Scaling new heights in the fight against heart disease

April 2025

Forward-looking statement

This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, that are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. All statements other than statements of historical facts contained in this presentation, including statements regarding business strategy, plans and 2025 strategic priorities; the clinical, therapeutic and market potential of and expectations regarding our product candidates, platforms and proprietary capabilities; clinical development plans for TN-201, TN-401 and TN-301; preclinical efforts and timelines; availability and content of data from MyPEAK™-1 and RIDGE™-1; targeted populations for clinical trials and treatments; the sufficiency of Tenaya's cash runway to fund operations, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "purpose," "focus," "plan," "potential," "may," "future," "anticipated," "objective," or the negative of these terms or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs.

These forward-looking statements are subject to time, risks, uncertainties and assumptions described in our filings with the SEC, including, but not limited to the section titled "Risk Factors" in our Form 10-K for year ended December 31, 2024, and other documents we have filed, or will file with the SEC. These filings, once filed, are or will be available on the SEC website at www.sec.gov. Such risks include, among other things: the availability of data at the referenced times; the timing of the initiation, progress, completion and potential results of our clinical trials and preclinical studies; our ability to advance product candidates into, and successfully complete, clinical trials and preclinical studies; the potential for clinical trials of our product candidates to differ from preclinical, preliminary, interim or expected results; the timing or likelihood of regulatory filings and approvals; our estimates of the number of patients who suffer from the diseases we are targeting and the number of patients that may enroll in our clinical trials; our ability to successfully manufacture and supply our product candidates for preclinical studies, clinical trials and for commercial use, if approved; our ability to commercialize our product candidates, if approved; future strategic arrangements and/or collaborations and the potential benefits of such arrangements and/or collaborations; our estimates regarding expenses, capital requirements and needs for financing, and our ability to obtain capital; our ability to retain the continued service of our key personnel and to identify, hire and retain additional qualified professionals; our ability to obtain and maintain intellectual property protection for our platforms, programs and product candidates; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the pricing, coverage and reimbursement of our product candidates, if approved; and developments relating to our competitors and our industry, including competing product candidates and therapies; general economic and market conditions; and other risks. These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. The forward-looking statements made in this presentation relate only to events as of the date on which such statements are made. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

This presentation discusses product candidates that are under clinical study and have not yet been approved for marketing by the U.S. Food and Drug Administration. No presentation is made as to the safety or efficacy of these product candidates for the use for which such product candidates are being studied.

Our purpose: To transform and extend lives through
the discovery, development and delivery of potentially curative therapies
that target the underlying causes of heart disease.

TENAYA™ THERAPEUTICS

Singular focus on the heart

3 clinical-stage programs and multiple near-term gene therapy data readouts

Deep expertise in cardiology, genetics and rare disease drug development

Foundational capabilities fuel innovation and first-in-class potential

Track record of execution on ambitious goals

Clinical-stage pipeline poised for progress

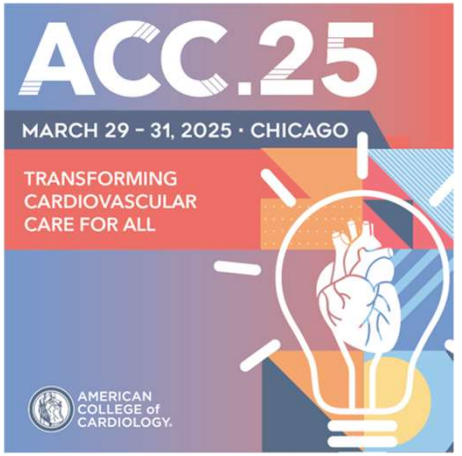
Program	Modality	U.S. Prevalence	Development Stage	Status
Clinical-Stage Programs				
TN-201 for *MYBPC3*+ HCM • FDA Orphan Drug, Fast Track and Rare Pediatric Disease designations • Orphan Medicinal Product designation from European Commission	AAV9 gene therapy	> 120K[1]	**MyPEAK™-1 Phase 1b/2** Seroprevalence study Natural history study	Cohort 1 enrolled Cohort 2 enrolling Completed >100 participants > 220 participants enrolled
TN-401 for *PKP2*+ ARVC • FDA Orphan Drug and Fast Track designations • Orphan Medicinal Product designation from European Commission	AAV9 gene therapy	> 70K[2]	**RIDGE™-1 Phase 1b** Natural history and seroprevalence study	Cohort 1 enrolling > 100 participants
TN-301 for HFpEF	Small molecule	> 3M[3]	**Phase 1 SAD/MAD**	Phase 1b/2a ready Dose escalation in healthy volunteers complete

