Tenaya Therapeutics Announces TN-201 IND Clearance and Anticipated 2023 Milestones

January 9, 2023

Phase 1b Clinical Trial for TN-201 in MYBPC3-associated HCM Patients Expected to Begin Dosing in Third Quarter 2023; Data Anticipated in 2024

Data from First-in-Human Clinical Trial of TN-301 Anticipated in Second Half 2023

TN-401 IND Submission Planned in Second Half 2023

Cash Runway Extended into First Half 2025

SOUTH SAN FRANCISCO, Calif., Jan. 09, 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, announced today that the U.S. Food and Drug Administration (FDA) has provided clearance of its Investigational New Drug (IND) application to initiate clinical testing of TN-201. In addition, Tenaya shared anticipated 2023 program milestones and updated cash runway guidance.

“Tenaya had a momentous year in 2022 in which we filed two INDs, transitioned into a clinical-stage company, launched operations of our Genetic Medicines Manufacturing Center - where we successfully produced clinical drug supply for TN-201 - and significantly extended our cash runway,” said Faraz Ali, Chief Executive Officer of Tenaya. “We are pleased to start 2023 with clearance of the IND for our TN-201 gene therapy program and look forward to dosing patients with *MYBPC3*-associated HCM in our Phase 1b study in the coming months. We are also starting 2023 with confirmation of target engagement in our TN-301 Phase 1 study and look forward to reporting clinical data for this program later this year. We are enrolling patients across three non-interventional studies for our gene therapy programs and plan to file an IND for TN-401. Taken altogether, we are making tremendous strides on our mission and are solidifying our leadership position in the field of precision medicine therapies for heart disease.”

TN-201 IND Clearance and Phase 1 Protocol
Tenaya received notification from the FDA indicating that, following review of the company’s IND package, clinical testing of TN-201 may proceed. TN-201 is Tenaya’s first-in-class adeno-associated virus (AAV)-based investigational gene therapy product candidate for the treatment of hypertrophic cardiomyopathy (HCM) caused by mutations in the *MYBPC3* gene, the most common genetic cause of HCM. TN-201 is designed to deliver a fully functional *MYBPC3* gene to restore normal levels of MYBPC3 protein and thereby potentially halt disease progression and reverse the course of genetic HCM after a single treatment.

The TN-201 Phase 1b clinical trial is a multi-center, open-label study to assess the safety, tolerability and clinical efficacy of a one-time intravenous infusion of TN-201. The trial will 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.

The trial protocol includes assessments of safety, markers of cardiac transduction and transgene expression in right ventricular biopsy samples, changes in circulating cardiac biomarkers, imaging biomarkers relevant to HCM as measured by echocardiogram and changes in exercise capacity, symptom burden and quality of life. Tenaya expects to assess two dose levels of TN-201, starting with 3E13 vg/kg, a dose associated with near-maximal efficacy in preclinical studies. An independent safety review following the initial cohort will inform plans for dose escalation to 6E13 vg/kg, as needed, and/or enrollment of additional patients in the initial cohort.

“We look forward to initiating our Phase 1b clinical trial of TN-201 in symptomatic adults living with the nonobstructive form of hypertrophic cardiomyopathy later this year,” said Whit Tingley, M.D., Ph.D., Tenaya’s Chief Medical Officer. “HCM patients whose disease is caused by *MYBPC3* mutations are at increased risk for early disease onset and rapid disease progression, but the clinical management for nonobstructive HCM is limited to nonspecific medications intended to reduce symptoms. TN-201 is being developed by Tenaya to correct the underlying genetic cause of HCM after a single dose, offering the hope of restoring normal contractility and preventing the serious complications associated with this disease.”

2023 Anticipated Milestones and Recent Progress

- **TN-201 – *MYBPC3* Gene Therapy Program for Genetic Hypertrophic Cardiomyopathy (HCM)**
  - Tenaya is conducting two non-interventional studies to support the development of TN-201: a study evaluating seroprevalence to AAV9 antibodies among adults with *MYBPC3*-associated HCM, and MyClimb, a natural history study of pediatric patients with *MYBPC3*-associated HCM for which the company has activated more than 15 sites in the U.S. and Europe and enrolled more than 80 subjects.
  - Tenaya has produced sufficient clinical trial material at the company’s Genetic Medicines Manufacturing Center to support the entire anticipated enrollment in the Phase 1b clinical trial.
  - Tenaya anticipates dosing the first patient in the Phase 1b clinical trial of TN-201 in the third quarter 2023.

- Initial data from the TN-201 Phase 1b clinical trial is anticipated in 2024.

