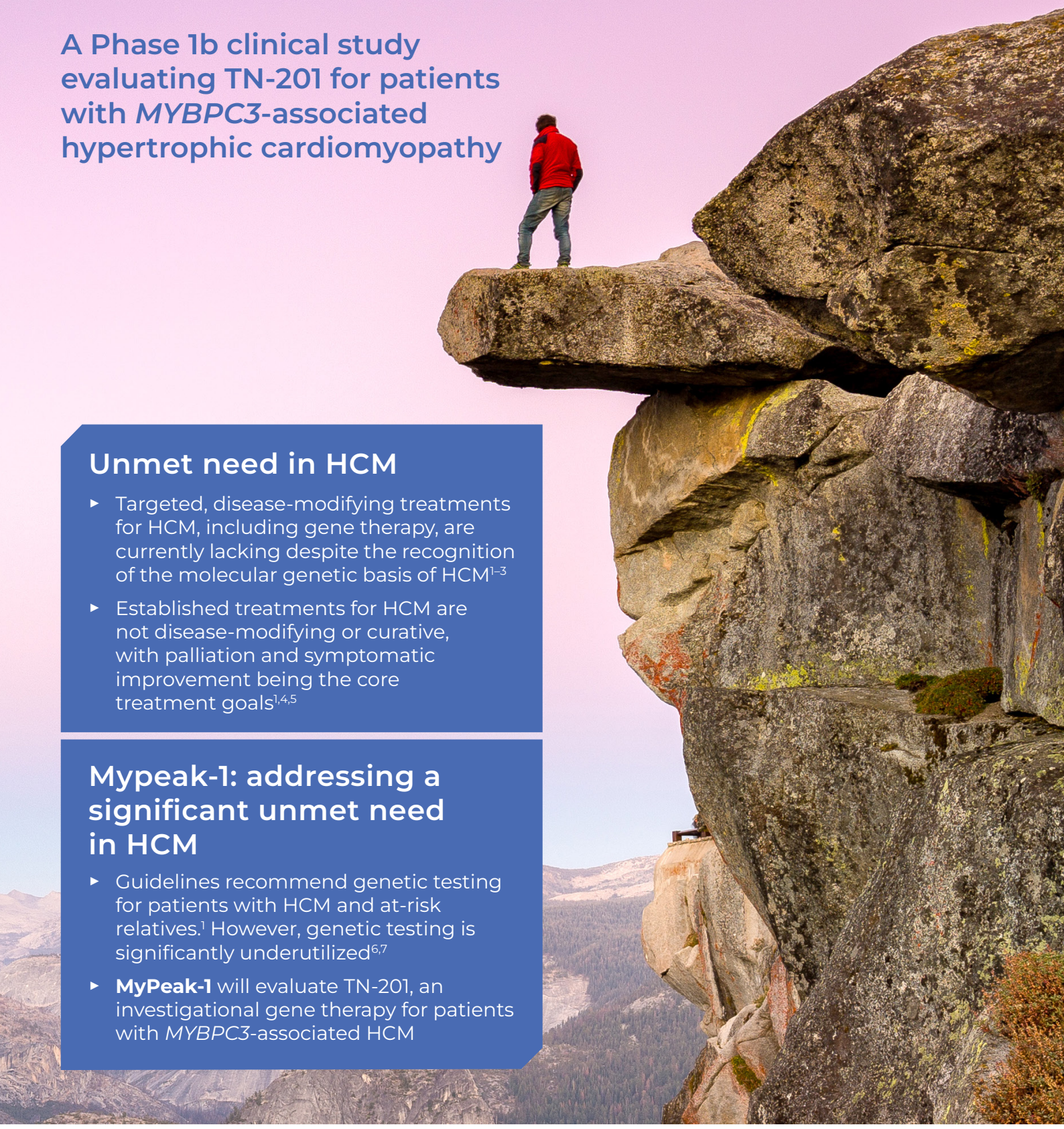
MyPeak-1

A Phase 1b clinical study evaluating TN-201 for patients with *MYBPC3*-associated hypertrophic cardiomyopathy



