Tenaya Therapeutics Announces FDA Clearance of Investigational New Drug Application and Initiation of Phase 1 Safety Study for TN-301, an HDAC6 Inhibitor for Heart Failure with Preserved Ejection Fraction

September 6, 2022

SOUTH SAN FRANCISCO, Calif., Sept. 06, 2022 (GLOBE NEWSWIRE) -- Tenaya Therapeutics, Inc. (NASDAQ: TNYA), a biotechnology company with a mission to discover, develop and deliver potentially curative therapies that address the underlying causes of heart disease, announced clearance of its Investigational New Drug (IND) application to begin clinical testing of TN-301 by the U.S. Food and Drug Administration (FDA). TN-301 is Tenaya's highly selective small molecule inhibitor of histone deacetylase 6 (HDAC6), initially being developed for the potential treatment of heart failure with preserved ejection fraction (HFpEF). Tenaya has initiated its first-in-human Phase 1 clinical trial of TN-301 in healthy adult participants.

"HFpEF accounts for approximately half of all heart failure cases and its prevalence is increasing, yet there are few effective treatment options. We are excited by the prospects for TN-301, which has shown compelling promise in preclinical models of HFpEF by improving left ventricular relaxation and filling, a hallmark of the disease," said Whit Tingley, M.D., Ph.D., Tenaya's Chief Medical Officer. "The FDA clearance of our IND application for TN-301 is an important milestone for Tenaya as we transition to a clinical-stage biotechnology company and advance the first of our internally discovered candidates to address heart disease into first-in-human safety studies. In conjunction with IND clearance, we have initiated the Phase 1 clinical study of TN-301."

HFpEF is a complex syndrome with many contributing causal factors and is estimated to affect more than three million people in the U.S. alone.[1] It is a disease that involves systemic inflammation, left ventricular hypertrophy, fibrosis, and diastolic dysfunction, resulting in high morbidity and mortality. In preclinical studies, Tenaya's proprietary HDAC6 inhibitors have shown evidence of improvements in multiple parameters of HFpEF, including reducing inflammation, normalizing metabolic dysfunction and improving diastolic dysfunction[2], all of which have been linked to the pathogenesis of the disease. The IND clearance was based on preclinical studies that characterized the safety and mechanistic profile of TN-301.

Tenaya's Phase 1 randomized, double-blind, placebo-controlled clinical study is designed to evaluate the safety and tolerability of escalating oral doses of TN-301. Secondary objectives of the study will be to assess pharmacokinetics and pharmacodynamics (PD) measures. The Phase 1 trial will enroll healthy adult participants in two stages. In Stage 1, participants will receive single ascending doses (SAD) of either TN-301 or placebo. Based on emerging data from the SAD portion of the study, including PD evidence of target engagement, participants in Stage 2 will receive multiple ascending doses of TN-301 at dose levels of interest to help guide dosing in future studies.

About TN-301 and HFpEF
HFpEF is characterized by a stiffening of the heart muscle resulting in an inability for the left ventricle to relax properly during normal heart rhythm, referred to as diastolic dysfunction. There are several cellular processes thought to underly the pathophysiology of HFpEF including increases in fibrosis and inflammation and defects in metabolism. Although HFpEF accounts for approximately 50 percent of all heart failures, there are few proven treatment options.

TN-301 is Tenaya's highly specific first-in-class small molecule histone deacetylase (HDAC) 6 inhibitor, initially being developed for the potential treatment of HFpEF. TN-301 has a multi-modal mechanism of action that includes modifying cytoskeletal and other proteins to coordinate cellular processes. In preclinical studies, TN-301 has been shown to reverse many of the signs and symptoms of HFpEF, with evidence of improved cardiac function and improved glucose tolerance and reduced inflammation and fibrosis.

About Tenaya Therapeutics
Tenaya Therapeutics is a biotechnology company committed to a bold mission: to discover, develop and deliver 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.

[1] Shah, S.; "Research Priorities for Heart Failure with Preserved Ejection Fraction;" Circulation 2020
[2] Yang, J.; European Society of Cardiology Heart Failure Congress 2022

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 "potential," "promise," "will," and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, the therapeutic potential of TN-301 as a treatment for patients with HFpEF and Tenaya's clinical development plans for TN-301. 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, progress and results of clinical studies for TN-301; 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 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 clinical trials for its product candidates; the timing, scope and likelihood of regulatory filings and approvals; Tenaya'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 operations, including planned clinical trials; 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.

Investors
Michelle Corral
Tenaya Therapeutics
mcorral@tenayathera.com

Media
Wendy Ryan
Ten Bridge Communications
wendy@tenbridgecommunications.com