Positive Interim Data from Cohorts 1 and 2 of Tenaya's RIDGE™-1 Phase 1b/2 Clinical Trial of TN-401 Demonstrated Consistent Reductions in Arrhythmia Burden for Adults with PKP2-associated ARVC

May 15, 2026

All Patients Achieved Meaningful Decreases (Mean = 64%) in Daily Premature Ventricular Contraction Count

TN-401 Gene Therapy was Well Tolerated at 3E13 vg/kg and 6E13 vg/kg Doses

Post-dose Biopsies Provide Evidence of TN-401 Activity in Heart Muscle Cells

PRIME Designation Granted by European Medicines Agency

Tenaya Management to Host a Webcast Conference Call to Review Results on Friday, May 15 at 10:30 a.m. ET / 7:30 a.m. PT Following Late-Breaker Presentation at ASGCT 2026

SOUTH SAN FRANCISCO, Calif., May 15, 2026 (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, presented interim data from the ongoing RIDGE™-1 Phase 1b/2 clinical trial of TN-401 gene therapy at the American Society of Gene and Cell Therapies (ASGCT) 2026 Annual Meeting. In adults with arrhythmogenic right ventricular cardiomyopathy (ARVC), caused by mutations in the *plakophilin-2* (*PKP2*) gene, treatment with a single infusion of TN-401 at either the 3E13 vg/kg (Cohort 1) or 6E13 vg/kg (Cohort 2) dose resulted in consistent and deep reductions in premature ventricular contractions (PVCs) in all six Cohort 1 and 2 patients. TN-401 was well tolerated at both dose levels, and post-dose biopsies provided evidence of robust transduction and TN-401-specific expression for the first five patients for whom data was available at the time of cut off.

"The most prominent and troubling clinical feature of *PKP2*-related ARVC is potentially life-threatening heart rhythm problems or ventricular arrhythmias, so the substantial reduction in ventricular arrhythmia events observed across the first six adults to receive TN-401 gene therapy is exciting. While additional follow-up is needed to appropriately assess TN-401's full potential, the emerging safety profile and early evidence of activity observed are promising," said John R. Giudicessi, M.D., Ph.D., a Genetic Cardiologist who oversees the Clinical Cardiac Gene Therapy section of the Windland Smith Rice Comprehensive Sudden Death Program at Mayo Clinic and a principal investigator for the RIDGE-1 clinical trial. "A gene therapy approach offers the potential of transformative treatment by correcting the genetic defect underlying *PKP2*-related ARVC, whereas existing care – which includes the use of implantable defibrillators, heart failure or anti-arrhythmic medicines, or ablation of parts of the heart muscle – does not address the underlying cause of disease or slow its progression."

"We are encouraged by the consistent improvements in ventricular electrical stability in the RIDGE-1 trial of TN-401, with substantial reductions in PVCs and NSVTs, along with clear evidence from heart biopsies of TN-401 transduction and expression, and a promising safety profile at both doses," said Whit Tingley, M.D., Ph.D., Tenaya's Chief Medical Officer. "The improved electrical stability of the RIDGE-1 patients is predicted to decrease the risk for more serious, life-threatening arrhythmias."

Interim results from the RIDGE-1 Phase 1b/2 Clinical Trial

The dose-escalating RIDGE-1 clinical trial is designed to assess the safety, tolerability and activity of a one-time dose of TN-401 gene therapy. Data reported today include electrophysiology, biopsy and safety results from a total of six patients who received a single infusion of TN-401 at a dose of 3E13vg/kg or 6E13vg/kg. As of the April 2026 data cut off, available follow up included assessments out to 20-52 weeks post-dose. Two additional patients have subsequently been dosed in the 6E13 vg/kg expansion cohort and will be included in future RIDGE-1 readouts.

Clinical Data (N=6)

Electrophysiology data was collected at regular time intervals post-treatment using an ambulatory monitoring device worn for seven days. Exploratory endpoints, including electrocardiographic (ECG) changes, heart structure and function, and symptom burden were also collected as part of the RIDGE-1 trial.

