Tenaya Therapeutics Unveils Preclinical Research Supporting Product Candidate for Rare and Prevalent Heart Disease Indications at ESC Heart Failure 2021

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- Highly specific HDAC6 inhibitors (HDAC6i) demonstrated improved cardiac function in mouse models of heart failure with preserved ejection fraction (HFpEF) and genetic dilated cardiomyopathy (gDCM)
- Potential utility of HDAC6 as a target in heart disease was validated using Tenaya's Precision Medicine platform
- HDAC6i product candidate TYA-11631 is currently in IND-enabling studies

SOUTH SAN FRANCISCO, Calif – July 13, 2021 – Tenaya Therapeutics, a biotechnology company with a mission to discover, develop and deliver curative therapies that address the underlying causes of heart disease, has unveiled preclinical data supporting drug discovery efforts involving its Precision Medicine Platform at the European Society of Cardiology Heart Failure 2021 (ESC-HF) meeting. The company shared data illustrating the use of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) to identify cardioprotective agents, as well as data supporting the beneficial effect of its proprietary and highly specific histone deacetylase 6 inhibitors (HDAC6i) – including TYA-11631 and TYA-11018 – in models of heart failure with preserved ejection fraction (HFpEF) and genetic dilated cardiomyopathy (gDCM).

"We are very encouraged by the preclinical data that supports the potential multi-modal benefit of TYA-11631 in HFpEF, one of the greatest areas of unmet need in heart disease," said Faraz Ali, Chief Executive Officer of Tenaya Therapeutics. "The data presented also provide important proof of concept for the utility of Tenaya's Precision Medicine platform that combines human disease models with machine learning algorithms to support modality agnostic drug discovery."

The data shared at ESC-HF demonstrated significant reversal of cardiac disease in two HFpEF models following once-daily oral dosing with TYA-11631, Tenaya's highly specific HDAC6i compound (see abstract titled *"HDAC6 Inhibition Improves Diastolic Function in a Mouse Model of Heart Failure with Preserved Ejection Fraction"*). HFpEF is a condition involving systemic inflammation, left ventricular hypertrophy, fibrosis, and diastolic dysfunction. It affects an estimated more than 3 million patients in the U.S. and there are no approved disease-modifying therapies. TYA-11631 has been well-tolerated in small and large animal models and is currently in IND-enabling studies.

Additional data shared at ESC-HF also illustrate Tenaya's ability to successfully use phenotypic screening of iPSC-CMs coupled with deep learning algorithms for target discovery (see abstract titled *"Phenotypic Screening Identifies HDAC6 Inhibitors as Cardioprotective Agents in BAG3 Cardiac-Knockout Mouse Model of Dilated Cardiomyopathy*"). HDAC6i were one of many potentially cardioprotective agents identified *in vitro* via a blinded screen of hiPSC-CMs mimicking gDCM due to *BAG3* deficiency. The benefit of HDAC6i was subsequently verified *in vivo* in a *BAG3* deficient mouse model as well as the HFpEF models, confirming that the hiPSC-CM disease models can yield biologically relevant targets. Tenaya has established more than 40 in-house hiPSC-CM disease models and is pursuing more targets identified through ongoing screening efforts.

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

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