose are an encouraging early signal of TN-201's activity," said Whit Tingley, M.D., Ph.D., Tenaya's Chief Medical Officer. "We look forward to building on these data with continued long-term follow-up of Cohort 1 and the maturation of early results for Cohort 2, which will inform our plans for TN-201's late-stage development."

Interim results from the MyPEAK-1 Phase 1b/2a Clinical Trial
Data reported today includes safety, biopsy and leading indicators of efficacy for the three patients enrolled in Cohort 1 with follow-up ranging from Week 52-78, and safety for the three patients in Cohort 2, Week 12 biopsy for Patient 6 and Week 26 assessments for Patient 4 as of the July 2025 data cut off. Patient 5 was lost to further follow-up after week 12. All patients other than Patient 5 have completed every visit and remain on study.

- **All patients enrolled in MyPEAK-1 had serious burden of disease at baseline.**
  - All six had objectively severe nonobstructive HCM with levels of hypertrophy significantly above average for people with HCM
  - All six were at sufficiently high risk of sudden cardiac death to warrant an implantable cardiac defibrillator (ICD) device
  - All experienced mild-to-moderate symptoms of heart failure that interfered in activities of daily living (New York Heart Association, or NYHA, Class II-III)
  - Four of the six have previously undergone surgical myectomy

- **Safety data for all six patients in Cohorts 1 and 2 showed that TN-201 was generally well tolerated at both the 3E13 vg/kg and 6E13 vg/kg doses. No dose-limiting toxicities were observed and all patients have tapered off immunosuppressive medicines.**

  - Reversible, asymptomatic liver enzyme elevations (Grade 1-3) were the most common treatment-related adverse events (AEs) reported

- There were no signs of cardiotoxicities, including no declines in left ventricular ejection fraction, clinical myocarditis or ventricular arrhythmias
- There were two treatment-related AEs classified as serious due to inpatient treatment or monitoring: a Cohort 1 patient with Grade 2 transaminase elevation that responded to steroids and a Cohort 2 patient with Grade 1 elevation of complement factors that resolved without additional intervention
- Adjustments to monitoring and immunosuppression during Cohort 1 resulted in faster tapers and lower cumulative corticosteroid doses in Cohort 2, despite the higher TN-201 dose

- **MyBP-C protein levels increased over time, with early evidence of a substantial increase commensurate with higher dose in Cohort 2. TN-201 DNA transduction and TN-201 mRNA expression following similar dose response.**
  - Tenaya reported that TN-201 transduction and TN-201 mRNA expression were robust. All three patients in Cohort 1 demonstrated sustained presence of TN-201 DNA in the heart and mRNA expression that increased over time, supporting the observed increases in MyBP-C level changes.
  - In Cohort 1 patients, protein levels increased by an average of 4% from the first biopsy taken to Week 52. In Patient 3, the first patient for whom baseline biopsies were available, MyBP-C protein was shown to increase by 5% at Week 52.
  - The first evaluable patient in Cohort 2 (Patient 6) demonstrated a clear dose response, and early MyBP-C expression increased by 14% after only 12 weeks post-dose. Of note, Patient 6 had a greater than 2-fold increase in transduction and expression at Week 12 relative to the averages for these measures observed across Cohort 1.

- **Multiple parameters, including biomarkers, hypertrophy, heart failure symptoms, associated with increased risks of complications or reduced survival, have improved among a majority of patients with greater than 26 weeks of follow-up.**
  - Cardiac Troponin I levels declined significantly (48%-74%) to normal or near-normal levels in all Cohort 1 patients. Cardiac troponin I is a predictive risk factor of cardiac AEs such as ventricular arrhythmias, sudden cardiac death, and progression to end-stage heart failure.[(1)]
  - NT-proBNP, a biomarker of cardiac muscle strain, improved or remained stable in two of three Cohort 1 patients
  - Cardiac Troponin I remained within the normal range and NT-proBNP remained stable for Patient 4 from Cohort 2 at their 26-Week assessment
  - All three patients in Cohort 1 now have evidence of significant improvement in one or more measures of hypertrophy at Week 52, including notable reductions in left ventricular posterior wall thickness (LVPWT) of between 21% and 39%. LVPWT for Patient 4 in Cohort 2 was stable at Week 26. Greater LVPWT is an independent risk factor for reduced long-term survival after septal myectomy.[(2)]
  - Two out of three Cohort 1 patients saw reductions in overall left ventricular mass index (LVMI) of between 12% and 22% at Week 52. LVMI for Patient 4 in Cohort 2 was stable at Week 26
  - NYHA classification, a measure of the impact of heart failure symptoms on activities of daily living, improved in all patients by at least one class by Week 26, and all Cohort 1 patients are now NYHA Class I (asymptomatic).

