Tenaya Therapeutics Doses First Patient in the MyPeak-1™ Phase 1b Clinical Trial of TN-201 for the Treatment of MYBPC3-Associated Hypertrophic Cardiomyopathy

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TN-201 is the First Gene Therapy for the Leading Genetic Cause of HCM to be Assessed in Humans; Adds Working MYBPC3 Gene to Heart Cells to Address Underlying Cause of Disease

SOUTH SAN FRANCISCO, Calif., Oct. 05, 2023 (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 first patient has been dosed with TN-201 gene therapy for the treatment of Myosin Binding Protein C3 *(MYBPC3)*-associated HCM in the MyPeak-1 Phase 1b clinical trial at the Cleveland Clinic, Cleveland, Ohio. Tenaya anticipates sharing initial data from the MyPeak-1 trial in 2024.

TN-201 is Tenaya's potential first-in-class adeno-associated virus (AAV)-based gene therapy designed to deliver a working, full-length copy of the human *MYBPC3* gene to heart muscle cells. The working *MYBPC3* gene is intended to restore normal levels of myosin-binding protein, which regulates the contraction and relaxation of the heart muscle. In preclinical studies, TN-201 halted disease progression and demonstrated significant and durable disease reversal and survival benefit following a single dose.

"*MYBPC3* gene mutations are the most common genetic cause of HCM and people with *MYBPC3*-associated HCM are at increased risk for accelerated decline and serious complications associated with their condition," said Milind Desai, M.D., MBA, Director at the Cleveland Clinic Hypertrophic Cardiomyopathy Center and Vice Chair, Heart Vascular Thoracic Institute, Cleveland Clinic, and an investigator for the MyPeak-1 Phase 1b clinical trial. "TN-201, a gene therapy for *MYBPC3*-associated HCM, offers the potential of a one-time treatment to correct the underlying genetic cause of disease and improve patient outcomes. We are pleased to participate in the first-in-human clinical trial of TN-201 to explore this new use of gene therapy treatment."

The MyPeak-1 Phase 1b clinical trial is a 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. The trial will initially seek to enroll at least six symptomatic (New York Heart Association Class II or III) adults who have been diagnosed with *MYBPC3*-associated nonobstructive HCM and have an implantable cardioverter defibrillator, and potentially treat up to 15 subjects in total from the U.S. and outside the U.S.

"The initiation of the MyPeak-1 clinical trial of TN-201 – the first gene therapy for *MYBPC3*-associated HCM to be studied in humans and the first of Tenaya's gene therapy candidates to reach clinical stage – is a significant milestone in our efforts to improve patients' lives through the development of new treatments that target the genetic underpinnings of heart disease," said Whit Tingley, M.D., Ph.D., Tenaya's Chief Medical Officer. "We are grateful for the support of study sites, referral centers, patient advocacy organizations, and patients and families who are actively engaged with Tenaya in our efforts to explore the potential of TN-201 as a novel treatment for *MYBPC3*-associated HCM. We look forward to continuing this close partnership as we enroll additional patients in the MyPeak-1 study and in subsequent studies."

The first dose of TN-201 being assessed in the MyPeak-1 clinical trial is 3E13 vg/kg, a dose associated with near-maximal efficacy in preclinical studies. Once three patients have been dosed at the 3E13 vg/kg level, a data safety and monitoring board (DSMB) of external advisors will review safety data and advise Tenaya on plans to enroll patients at the dose level of 6E13vg/kg and enroll additional patients in the initial dose cohort.

The MyPeak-1 clinical trial will be conducted at up to twelve leading U.S. centers specializing in HCM care. The first site that is actively recruiting patients is the Hypertrophic Cardiomyopathy Center at the Cleveland Clinic, Cleveland, Ohio. To learn more about gene therapy for HCM and participation in the MyPeak-1 study, please visit HCMStudies.com or ClinicalTrials.gov (NCT05836259).

About *MYBPC3*-Associated Hypertrophic Cardiomyopathy
Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiac disorder, and variants in the Myosin Binding Protein C3 (*MYBPC3)* gene are the most common genetic cause of HCM. *MYBPC3*-associated HCM is estimated to account for approximately 20 percent of the overall HCM population and to affect approximately 115,000 patients in the United States alone. In *MYBPC3*-associated HCM, mutations of the *MYBPC3* gene result in insufficient expression of a protein needed to regulate heart contraction. It is a chronic, progressive condition characterized by left ventricular thickening, hypercontractility, fibrosis, abnormal heart rhythms, cardiac dysfunction and impaired diastolic relaxation. This in turn leads to serious complications including debilitating symptoms such as shortness of breath, fainting and palpitations; heart failure; significant impairment in overall quality of life; and sudden cardiac death in some adults and children. There are currently no approved therapeutics that address the underlying genetic cause of HCM.

About TN-201
TN-201 is an investigational first-in-class adeno-associated virus (AAV)-based gene therapy being developed to treat HCM due to disease-causing variants in the *MYBPC3* gene. TN-201 gene therapy is intended to deliver a working *MYBPC3* gene to specific cells of the heart via a single infusion to address the underlying cause of *MYBPC3*-associated HCM. The U.S. Food and Drug Administration has granted TN-201 Fast Track and Orphan Drug Designation. TN-201 has also received orphan medicinal product designation from the European Commission.

Tenaya is conducting the Phase 1b MyPeak-1 clinical trial in symptomatic adults diagnosed with *MYBPC3*-associated nonobstructive HCM. As safety and dosing are established, Tenaya plans to develop TN-201 for any patient with a pathogenic *MYBPC3* mutation, including adults with obstructive disease and infants, children and teens with heterozygous or homozygous mutations.

A non-interventional natural history study designed to understand *MYBPC3*-associated HCM in infants, children and teens known as the MyClimb Natural History study is also ongoing at twenty-four sites in the U.S., Canada, and Europe. More information can be found HCMStudies.com or ClinicalTrials.gov NCT05112237.

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. Leveraging its integrated and interrelated Gene Therapy, Cellular Regeneration and Precision Medicine platforms and proprietary core capabilities, the company is advancing a pipeline of novel therapies with diverse treatment modalities for rare genetic cardiovascular disorders and more prevalent heart conditions. Tenaya's most advanced candidates include 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 small molecule HDAC6 inhibitor being initially developed for heart failure with preserved ejection fraction (HFpEF). Tenaya also has multiple early-stage programs progressing through 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 "anticipates," "potential," "seek," "look forward," "will," "plan," and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, the expected timing for sharing initial clinical data from MyPeak-1; the clinical and therapeutic potential of TN-201 as a one-time treatment to correct the underlying genetic cause of *MYBPC3*-associated HCM and improve patient outcomes; enrollment targets for MyPeak-1; and clinical development plans for TN-201. 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; unexpected concerns that may arise as a result of the occurrence of adverse safety events in MyPeak-1; the potential failure of TN-201 to demonstrate safety and/or efficacy in clinical testing; the potential for MyPeak-1 initial clinical trial results to differ from preclinical or expected results; the timing, scope and likelihood of regulatory filings and approvals for TN-201; Tenaya's ability to successfully operate a manufacturing facility for clinical supply for TN-201; 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 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 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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