Unmet need in HCM

- Targeted, disease-modifying treatments for HCM, including gene therapy, are currently lacking despite the recognition of the molecular genetic basis of HCM[1–3]
- Established treatments for HCM are not disease-modifying or curative, with palliation and symptomatic improvement being the core treatment goals[1,4,5]

Mypeak-1: addressing a significant unmet need in HCM

- Guidelines recommend genetic testing for patients with HCM and at-risk relatives.[1] However, genetic testing is significantly underutilized[6,7]
- **MyPeak-1** will evaluate TN-201, an investigational gene therapy for patients with *MYBPC3*-associated HCM

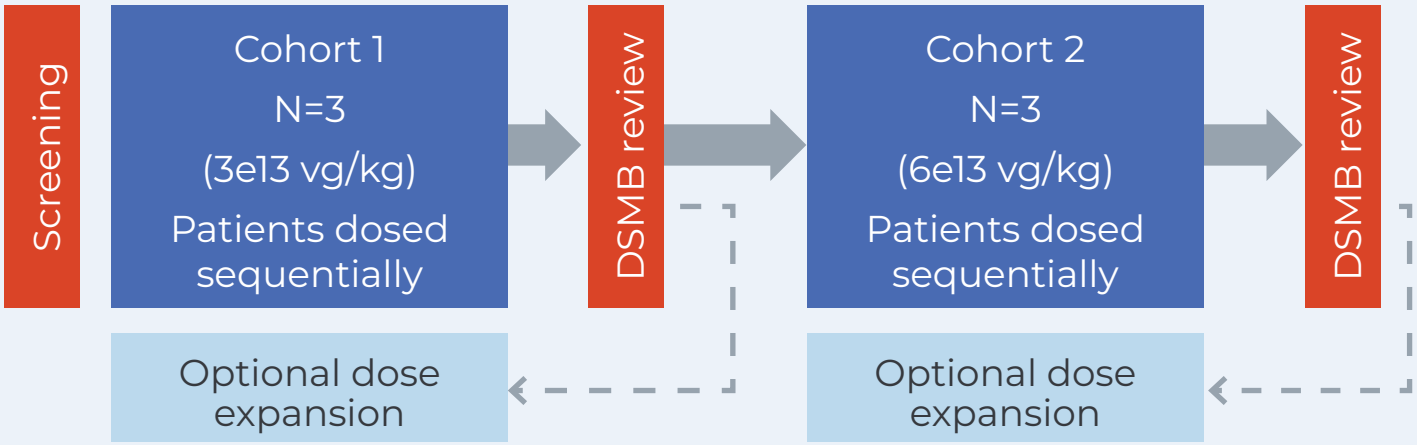
HCM = hypertrophic cardiomyopathy; *MYBPC3* = myosin binding protein C3 gene.

1. Ommen SR, et al. *Circulation* 2020;142:e558–e631; 2. Repetti GG, et al. *Circ Res* 2019;124:1536–1550; 3. Cheng Z, et al. *Front Cardiovasc Med* 2021;8:722340; 4. Ammirati E, et al. *Eur J Heart Fail* 2016;18:1106–1118; 5. Maron BJ, et al. *J Am Coll Cardiol* 2022;79:390–414; 6. Bhasin K, et al. *J Am Coll Cardiol* 2023;81(8_Supplement):1853. https://doi.org/10.1016/S0735-1097(23)02297-0; 7. Cirino AL, et al. *J Genet Couns* 2022;31:1290–1305.

MyPeak-1: A Phase 1b Gene Therapy Study

The study objectives are to evaluate the safety and tolerability of TN-201, and to explore the potential clinical and functional benefits of TN-201 treatment in adults with *MYBPC3*-associated hypertrophic cardiomyopathy

MyPeak-1 study design: An open-label, multicenter dose-escalation and dose-expansion study of TN-201, an investigational gene therapy candidate



ClinicalTrials.gov Identifier: NCT05836259

MyPeak-1 study endpoints:

- Safety and tolerability of TN-201
- Functional and symptomatic changes (assessment of NYHA class, exercise capacity, patient-reported outcomes)
- Pharmacokinetics (assessment of cardiac transduction and transgene expression)
- Pharmacodynamics (assessment of immunologic response, plasma biomarkers & echocardiography parameters)

Select inclusion criteria:

- **Adults** (age 18–65 years)
- Nonobstructive hypertrophic cardiomyopathy
- **Pathogenic/likely pathogenic truncating mutations in the *MYBPC3* gene**
- Symptomatic (NYHA Functional Class II or III)
- NT-proBNP ≥300 pg/ml
- Functioning ICD

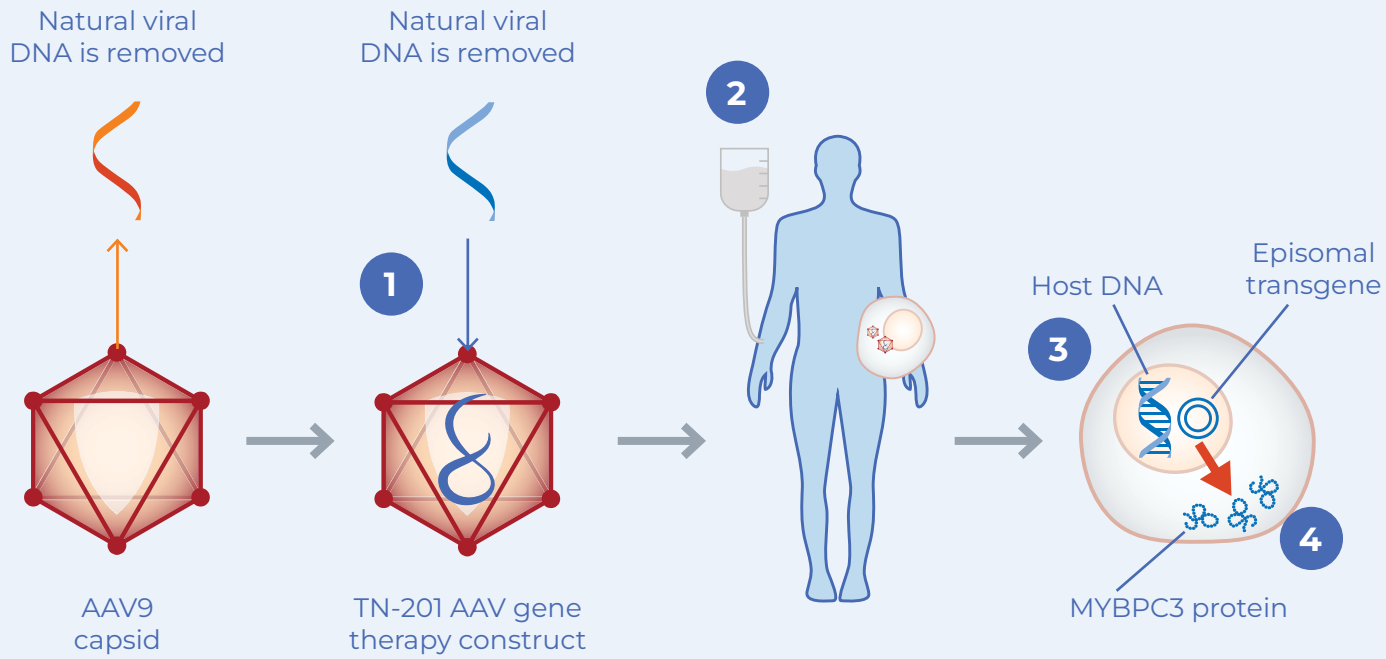
Exclusion criteria:

- Seropositive for AAV9-neutralizing antibody titer

AAV9 = adeno-associated virus serotype 9; DSMB = Data Safety Monitoring Board; ICD = implantable cardioverter defibrillator; *MYBPC3* = myosin binding protein C3; NT-proBNP = N-terminal pro B-type natriuretic peptide; NYHA = New York Heart Association.