1. Sedaghat-Hemedani, et al., *Clin Res Cardiol*. 2018
2. Groeneweg, et al, *Circ Cardiovasc Gen 2015* & McKenna, et al, *Nature Rev Cardio* 2021
3. Abovich, et al, *Am J Prev Cardio* 2023

MYBPC3 = Myosin binding protein C-3
HCM = Hypertrophic cardiomyopathy (HCM)
AAV9 = Adeno-associated virus serotype 9

PKP2 = Plakophilin-2
ARVC = = Arrhythmogenic right ventricular cardiomyopathy
HFpEF = Heart failure with preserved ejection fraction

ACC.25 Cohort 1 Update:
Positive early signals of TN-201's clinical impact



1. **Safety: TN-201 well tolerated at 3E13 vg/kg dose; safety profile is consistent with other gene therapies**
   - No cardiotoxicities
   - Liver enzyme elevations manageable and reversible
   - All patients have completed every visit and remain on study

2. **Biopsy: TN-201 reaches heart cells and achieves RNA expression**
   - Consistently robust cardiac transduction that exceeds expectations
   - Durable and increasing mRNA expression in line with peer clinical-stage gene therapy program
   - Protein levels modestly higher from Week 8 to Week 52 in two patients

3. **Clinical Endpoints: Two of three patients saw improvements in ≥ 1 measures of hypertrophy**
   - All three patients improved from NYHA class II/III to NYHA class I
   - Elevated troponin levels dropped by 60% in two patients into normal ranges
   - Diastolic function measures are stable

Initial results from Cohort 2 + additional Cohort 1 follow-up planned for 2H'25

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mRNA = messenger ribonucleic acid
NYHA = New York Heart Associations

Global clinical execution is building momentum for TN-201 and TN-401

Broad clinical footprint positions current and future genetic therapy programs for success

>400 study participants

5 interventional, non-interventional and/or natural history studies

~45 clinical sites activated

8 countries

- ✓ **Providing deeper insights** about disease severity, progression, and approvable endpoints
- ✓ **Fostering stronger relationships** with global cardiomyopathy community
- ✓ **Enabling us to move quickly** toward clinical data and pivotal studies
- ✓ **Paving the path** for future gene therapy and gene editing pipeline product candidates

Significant clinical progress expected in 2025 and beyond

	1H'25	2H'25	2026+
TN-201			
MyPEAK-1	✓ **Present additional Cohort 1 data** • Complete Cohort 2 enrollment	• **Provide Cohort 1 data update & present initial Cohort 2 data**	• **1H'26: Present two-year Cohort 1 and one-year Cohort 2 data** • Pursue regulatory alignment on pivotal studies • Initiate pediatric pivotal study
MyClimb	• Present initial natural history data		
TN-401			
RIDGE-1	• Complete Cohort 1 enrollment • Ex-US expansion	• **Cohort 1 initial data** • Cohort 2 and/or expansion cohort enrollment	• **1H'26: Present one-year Cohort 1 data and early Cohort 2 data** • Pursue regulatory alignment on pivotal study
RIDGE	• Present additional seroprevalence + natural history data		

Increasing clinical and regulatory momentum across the sector bodes well for the future

Cardiomyopathy clinical guidelines recommend genetic testing in the U.S. and Europe

Gene therapies for rare diseases in Phase I have **2x-3.5x higher likelihood of an approval**[1, 2]

7 approvals for potentially curative AAV gene therapies for diseases of the eye, brain, liver, & muscle[3]

Growing number of AAV gene therapy sponsors have announced **regulatory alignment on pivotal studies or approvals based on surrogate endpoints** following clinical data from modest number of patients

rocket pharma
LEXEO therapeutics
SAREPTA THERAPEUTICS
REGENXBIO
uniQure
PTC THERAPEUTICS
ultragenyx
Sangamo THERAPEUTICS

