Tenaya Therapeutics Receives Orphan Drug Designation from the U.S. Food and Drug Administration for its Gene Therapy for Genetic Arrhythmogenic Right Ventricular Cardiomyopathy

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TN-401 is being developed for the treatment of genetic arrhythmogenic right ventricular cardiomyopathy (ARVC) caused by mutations in the PKP2 gene

Orphan Drug Designation for TN-401 is the first for a gene therapy treatment for ARVC

Expect to submit TN-401 IND application to the FDA in 2023

SOUTH SAN FRANCISCO, Calif., Nov. 28, 2022 (GLOBE NEWSWIRE) -- Tenaya Therapeutics, 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 U.S. Food and Drug Administration (FDA) has granted orphan drug designation for its second gene therapy product candidate, TN-401, for the treatment of arrhythmogenic right ventricular cardiomyopathy (ARVC).

TN-401 is an adeno-associated virus (AAV)-based gene therapy being developed for the treatment of genetic ARVC caused by Plakophilin-2 (*PKP2)* gene mutations. Mutations of the *PKP2* gene can cause severe disease, including enlargement of the right ventricle in affected individuals, cardiac dysfunction, significant arrhythmia and sudden cardiac death in adults and children. *PKP2* mutations are the most common genetic cause of ARVC, estimated to represent approximately 40 percent of the overall ARVC population and to effect more than 70,000 people in the U.S. alone. TN-401 is designed to use an AAV9 vector to deliver a healthy copy of the *PKP2* gene to the heart muscle of affected patients via a single intravenous dose. Current treatments do not address the underlying genetic cause of disease and do not appear to affect disease progression.

The FDA Orphan Drug program provides orphan designation to drugs and biologics that are intended for the treatment of rare diseases (those affecting fewer than 200,000 people in the United States). Orphan designation qualifies Tenaya for various development incentives as part of the Orphan Drug Act, including tax credits for certain clinical trial expenses. This designation is not an assurance that regulatory approval will be received, but if approved, would allow TN-401 to become eligible for seven years of market exclusivity in the United States.

Tenaya intends to initiate a global non-interventional study of ARVC *PKP2* gene mutation carriers by the end of this year in order to collect treatment history and data on seroprevalence to AAV antibodies. Tenaya expects to submit an Investigational New Drug (IND) application for the program to the FDA in 2023.

Tenaya presented preclinical data supporting TN-401's activity in a *Pkp2*-deficient murine model of ARVC earlier this year at the annual meeting of the Heart Rhythm Society (HRS), as well as at the annual meeting of the American Society of Gene and Cell Therapy (ASGCT). These data demonstrated significant improvement of right ventricular dilation, cardiac dysfunction, and electrophysiological deficits, including the hallmark arrythmia associated with *PKP2* mutations. The effects were dose-dependent and stable following a single infusion, and a significant survival benefit was observed compared to untreated controls. No safety signals have been observed to date.

About Tenaya Therapeutics
Tenaya Therapeutics is a clinical-stage 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.

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 "expect," "would," "intends," and similar expressions are intended to identify forward-looking statements. Such forward-looking statements include, among other things, the expected timing for submission of an IND application for TN-401; the therapeutic and commercial potential of TN-401 as a treatment for patients with ARVC; the potential benefits of receipt of orphan drug designation by the FDA for TN-401; and plans to initiate a global non-interventional study of patients with ARVC. 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 for TN-401 and Tenaya's other product candidates; Tenaya's ability to develop, initiate or complete preclinical studies and clinical trials for TN-401 and its other product candidates; 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; 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 preclinical studies and 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.

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