- **TN-301 – Small Molecule *HDAC6* Inhibitor for Heart Failure with Preserved Ejection Fraction (HFpEF)**

Tenaya is conducting a Phase 1 clinical trial designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics, including target engagement, of escalating oral doses of TN-301, a highly selective small molecule inhibitor of HDAC6 being developed for the potential treatment of HFpEF. The Phase 1 clinical trial began dosing healthy adult participants in September 2022 with single ascending doses (SAD) of TN-301 or a placebo.

- To date, no dose-limiting toxicities have been observed in the ongoing SAD portion of the study.
- Initial target engagement, measured by the biomarker of tubulin acetylation, has been achieved. In preclinical studies, dose dependent tubulin acetylation measured in circulating blood cells was found to correlate to levels in the heart.
- The company expects to commence dosing in the multiple-ascending dose (MAD) stage of the Phase 1 trial in the first quarter 2023.
- Tenaya plans to present clinical data from both the SAD and MAD stages of the Phase 1 clinical trial in the second half 2023.
- The company expects to also present additional preclinical data supporting the efficacy of TN-301, the mechanism of action (MOA) of HDAC6 inhibition, and comparisons with SGLT2 inhibitors at major conferences in 2023.

- **TN-401 – *PKP2* Gene Therapy Program for Genetic Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)**

Tenaya is preparing for the submission of an IND for TN-401, the company's second gene therapy candidate, being developed for the treatment of genetic ARVC. TN-401 IND-enabling studies and process development for manufacturing are currently underway.

- Tenaya has initiated a global non-interventional study to collect treatment history and seroprevalence to AAV9 antibodies data among ARVC *PKP2* gene mutation carriers.
- Tenaya plans to submit an IND application to the FDA in the second half 2023 to enable clinical development of TN-401.
- Clinical supply of TN-401 will be produced at Tenaya's cGMP Genetic Medicines Manufacturing Center to support the IND filing. These efforts leverage significant learnings from related nonclinical, regulatory, clinical and manufacturing efforts for TN-201.

- **Early-stage Research Efforts**

- Tenaya plans to present and publish new preclinical data related to its research on new targets, novel AAV capsid engineering efforts and manufacturing process improvements throughout 2023.
- Tenaya continues to conduct research on numerous promising targets for potential therapeutic utility and is also pursuing platform enhancements that may further the company's ability to deliver on its mission of discovering and developing disease-modifying medicines for heart disease.

- **Cash Position and Updated Cash Guidance**

Tenaya ended the third quarter of 2022 with $149.5 million in cash, cash equivalents and investments in marketable securities. With the additional estimated net proceeds of $76.8 million from the November 2022 public offering, Tenaya expects that such resources will be sufficient to fund the company into the first half 2025.

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. Founded by leading cardiovascular scientists from Gladstone Institutes and the University of Texas Southwestern Medical Center, Tenaya is developing therapies for rare genetic cardiovascular disorders, as well as for more prevalent heart conditions, through three distinct but interrelated product platforms: Gene Therapy, Cellular Regeneration and Precision Medicine. For more information, visit www.tenayatherapeutics.com.

Forward-looking Statement
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," "anticipated," "planned," "look forward," "potentially," "will," and "may," and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, statements regarding key milestones anticipated in 2023, including the

timing for dosing of patients in the Phase 1b clinical trial evaluating TN-201, data from the Phase 1 trial of TN-301 and the submission of the TN-401 IND; the sufficiency of cash resources to fund Tenaya into the first half 2025; the therapeutic potential of TN-201 for *MYBPC3*-associated HCM patients; enrollment and clinical development plans for the TN-201 Phase 1b clinical trial and the related availability of data from the trial; the expected timing to commence dosing in the MAD stage of the Phase 1 trial for TN-301; the plan to present additional TN-301 preclinical data at major conferences; the plan to produce clinical supply for TN-401 at the company's cGMP Genetic Medicined Manufacturing Center; and the potential of, and plans to present, new preclinical data related to the company's research and manufacturing efforts; and statements by Tenaya's Chief Executive and Chief Medical Officers. 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, scope and likelihood of regulatory filings and approvals; the impact of any future communications from the FDA regarding Tenaya's TN-201 IND; Tenaya's ability to develop, initiate or complete preclinical studies and clinical trials for its product candidates; the availability of data at the referenced times; 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; the level of costs associated with Tenaya's research, development, manufacturing and other activities and the company's ability to raise any additional funding it will need to continue to pursue its business and product development plans; negative impacts of the COVID-19 pandemic on Tenaya's manufacturing and operations, including preclinical studies and planned clinical trials; the potential for any clinical trial results to differ from preclinical, interim, preliminary, topline or expected results; Tenaya's ability to successfully operate a manufacturing facility for clinical or commercial supply; 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 reliance on third parties; 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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