1. FDA Draft Guidance for heart failure; for cell and gene therapies
2. Tufts NEWDIGS FoCUS Project
3. FDA; EMA

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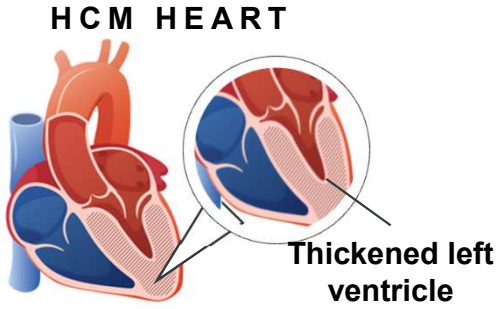
TN-201 for *MYBPC3*-associated HCM

MYBPC3-associated HCM is estimated to affect 120,000 people in the U.S. alone(1)

A severe and progressive autosomal dominant condition affecting adults, teens, children and infants

~57% of identified genetic variants underlying familial HCM are *MYBPC3* mutations(2)

>30% of genetic variants underlying childhood-onset HCM are *MYBPC3* mutations(3)

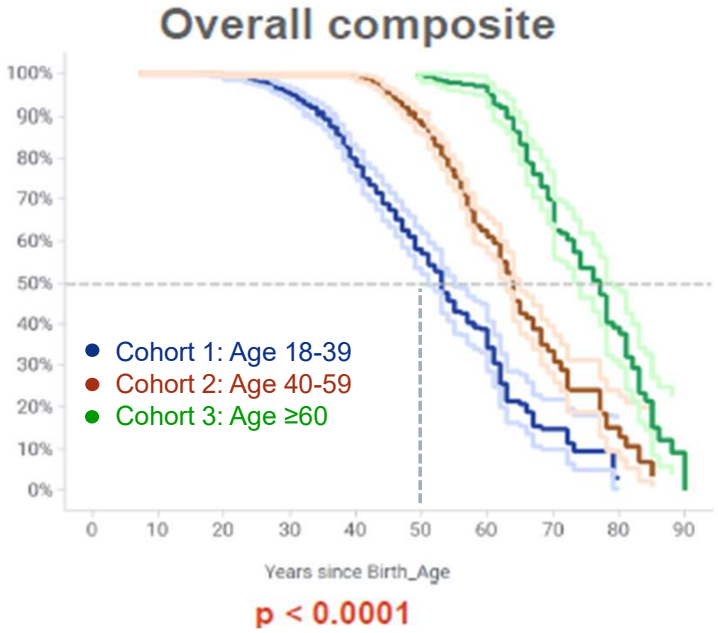


- Significant functional impairment
- Social and psychological impacts
- Symptoms include shortness of breath, fainting, chest pain, fatigue, palpitations, arrhythmias
- Elevated risk of sudden cardiac death and heart failure

1. Sedaghat-Hemedani, et al., *Clin Res Cardiol* 2018
2. Ho, et al, *Circulation* 2018
3. Marston, et al, *Eur Heart Jrnl* 2021

Patients with *MYBPC3*+ HCM are at high risk for serious cardiac events[1]

Younger onset correlates with greater rates of morbidity and mortality



***Overall composite** = NYHA class III/IV or transplant or ventricular assist device or sudden cardiac arrest/death or ICD-appropriate firing or atrial fibrillation or stroke or death*

SHaRE analyses of 1,637 adults with *MYBPC3*-associated HCM

50% of adults diagnosed before age 40 experience a serious cardiac event by age 50

28% rate of SCD among Cohort 1 vs.15% or 12% for Cohorts 2 and 3, respectively

>1in 5 young adults elected to receive a septal reduction surgery

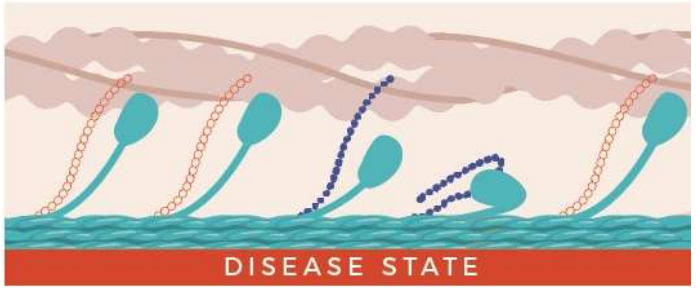
18-39 year old adults were just as likely to be hospitalized due to heart failure symptoms as those ≥ age 60