- Treatment with TN-401 resulted in dramatic improvements in electrical stability, as measured by PVCs and non-sustained ventricular tachycardias (NSVTs)
  - All six patients demonstrated meaningful reductions in arrhythmia burden as measured by PVCs, with a mean reduction of 60% for Cohort 1 and 67% for Cohort 2.
  - Two patients with a high rate of NSVTs at baseline experienced substantial decreases, apparent as early as Week 20. Patient 2 had a NSVT burden of 78 counts per 24-hours, which dropped to zero and remained stable at Week 52. At baseline, Patient 5 had a NSVT count of 43 per 24 hours, which dropped to 4 per 24 hours at Week 20. Four patients had low NSVT burden at baseline and remained low.

Change in Average 24-hour PVC Burden Following TN-401 Treatment

PVC COUNT	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
At screening	2,462	618	2,666	1,571	7,819	8,634
Most recent assessment	1,707	99	1,518	1,064	1,412	2,543
Percent change	**-31%**	**-84%**	**-43%**	**-32%**	**-82%**	**-71%**

- Other measures of clinical response including ECG changes (QRS duration and T wave inversions), heart structure and function and New York Heart Association (NYHA) class were in the normal range or remained stable during the post-dose follow-up period.

TN-401 Biopsy Findings (N=5)

Biopsy samples were collected from the right ventricular septum at eight weeks for the first four patients and at 22 weeks for Patient 5, with results from 52-week biopsies available for Cohort 1 patients. Biopsy sample analysis from Patient 6 was not completed as of the data cut off.

- The totality of the biopsy data provides evidence that TN-401 is being transduced within the heart muscle cells, achieving transcription into messenger RNA and resulting in PKP2 protein.
  - Mean TN-401 DNA levels were 3.4 vg/dg and 3.8 vg/dg in Cohorts 1 and 2, respectively. These levels were measured as early as 8 weeks post dose.
  - At Week 8 for the first four patients, TN-401 mRNA expression ranged from 1.0E+04 - 2.9E+05 copies per microgram TN-401 mRNA was 7.1E+04at Week 22 for Patient 5.
  - Measures of PKP2 protein levels in heart muscle cells from baseline to the most recent timepoints ranged from -4% to +15% as measured by liquid chromatography mass spectrometry normalized to myosin heavy chain, a sarcomere protein only found in cardiomyocytes.
  - Measurements of PKP2 protein levels are impacted by the varied composition of cardiac tissue in an ARVC heart.

Safety Update (N=6)

Safety is monitored throughout the RIDGE-1 trial, including one-week of inpatient observation and close monitoring of lab values throughout post-dose immunosuppressive tapering. As of the April data cut, all patients have successfully tapered off immunosuppressives.

- TN-401 has been generally well tolerated at both doses.
- The prophylactic immune suppression regimen of sirolimus and prednisone successfully managed immune responses, with similar dosing and duration of immunosuppressive medications utilized at both dose levels.
- Adverse events (AEs) associated with TN-401 treatment were asymptomatic and self-resolved or responded to treatment. As previously reported, the most frequent AEs attributed to TN-401 were transient elevations in troponins and/or transaminase. Among these, there was a Grade 3 liver enzyme elevation in Cohort 2 due to a medication error and interruption to steroid treatment.
- There was no clinical thrombotic microangiopathy (TMA), no ventricular arrhythmias related to TN-401, and no other cardiotoxicities associated with TN-401.
- All patients remain on study and no dose-limiting toxicities have occurred.
- The independent Data Safety Monitoring Board endorsed continuing the expansion portion of the study as planned.

Tenaya also announced that the European Medicines Agency (EMA) has granted TN-401 PRIority MEdicine (PRIME) designation. The designation recognizes the potential of TN-401 to address significant unmet medical needs in patients with *PKP2*-associated ARVC. The PRIME program enables the EMA to offer early and proactive support to sponsors in an effort to optimize the generation of robust safety and efficacy data in order to accelerate assessment of medicines applications.

Webcast Conference Call

Tenaya management will host a conference call on Friday, May 15, 2026, at 10:30 a.m. EDT / 7:30 a.m. PDT to discuss the TN-401 data presented at ASGCT. 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 *PKP2*-Associated ARVC

Plakophilin-2 (*PKP2*) mutations are the most common genetic cause of arrhythmogenic right ventricular cardiomyopathy (ARVC, also known as arrhythmogenic cardiomyopathy or ACM), occurring in approximately 40 percent of the overall ARVC population. The prevalence of *PKP2*-associated ARVC is estimated at more than 70,000 people in the U.S. alone.

