Tenaya Therapeutics Presents Preclinical Data at MDA 2026 Highlighting TN-301's Potential to Correct Skeletal and Cardiac Muscle Decline in Duchenne Muscular Dystrophy

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Tenaya's Highly Selective HDAC6 Inhibitor TN-301 Outperformed Approved Pan-HDAC Inhibitor Givinostat in Improving Muscle Function and Correcting Drivers of DMD Cardiomyopathy

New Data Confirm TN-301's Differentiated Mechanism and Opportunities to Positively Address Rare and Prevalent Cardiac, Metabolic and Muscular Conditions

Tenaya Plans to Advance TN-301 Toward Phase 2 Clinical Development

ORLANDO, Fla. and SOUTH SAN FRANCISCO, Calif., March 09, 2026 (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 presented encouraging preclinical data evaluating TN-301, the company's highly selective HDAC6 inhibitor, at the Muscular Dystrophy Association's Clinical & Scientific Conference 2026 (MDA 2026). In *in vitro* and *in vivo* models of Duchenne muscular dystrophy (DMD), TN-301 improved muscle performance and corrected key drivers of DMD cardiomyopathy.

TN-301 is Tenaya's potent and highly selective small molecule HDAC6 inhibitor with a multi-modal mechanism of action, including reducing inflammation, metabolic and mitochondrial dysregulation and fibrosis, and improving autophagy, which may have potential benefit in rare or prevalent cardiac, metabolic, muscle and pulmonary diseases. In a Phase 1 safety study in healthy adults, TN-301 was generally well tolerated over a wide dose range and did not demonstrate serious adverse events or dose-limiting toxicities. Based on this profile, Tenaya has identified several potential indications of interest, supported by the company's previously published preclinical results in heart failure with preserved ejection fraction (HFpEF) and genetic dilated cardiomyopathy.

Today's presentation at MDA 2026 adds to this body of research, highlighting TN-301's potential in DMD cardiomyopathy and muscle degeneration. Tenaya plans to advance TN-301 toward clinical studies in patients, with HFpEF and DMD being among the most promising potential indications identified to date.

"DMD-related cardiomyopathy is the most common cause of death among individuals with DMD, and despite advances in care, there is a profound unmet need for treatments that can address both skeletal muscle atrophy and cardiac decline," said Kathy Ivey, Ph.D., Senior Vice President, Research of Tenaya Therapeutics. "Recognizing that many of the drivers of DMD-related cardiomyopathy and skeletal muscle degeneration corresponded to TN-301's multi-modal mechanism of action, we conducted a series of studies and found that TN-301 outperformed the approved agent, givinostat, achieving functional improvements in *mdx* mice that restored muscle performance to wild-type levels while also correcting key DMD-associated cardiomyocyte defects."

The pan HDAC inhibitor, givinostat, is approved in the U.S. and EU for the treatment of DMD and has been shown to slow skeletal muscle decline in DMD patients as demonstrated clinically by the 4 Stair Climb (4SC) and North Star Ambulatory Assessment (NSAA). However, its use is limited by side effects including thrombocytopenia, and by QT prolongation risk – liabilities not observed clinically in the Phase 1 study of TN-301. To test the hypothesis that TN-301 may delay or reverse both skeletal muscle pathology and cardiomyopathy in DMD, Tenaya researchers conducted studies comparing TN-301 with givinostat. Key findings presented at MDA 2026 include:

- TN-301 treatment at doses as low as 3 mg/kg improved grip strength to wild-type levels within five weeks, whereas *mdx* mice treated with givinostat (10 mg/kg, approximating clinical exposures) failed to reach wild-type performance.
- TN-301-mediated functional improvements were accompanied by reductions in circulating creatine kinase activity and favorable changes in gene expression, indicating reduced muscle cell injury.
- In cardiomyocytes derived from human DMD induced pluripotent stem cells, TN-301 corrected calcium handling abnormalities and mitochondrial dysfunction, while givinostat exacerbated these established drivers of DMD cardiomyopathy.

These positive preclinical data – as well as data from others using HDAC6 inhibitors in DMD disease models – collectively suggest that HDAC6 inhibition may be substantially driving the benefits observed to date with pan-HDAC inhibitors in DMD clinical studies.

These results were presented at MDA 2026 by Dr. Ivey in a poster presentation, titled "*TN-301, Tenaya's HDAC6 Inhibitor, Improves Muscle Function and Molecular Pathology in mdx Mice and Corrects Human DMD iPSC-Cardiomyocyte Phenotypes*".

About TN-301
TN-301 is Tenaya's highly specific small molecule histone deacetylase (HDAC) 6 inhibitor, which has demonstrated promising preclinical potential for the treatment of heart failure with preserved ejection fraction (HFpEF) and Duchenne muscular dystrophy (DMD). In a Phase 1 clinical trial of healthy volunteers, TN-301 was generally well tolerated across the broad range of doses studied, with dose-responsive pharmacokinetics and a half-life supportive of once-daily dosing. Notably, there were no changes in histone acetylation with TN-301, underscoring the >3000-fold selectivity of TN-301 for HDAC6 over other HDACs and supporting the potential to avoid the off-target effects observed with less selective HDAC6 or pan-HDAC inhibition.

HDAC6 inhibition exerts its benefits on the heart and other organs in the body by modifying cytoskeletal and other proteins to coordinate cellular processes through a multi-modal mechanism of action. In preclinical studies, Tenaya's HDAC6 inhibitors have been shown to reduce inflammation, oxidative stress, fibrosis, and metabolic dysregulation, as well as improve autophagy, protein quality control, mitochondrial metabolism, and lipid metabolism. Tenaya is committed to exploring opportunities to advance TN-301 into clinical studies of patients with cardiac, metabolic, muscular or pulmonary disorders where there is strong alignment between the activity of HDAC6 inhibition and the pathophysiology of disease.

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's pipeline includes clinical-stage candidates TN-201, a gene therapy for *MYBPC3*-associated hypertrophic cardiomyopathy (HCM) and TN-401, a gene therapy for *PKP2*-associated arrhythmogenic right ventricular cardiomyopathy (ARVC). Tenaya has employed a suite of integrated internal capabilities, including modality agnostic target validation, capsid engineering and manufacturing, to generate a portfolio of novel medicines based on genetic insights, including TN-301, a clinical-stage small molecule HDAC6 inhibitor for the potential treatment of heart failure and related cardio/muscular disease, and multiple early-stage programs in preclinical development aimed at the treatment of both rare genetic disorders and more prevalent heart conditions. 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 "opportunities," "plans," "may," "potential," "promising," "committed," 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 TN-301 as a treatment for HFpEF, DMD and other cardiac, metabolic, muscle and pulmonary diseases and Tenaya's commitment to exploring opportunities to advance TN-301 into clinical studies in such indications. 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 potential failure of TN-301 to demonstrate safety and/or efficacy in clinical testing; unexpected concerns that may arise as a result of the occurrence of adverse safety events or additional data analyses of clinical trials evaluating TN-301; the timing, scope and likelihood of regulatory filings and approvals for TN-301; 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 TN-301 or 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 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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