TN-201 is intended to deliver a working copy of the *MYBPC3* gene to correct *MYBPC3*-associated HCM

TN-201 is an AAV9-based gene therapy that has been designed to selectively deliver the *MYBPC3* transgene to the cardiomyocytes



1. The *MYBPC3* transgene is packaged into an **AAV9** capsid, producing TN-201
2. TN-201 is administered as a **one-time only** intravenous infusion
3. The *MYBPC3* transgene stabilizes as a circular episome (i.e., DNA that does not integrate or modify the genome)
4. The *MYBPC3* transgene leads to cardiomyocyte-specific expression of functioning myosin binding protein, which may reverse the course of HCM

AAV9 is the only capsid with broad biodistribution and robust transduction and expression data from human heart biopsies[1,2]

AAV9 = adeno-associated virus serotype 9; HCM = hypertrophic cardiomyopathy; *MYBPC3* = myosin binding protein C3.

1. Greenberg B, et al. *Circulation* 2021;144:A10727. https://doi.org/10.1161/circ.144.suppl_1.10727; 2. Rossano J, et al. *Circulation* 2022;146:A11117. https://doi.org/10.1161/circ.146.suppl_1.11117.

The efficacy and safety risks of gene therapy have been established by several FDA-approved therapies

8

FDA-approved gene therapies[1,2]*; 5 therapies use AAV[3]

>10 years

therapeutic gene expression after a single dose[4]

>3,000

patients on AAV gene therapy[5]

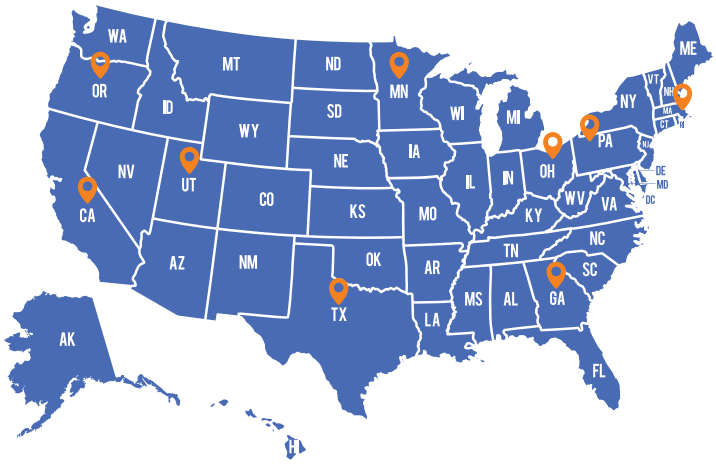
*As of 30 June 2023. AAV = adeno-associated virus; FDA = US Food and Drug Administration.

1. McKinsey & Company March 29, 2022. Available at: https://www.mckinsey.com/industries/life-sciences/our-insights/viral-vector-therapies-at-scale-todays-challenges-and-future-opportunities. Accessed Jul 2023; 2. FDA Approved cellular and gene therapy products. Available at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products. Accessed Jul 2023; 3. Mietzsch M, et al. *Mol Ther Clin Dev* 2023;29:460–472; 4. Muhuri M, et al. *Mol Ther* 2022;30:1364–1380; 5. Ramamurthy RM, et al. *Front Immunol* 2022;13:1011143. https://doi.org/10.3389/fimmu.2022.1011143.

The focus of the MyPeak-1 study will be patient safety

- Immunosuppressive regimen to minimize immunogenicity
- Rigorous laboratory safety monitoring with frequent safety assessments
- Independent Data and Safety Monitoring Board (DSMB) review to ensure ongoing safety

MyPeak-1 study sites



1) La Jolla, CA
2) San Francisco, CA
3) Atlanta, GA
4) Boston, MA
5) Rochester, MN
6) Cincinnati, OH
7) Cleveland, OH
8) Portland, OR
9) Philadelphia, PA
10) Pittsburgh, PA
11) Houston, TX
12) Salt Lake City, UT

If you have a patient that may meet the MyPeak-1 study eligibility criteria:

Please contact medicalaffairs@tenayathera.com

The following websites provide more information on:

Genetic testing:
4hcm.org/genetic-testing-an-overview/

The MyPeak-1 Study:
www.clinicaltrials.gov/study/NCT05836259