While the interim results from MyPEAK-1 are promising, longer-term follow-up for all patients is required to further inform Tenaya's understanding of TN-201's potential as a treatment for MYBPC3-associated HCM. Tenaya plans to periodically report additional results from longer-term follow-up. These interim data were presented during the "Forgotten No More: The Current Belle of the Ball? Breakthrough Evolutions in Hypertrophic Cardiomyopathy" Late-Breaking Science: Main Event session during AHA 2025 and were published simultaneously in an article titled "First-in-human study of AAV9:MYBPC3 gene replacement therapy (TN-201) in hypertrophic cardiomyopathy: Initial safety, pharmacodynamic, and imaging results from MyPEAK-1" in *Cardiovascular Research*.

Conference Call and Webcast
Tenaya management will host a conference call on Monday, November 10, 2025, at 8:00 a.m. ET/5:00 a.m. PT to discuss the TN-201 data presented and published today and the status of the MyPEAK-1 clinical trial. The webcast conference call, including an accompanying slide presentation, can be accessed from the Investor section on the "Events and Presentations" page of the Tenaya website at www.tenayatherapeutics.com.

About the MyPEAK-1 Phase 1b/2a Clinical Trial
The MyPEAK-1 Phase 1b/2 clinical trial (Clinicaltrials.gov ID: NCT05836259) is a multi-center, open-label, dose-escalating (3E13 vg/kg and 6E13 vg/kg) study of symptomatic adults (up to 24) who have been diagnosed with *MYBPC3*-associated HCM. MyPEAK-1 is designed to assess the safety, tolerability and clinical efficacy of a one-time intravenous infusion of TN-201 gene replacement therapy. MyPEAK-1 has tested doses of 3E13 vg/kg and 6E13 vg/kg in two cohorts of three patients each. On July 30, 2025, Tenaya reported that the trial's independent Data Safety Monitoring Board (DSMB) concluded that TN-201 had an acceptable safety profile to allow enrollment of expansion cohorts at either the 3E13 vg/kg (Cohort 1) or 6E13 vg/kg (Cohort 2) dose levels. On November 7, 2025, Tenaya announced the FDA placed MyPEAK-1 on a clinical hold. Tenaya is working with the FDA to address the agency's concerns through an amendment to the trial protocol.

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

About *MYBPC3*-Associated Hypertrophic Cardiomyopathy (HCM)
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. *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. 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 address the underlying cause of *MYBPC3*-associated hypertrophic cardiomyopathy (HCM) by delivering a working *MYBPC3* gene to heart muscle cells via a single intravenous infusion and thereby increasing insufficient MyBP-C protein levels 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's pipeline includes clinical-stage candidates TN-201, a gene therapy for *MYBPC3*-associated hypertrophic cardiomyopathy (HCM) and TN-401, a gene therapy for *PKP2*-associated arrhythmogenic right ventricular cardiomyopathy (ARVC). Tenaya has employed a suite of integrated internal capabilities, including modality agnostic target validation, capsid engineering and manufacturing, to generate a portfolio of novel medicines based on genetic insights, including TN-301, a clinical-stage small molecule HDAC6 inhibitor for the potential treatment of heart failure and related cardio/muscular disease, and multiple early-stage programs in preclinical development aimed at the treatment of both rare genetic disorders and more prevalent heart conditions. For more information, visit www.tenayatherapeutics.com.

(1) Kubo, et al, Journal Am Coll Cardiol, 2013
(2) Schaff, et al, JACC Heart Failure, 2022

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 "promising," "opportunity," "expectations," "encouraging," "look forward," "will," "potential," and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, the clinical, therapeutic and commercial potential of, and expectations regarding, TN-201 as a treatment for *MYBPC3*-associated HCM; the potential for additional MyPEAK-1 data to inform plans for TN-201's late stage development; statements regarding the continued development of TN-201, clinical hold, anticipated timelines, TN-201 clinical outcomes and risk/benefit profile, which may materially change as more patient data become available and statements made by Tenaya's Chief Medical Officer and the 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: the expected timing and outcome of Tenaya's regulatory interactions related to the clinical hold on MyPEAK-1; the timing and availability of MyPEAK-1 data; the potential 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; the potential for the FDA and/or other regulatory agencies to conclude at any time that TN-201 may not have an appropriate risk/benefit profile; 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 June 30, 2025, 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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