Tenaya Receives Positive Safety Reviews from Independent DSMBs to Advance Both TN-201 and TN-401 Gene Therapy Clinical Trials as Designed

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Enrollment in Both Dose Cohorts of the MyPEAK™-1 Phase 1b/2 Clinical Trial ofTN-201 for Hypertrophic Cardiomyopathy (HCM) Complete; Follow-up Data from Cohort 1 and Initial Data from Cohort 2 Expected in Fourth Quarter of 2025

First Patient Dosed in 6E13 vg/kg Cohort 2 of RIDGE™-1 Phase 1b Clinical Trial ofTN-401 for Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

Initial Cohort 1 Data for TN-401 and Enrollment of Additional Patients in Both Dose Cohorts Planned for Fourth Quarter of 2025

SOUTH SAN FRANCISCO, Calif., July 30, 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 announced positive endorsements from each trial's independent Data Safety and Monitoring Board (DSMB) to proceed per protocol with its two cardiovascular gene therapy clinical trials, MyPEAK-1 for TN-201 and RIDGE-1 for TN-401.

"Safety is paramount, and this milestone reinforces the favorable tolerability profile emerging for both TN-201 and TN-401 and highlights the appropriateness of our immunosuppressant regimen to manage patients. We are very encouraged by the DSMBs' endorsements to proceed per protocol into expansion cohorts at either dose level for TN-201, and to expand at the current dose and escalate to the higher dose level for TN-401, with our first Cohort 2 patient already dosed," said Whit Tingley, M.D., Ph.D., Tenaya's Chief Medical Officer. "We look forward to sharing clinical data from both programs later this year as we continue to advance our mission to transform the treatment landscape for patients with serious cardiovascular diseases."

MyPEAK-1 DSMB Review
This is the second positive DSMB review for the MyPEAK-1 Phase 1b/2 clinical trial of TN-201 for *MYBPC3*-associated hypertrophic cardiomyopathy, a condition caused by insufficient levels of myosin-binding protein C (MyBP-C). Following enrollment of the first three patients at the 6E13 vg/kg dose (Cohort 2), all available data from Cohorts 1 and 2 were reviewed by the MyPEAK-1 DSMB, a panel of experts in gene therapy, cardiology and/or immunology. The DSMB determined that TN-201 has an acceptable safety profile to allow enrollment of expansion cohorts at either the 3E13 vg/kg or 6E13 vg/kg dose levels. Tenaya currently anticipates enrolling patients in the 6E13 vg/kg dose expansion cohort.

Initial data from the first three patients to receive TN-201 at the 3E13 vg/kg dose level (Cohort 1) were reported earlier this year at the American College of Cardiology meeting, showing that TN-201 reached cardiomyocytes, resulting in robust RNA expression. Increased MyBP-C protein levels were observed in two patients for whom serial biopsies were available. All three patients had objectively severe disease at baseline and achieved New York Heart Association (NYHA) Class I post-treatment, indicating a resolution of heart failure symptoms. Two of the three patients in Cohort 1 experienced improvement in one or more measures of hypertrophy. 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.

Tenaya plans to report longer-term follow-up data from Cohort 1 and initial data from Cohort 2 in the fourth quarter of this year. Data from MyPEAK-1 is intended to inform dose selection and pivotal study design in pediatric and adult individuals with *MYBPC3*-associated HCM.

RIDGE-1 DSMB Review
Tenaya enrolled the first three patients (Cohort 1) at the 3E13 vg/kg dose in the RIDGE-1 Phase 1b clinical trial of TN-401 for the potential treatment of *PKP2*-associated arrhythmogenic right ventricular cardiomyopathy. In *PKP2*-associated ARVC, mutations of the *PKP2* gene result in insufficient expression of the plakophilin-2 protein, leading to irregular heart rhythms. In July, the RIDGE-1 trial DSMB reviewed all available data and endorsed dose escalation to the 6E13 vg/kg level and expanding enrollment of Cohort 1, per protocol. The first of three patients in the higher dose cohort (Cohort 2) has been dosed and Tenaya may enroll additional patients in a 3E13 vg/kg dose expansion cohort. Up to 15 adults with *PKP2*-associated ARVC may be enrolled in the RIDGE-1 clinical trial, which is being conducted at clinical sites across the U.S. and in the UK.

Tenaya expects to report initial data from Cohort 1 of the RIDGE-1 clinical trial in the fourth quarter of 2025. The readout is anticipated to focus on safety and tolerability and analyses of cardiac biopsy data.

About 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 therapy. TN-201 gene replacement therapy is designed to increase protein levels of MyBP-C to slow or even reverse the course of disease by delivering a functional copy of the *MYBPC3* gene to heart muscle cells. 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.

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

About TN-201 Gene Therapy
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. The MyBP-C protein

plays a crucial role in regulating the heart's contractility. In preclinical studies of *MYBPC3* knock-out models, TN-201 halted disease progression and demonstrated significant and durable disease reversal and survival benefit 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 RIDGE-1 Phase 1b Clinical Trial
Tenaya is conducting the RIDGE-1 Phase 1b clinical trial (ClinicalTrials.gov ID: NCT06228924) of TN-401 in patients with *PKP2*-associated ARVC. The RIDGE-1 Phase 1b clinical trial is a multi-center, open-label, dose escalation study being conducted in the U.S. and UK. RIDGE-1 will assess the safety, tolerability and preliminary clinical efficacy of a one-time intravenous infusion of TN-401. RIDGE-1 will seek to enroll up to fifteen adults who have been diagnosed with *PKP2*-associated ARVC, have an implantable cardioverter defibrillator (ICD) and are at increased risk for arrhythmia as determined by premature ventricular contraction (PVC) count during screening. RIDGE-1 is designed to test doses of 3E13vg/kg and 6E13 vg/kg in two cohorts of three patients each.

To learn more about gene therapy for ARVC and participation in the RIDGE-1 study, please visit ARVCstudies.com

About TN-401 Gene Therapy
TN-401 is an investigational AAV9-based gene therapy being developed for the treatment of ARVC due to mutations in the *PKP2* gene. In *PKP2*-associated ARVC, mutations of the *PKP2* gene result in insufficient expression of proteins needed for the proper functioning of the desmosomal complex that maintains physical connections and electrical signaling between heart muscle cells. In preclinical studies, Tenaya has shown that a single dose of TN-401 restored healthy levels of plakophilin 2 protein, normalized heart rhythms, improved right and left ventricular size and function and extended survival. TN-401 has received Orphan Drug and Fast Track Designations from the FDA.

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.

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 "expected," "is planned," "plans," "look forward," "is anticipated," "anticipates," "intends," "is intended," "may," 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 and TN-401; the planned timing to report data from MyPEAK-1 and RIDGE-1 and related focus of each data readout; enrollment plans for MyPEAK-1 and RIDGE-1; and statements made by Tenaya's Chief Medical 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: the timing and progress of MyPEAK-1 and RIDGE-1; the potential failure of TN-201 and/or TN-401 to demonstrate safety and/or efficacy in clinical testing; availability of MyPEAK-1 and RIDGE-1 data at the referenced times; the potential for any MyPEAK-1 and/or RIDGE-1 clinical trial results to differ from preclinical, interim, preliminary, topline or expected results; 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 entitled "Risk Factors" in 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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