RIDGE™-1 CLINICAL TRIAL

for *PKP2*-associated ARVC

Arrhythmogenic right-ventricular cardiomyopathy (ARVC), also known as Arrhythmogenic Cardiomyopathy (ACM), is an inherited condition often caused by mutations (changes) in the *PKP2* gene. The *PKP2* gene produces proteins necessary for heart muscle cells to connect and communicate with each other for typical heart function. *PKP2* gene mutations result in a loss of proteins and, over time, muscle cells in the heart lose their structure. This can lead to heart failure. The heart cells may also lose the ability to make consistent heartbeats, which can lead to dangerous heart rhythms, called arrhythmias, and sudden cardiac arrest.

WHAT IS TN-401?

The RIDGE-1 clinical trial is studying TN-401, an investigational gene therapy designed to reach heart muscle cells to address the uderlying genetic cause of ARVC.

- TN-401 uses adeno-associated virus 9 (AAV9) to deliver a working *PKP2* gene to heart muscle cells called cardiomyocytes
- Once in these cells, the working *PKP2* gene is expected to make the protein needed to restore typical heart function
- TN-401 is given as a one-time intravenous (IV) infusion

AAV9 is one type of virus commonly used as a vector (also called a capsid) because it is efficient at delivering new genes to cells and is not known to cause diseases in people.[1]

There are different types of AAV capsids. The AAV9 capsid used in TN-401 is the most extensively studied and is proven to reach heart muscle cells.[2,3]

WHAT IS THE PURPOSE OF THE RIDGE-1 CLINICAL TRIAL?

RIDGE-1 is a Phase 1b clinical trial. This means it is the first trial conducted by Tenaya Therapeutics to study TN-401 in humans. The goals are to understand:

- The safety of TN-401 in humans
- Any potential side effects
- The best dose of TN-401
- The effects of TN-401 on the body

The RIDGE-1 clinical trial will also look at how TN-401 affects overall health and quality of life based on feedback from participants and their doctors.

AAV gene therapy does carry some risk. Please ask your doctor about these risks.

WHO CAN TAKE PART IN THE RIDGE-1 CLINICAL TRIAL?

You may be able to take part in the trial if you

- Have ARVC caused by mutations in the *PKP2* gene
- Are between 18 and 65 years old
- If you have not had a ventricular tachycardia ablation or have had an ablation at least 6 months ago
- Have a working implantable cardiac defibrillator (ICD) with remote monitoring
- Have no heart failure symptoms, or mild to moderate heart failure symptoms affecting daily activities
- Have a low level of antibodies to the AAVs

These are not all of the eligibility criteria. Clinical trial staff will evaluate you and determine if you are eligible to participate in RIDGE-1.

WHAT TO EXPECT IN THE RIDGE-1 CLINICAL TRIAL

MAIN CLINICAL TRIAL		
8-12 Weeks	Informed Consent & Screening	• 1 visit to gather information about your health to determine whether you can participate • You will review informed consent materials to ensure you understand: ◦ The purpose of the clinical trial ◦ All participants will receive TN-401, the investigational gene therapy ◦ The expectations for participation, including required visits, procedures, and tests ◦ Potential risks and benefits ◦ Options for leaving the clinical trial if desired
About 7 days	Pre-dose Activities	• The clinical trial doctor will start you on medicines that will reduce the chances that your immune system will block the effect of TN-401 ◦ The doctor will review the reason these medicines are needed, the amount of time you will need to take these medicines, and any potential side effects • The doctor will gather more information about your health
About 8 Days	Hospitalization for Infusion of TN-401 & Monitoring	• Hospitalization for close monitoring, management, and treatment of any possible side effects
About 1 Year	First Year Visits	• 19 follow up visits after leaving the hospital to monitor safety and changes in heart function and ARVC symptoms*
LONG-TERM FOLLOW-UP		
About 4 Years	Follow-up Visits	• 5 visits total to monitor safety and changes in heart function and ARVC symptoms over time
TOTAL PARTICIPATION – ABOUT 5 YEARS		

**Most visits will be in person at the trial site with a select number of visits completed by phone or at your home.*

IF YOU ARE INTERESTED IN PARTICIPATING:

Talk to your doctor about whether you may be a candidate for this clinical trial

Visit ClinicalTrials.gov and enter identifier number **NCT06228924** to learn more

Contact Tenaya at Patient.Advocacy@tenayathera.com to request more information

THE USE OF TN-401 DESCRIBED HERE IS INVESTIGATIONAL. SAFETY AND EFFICACY HAVE NOT BEEN ESTABLISHED. TN-401 HAS NOT BEEN APPROVED BY THE U.S. FOOD AND DRUG ADMINISTRATION OR ANY OTHER COUNTRY'S HEALTH AUTHORITY OR REGULATORY AGENCY.

REFERENCES **1.** Li C, Samulski RJ. *Nat Rev Genet*. 2020;21(4):255-272. **2.** Sasaki N, et al. *Heart Lung Circ*. 2023;32:816-824. **3.** Novartis. https://www.novartis.com/sites/novartis_com/files/q4-2022-investor-presentation.pdf. Accessed April 9, 2024.

TENAYA THERAPEUTICS

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