Tenaya Therapeutics Announces Updates on TN-201 Gene Therapy Program for MYBPC3-associated HCM

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Independent Data Safety and Monitoring Board Endorsed Dose Escalation and Broadening of Eligibility Criteria; Cohort 2 Now Enrolling

Initial Data from Cohort 1 to be Reported in December 2024

Highlights Recently Presented Insights on Pediatric MYBPC3-associated HCM Disease Burden

SOUTH SAN FRANCISCO, Calif., Oct. 17, 2024 (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 shared updates related to its ongoing Phase 1b/2 MyPEAK-1 clinical trial of TN-201. 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). 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 MyPEAK-1 study of TN-201 is primarily intended to establish the safety profile of TN-201 gene therapy, and we are pleased to report that TN-201 has an appropriate tolerability profile at the 3E13 vg/kg dose without unexpected adverse reactions," said Whit Tingley, M.D., Ph.D., Tenaya's Chief Medical Officer. "The DSMB's recommendation to proceed with dose escalation and endorsement to expand eligibility criteria are further positive early indicators for TN-201's safety profile and enable Tenaya to explore the utility of TN-201 in different populations. We've implemented adjustments to the protocol, including the addition of a biopsy at baseline, broadening eligibility to include obstructive HCM patients and increasing the size of the overall MyPEAK-1 study."

Tenaya completed dosing of the first three patients (Cohort 1) at the 3E13 vg/kg dose in the MyPEAK-1 trial with no unexpected events or toxicities associated with study drug observed. Safety data from Cohort 1 were reviewed by an independent Data and Safety Monitoring Board (DSMB), showing a safety and tolerability profile consistent with other AAV gene therapies at this dose. Accordingly, the DSMB recommended that Tenaya proceed with dose escalation to the 6E13 vg/kg dose (Cohort 2), per protocol. Enrollment of Cohort 2 is underway.

Tenaya has implemented several changes in the MyPEAK-1 protocol intended to support future development, including:

- Adding a baseline biopsy, increasing the total number of cardiac biopsies from two to three, and permitting more flexible timing of post-dose biopsies to help characterize TN-201 expression over time
- Expanding eligibility to include participants who do not have an implantable cardioverter defibrillator device (ICD) and to permit adults with either obstructive or nonobstructive forms of HCM to enroll
- Increasing the potential number of total patients enrolled in the dose expansion portion of the clinical trial from nine to twenty-four adults

Tenaya plans to report initial data from Cohort 1 in December of this year. This readout is expected to focus on TN-201's safety and tolerability, analyses of cardiac biopsy, as well as changes from baseline in cardiac biomarkers. The MyPEAK-1 clinical trial is also collecting data to understand TN-201's effect on imaging biomarkers, heart function, exercise capacity, functional status, and patient quality of life.

As part of Tenaya's ongoing efforts to characterize the disease burden for children and adolescents with *MYBPC3*-associated HCM, Dr. Tingley recently presented data from a study conducted in partnership with the Sarcomeric Human Cardiomyopathy Registry (SHaRe):

- Of the nearly 1,800 *MYBPC3*-associated HCM individuals identified in SHaRe's database, approximately 13% were diagnosed prior to age 18.
- The cumulative lifetime risk of severe events for *MYBPC3*-associated pediatric patients is very high, with 50% experiencing significant morbidity by age 40.
- Both adult and pediatric *MYBPC3*-associated HCM individuals have high rates of serious complications, such as heart failure and ventricular arrhythmias, highlighting the need for timely diagnosis, active monitoring and new genetic medicines that can have a meaningful impact on outcomes**.**
- These data were presented at the virtual HCM Society Scientific Sessions and are available in the Publications page of Tenaya's website.

Tenaya also continues to characterize the pediatric *MYBPC3*-associated HCM population through the MyClimb natural history study (Clinicaltrials.gov ID: NCT05112237) with more than 200 children and adolescents enrolled across 29 sites in USA, Canada, Spain, and the United Kingdom.

About the 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 replacement therapy. 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. Following DSMB assessment of safety at each dose, planned dose expansion cohorts may enroll up to 24 *MYBPC3*-associated HCM adults with either nonobstructive or obstructive forms of HCM.

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

About *MYBPC3*-Associated Hypertrophic Cardiomyopathy 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.(1) *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.(2) 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 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 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 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.

(1) Sedaghat-Hemedani, et al., *Clinical Research Cardiology*, 2017
(2) Ho, et al., *Circulation* 2018

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 "plans," "will," "expected," 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; the planned timing to report initial data from MyPEAK-1 and related focus of the data readout; 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; the potential failure of TN-201 to demonstrate safety and/or efficacy in clinical testing; availability of MyPEAK-1 data at the referenced time; the potential for any MyPEAK-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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