In *PKP2*-associated ARVC, mutations of the *PKP2* gene results in insufficient expression of a protein needed for the proper functioning of the desmosomal complex that maintains physical connections and electrical signaling between heart muscle cells. As the desmosome structure degrades, cardiac muscle cells are replaced by fibrofatty tissue and electrical pulses in the heart become unstable, resulting in life potentially threatening heart rhythms. ARVC symptoms include arrhythmias, palpitations, lightheadedness, dizziness and fainting. It is typically diagnosed before age 40, and sudden cardiac arrest due to ventricular arrhythmia is frequently the first manifestation of disease. Current treatments include anti-arrhythmic medications, implantable cardioverter-defibrillators (ICDs) and ablation procedures, which do not address the underlying genetic cause of disease.

About TN-401 Gene Therapy and the RIDGE-1 Clinical Trial

TN-401 is an investigational AAV9-based gene therapy being developed for the treatment of ARVC due to mutations in the *PKP2* gene. AAV9 was selected as the vector for delivery of Tenaya’s *PKP2* gene therapy based on its extensive clinical and commercial safety record and demonstrated ability to target heart muscle cells. TN-401 has received Orphan Drug and Fast Track Designations from the U.S. Food and Drug Administration, as well as PRIME designation from the European Medicines Agency. Tenaya’s development of TN-401 is supported in part by a grant from the California

Institute for Regenerative Medicine (CIRM).

The RIDGE-1 Phase 1b/2 clinical trial of TN-401 in patients with *PKP2*-associated ARVC is a multi-center, open-label, dose escalation study being conducted in the U.S. and UK. RIDGE-1 is intended to assess the safety, tolerability and preliminary clinical efficacy of a one-time intravenous infusion of TN-401. RIDGE-1 seeks to enroll up to fifteen adults who have been diagnosed with *PKP2*-associated ARVC, have an ICD and are at increased risk for arrhythmias as determined by premature ventricular count (PVC) during screening.

To learn more about gene therapy for ARVC and the RIDGE-1 clinical trial, please visit ARVCstudies.com or ClinicalTrials.gov (NCT06228924).

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); TN-401, a gene therapy for *PKP2*-associated arrhythmogenic right ventricular cardiomyopathy (ARVC); and TN-301, a highly specific small molecule HDAC6 inhibitor with broad potential clinical utility in cardiac, metabolic and muscular conditions, including heart failure with preserved ejection fraction (HFpEF) and Duchenne muscular dystrophy (DMD). Tenaya has employed a suite of integrated internal capabilities including modality agnostic target discovery and validation, to generate a portfolio of novel medicines based on genetic insights, 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 "planned," "potential," "will," and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, the potential advantages of TN-401; clinical outcomes, which may materially change as patient enrollment continues or more patient data become available; the potential for improved electrical stability of the RIDGE-1 patients to decrease the risk for more serious, life-threatening arrhythmias; the timing and content of the RIDGE-1 data presentation and related conference call; and statements by Tenaya's Chief Medical Officer and Dr. Giudiscessi. 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 data at the referenced times; the timing and progress of RIDGE-1 and Tenaya's other ongoing clinical trials; the potential failure of Tenaya's product candidates to demonstrate safety and/or efficacy in clinical testing; changes in Tenaya's plans to develop and commercialize its product candidates; the potential for any clinical trial results to differ from preclinical, interim, preliminary, topline or expected results; risks associated with the process of discovering, developing and commercializing therapies that are safe and effective for use as human therapeutics; Tenaya's ability to develop, initiate or complete preclinical studies and clinical trials, and obtain approvals, for any of its product candidates; 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 business and 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 Tenaya's Quarterly Report on Form 10-Q for the quarter ended March 31, 2026, and future 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.

Tenaya Contacts
Michelle Corral
IR@tenayathera.com

Investors
Anne Marie Fields
Precision AQ
annemarie.fields@precisionaq.com

Media
Wendy Ryan
Ten Bridge Communications
wendy@tenbridgecommunications.com