Tenaya Therapeutics Receives $8 Million Clinical Grant from California Institute for Regenerative Medicine

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Funding will Support Ongoing RIDGE™-1 Clinical Trial of TN-401 Gene Therapy for the Potential Treatment of PKP2-Associated Arrhythmogenic Right Ventricular Cardiomyopathy

Initial Data from RIDGE-1 Phase 1b Clinical Trial Expected in 2H25

SOUTH SAN FRANCISCO, Calif., Feb. 03, 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 that the California Institute for Regenerative Medicine (CIRM), a state of California Agency that funds regenerative medicine, stem cell, and gene therapy research, has awarded Tenaya Therapeutics an $8.0 million CLIN2 grant. Proceeds from the grant will help fund clinical trial costs for Tenaya's ongoing Phase 1b RIDGE-1 clinical trial of TN-401 gene therapy.

TN-401 is being developed for the treatment of arrhythmogenic right ventricular cardiomyopathy (ARVC), (also known as arrhythmogenic cardiomyopathy or ACM), caused by mutations in the *plakophilin-2* (*PKP2)* gene. *PKP2* gene mutations result in insufficient levels of critical proteins needed to maintain the structural integrity and cell-to-cell signaling of heart muscle cells. TN-401 gene replacement therapy is designed to address the underlying cause of disease by delivering a functional *PKP2* gene into heart muscle cells using an adeno associated virus serotype 9 (AAV9) capsid. The RIDGE-1 clinical trial will assess the safety, tolerability and preliminary clinical efficacy of a one-time intravenous infusion of TN-401. The open-label, dose-escalation study is currently enrolling symptomatic adults who have been diagnosed with *PKP2*-associated ARVC.

"We are honored to be awarded this substantial grant and gratified to continue our collaboration with CIRM, whose efforts to accelerate world-class science and deliver transformative regenerative medicine treatments are making a profound impact on the advancement of novel treatments for serious conditions," said Faraz Ali, Chief Executive Officer of Tenaya Therapeutics. "Funds from this grant will support our ongoing RIDGE-1 clinical trial of TN-401, a potential best-in-class gene therapy for the treatment of *PKP2*-associated ARVC, a severe, progressive disease affecting an estimated 70,000 people in the U.S. RIDGE-1 is actively enrolling patients at leading centers, and we look forward to sharing initial data from the low-dose cohort in the second half of this year."

To learn more about gene therapy for ARVC and participation in the RIDGE-1 study, please visit ARVCstudies.com or ClinicalTrials.gov (NCT06228924). Tenaya is also conducting a global natural history and seroprevalence study of adults with *PKP2*-assocated ARVC (NCT06311708).

About *PKP2*-Associated ARVC
Plakophilin-2 (*PKP2*) mutations are the most common genetic cause of arrhythmogenic right ventricular cardiomyopathy (ARVC), estimated to represent 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 irregular heart rhythms. ARVC symptoms include arrhythmias, palpitations, lightheadedness, dizziness and fainting. It is typically diagnosed before age 40, and sudden cardiac arrest due to life-threatening ventricular arrhythmias 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
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. In preclinical studies, Tenaya has shown that a single dose of TN-401 restored healthy levels of PKP2 protein, normalized heart rhythms, improved right and left ventricular size and function and extended survival.

Tenaya is conducting the RIDGE-1 Phase 1b clinical trial of TN-401 in patients with *PKP2*-associated ARVC. To support TN-401's clinical development, the company is currently enrolling the RIDGE global non-interventional study to collect natural history and AAV9 antibody (seroprevalence) data among ARVC patients carrying *PKP2* gene mutations. TN-401 has received Orphan Drug and Fast Track Designations from the FDA.

About the California Institute for Regenerative Medicine (CIRM)
CIRM is a funding agency established by Californians to accelerate regenerative medicine research to deliver treatments for patients with unmet medical needs. Established in 2004 through the passage of Proposition 71, CIRM was initially funded with $3 billion from the state of California to support ongoing research, and in 2020, was funded again with another $5.5 billion through Proposition 14 to continue the Agency's important work.

CIRM has provided billions in funding to support stem cell, genetic research, and development programs in its portfolio. Through the Agency's research, infrastructure, and education programs, CIRM aims to transform the field of regenerative medicine, stimulate economic growth, and improve the lives of diverse communities throughout the state. For more information go to cirm.ca.gov.

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.

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," "will," "potential," "estimated," "look forward" and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, the planned timing to report initial data from RIDGE-1, the clinical, therapeutic and commercial potential of, and expectations regarding TN-401; clinical development plans for TN-401; targeted populations for *PKP2*-associated ARVC clinical trials and treatments; and statements made by Tenaya's Chief Executive 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 RIDGE-1; the potential failure of TN-401 to demonstrate safety and/or efficacy in clinical testing; availability of RIDGE-1 data at the referenced time; the potential for any RIDGE-1 clinical trial results to differ from preclinical, interim, preliminary, topline or expected results; our estimates of the number of patients who suffer from *PKP2*-associated ARVC; 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 the development of TN-401; 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 TN-401; 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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