SCD = Sudden cardiac death
ICD = implantable cardio defibrillator

1. Wang, et al; ACC 2025

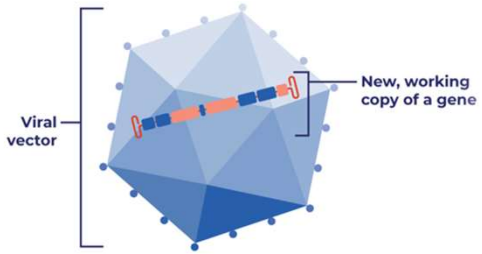
TN-201 is the first gene therapy being developed for *MYBPC3*-associated HCM[1]

MYBPC3+ Pathophysiology

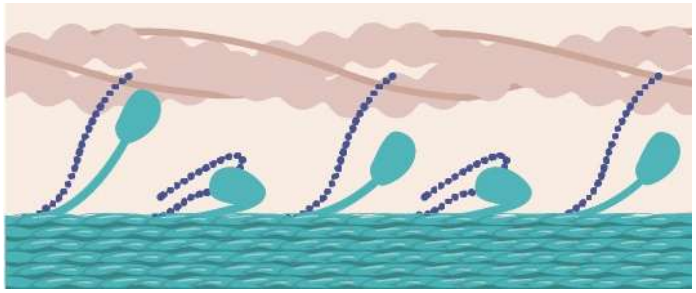


- MyBP-C is an essential structural protein regulating cardiac contractility via interactions with sarcomeric proteins
- Heterozygous mutations in the *MYBPC3* gene lead to lower levels of MyBP-C protein.
- Lower MyBP-C results in increased contractility, thickening of the left ventricle and impaired diastole

TN-201 Mechanism of Action



- TN-201 targets the underlying genetic cause of disease by delivering a full length copy of the *MYBPC3* gene to cardiomyocytes
- TN-201 utilizes an AAV9 capsid and a proprietary promoter with cardiac tropism



- Addition of a *MYBPC3* gene increases MyBP-C protein levels and is expected to halt disease progression, reverse disease pathophysiology, and improve symptoms and patient quality of life after a single dose

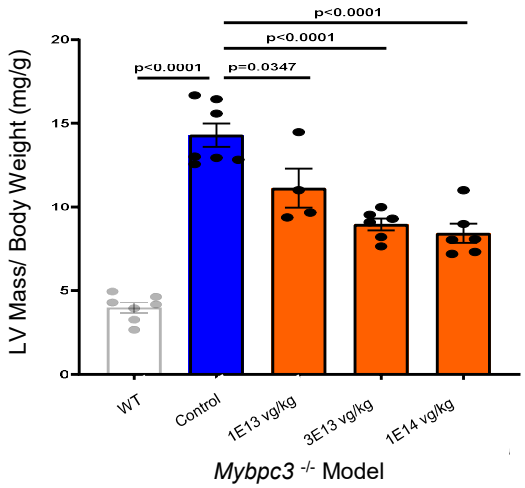
MyBP-C = Myosin-binding protein C

MyBP-C protein missing in sarcomere

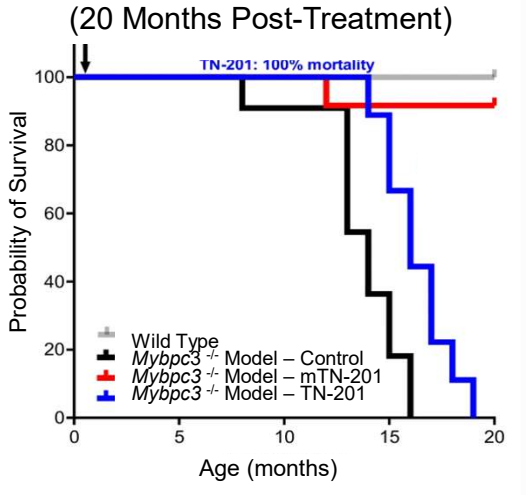
MyBP-C protein present in sarcomere

Single 3E13 vg/kg dose of TN-201 in preclinical KO mouse model reversed disease and increased survival

Reduced heart mass



Extended survival



Improved heart function

Multiple hallmarks of disease reverted toward normal following a single dose

- ✓ Restored WT MyBP-C protein levels
- ✓ Systolic function increased in severe model
- ✓ Diastolic dysfunction reduced

KO = knock-out
mTN-201 = mouse analog of TN-201
LV = left ventricular

Greer-Short, et al; *Nature Communicaitons* 2025

MyPEAK-1 Phase 1b/2 clinical trial design

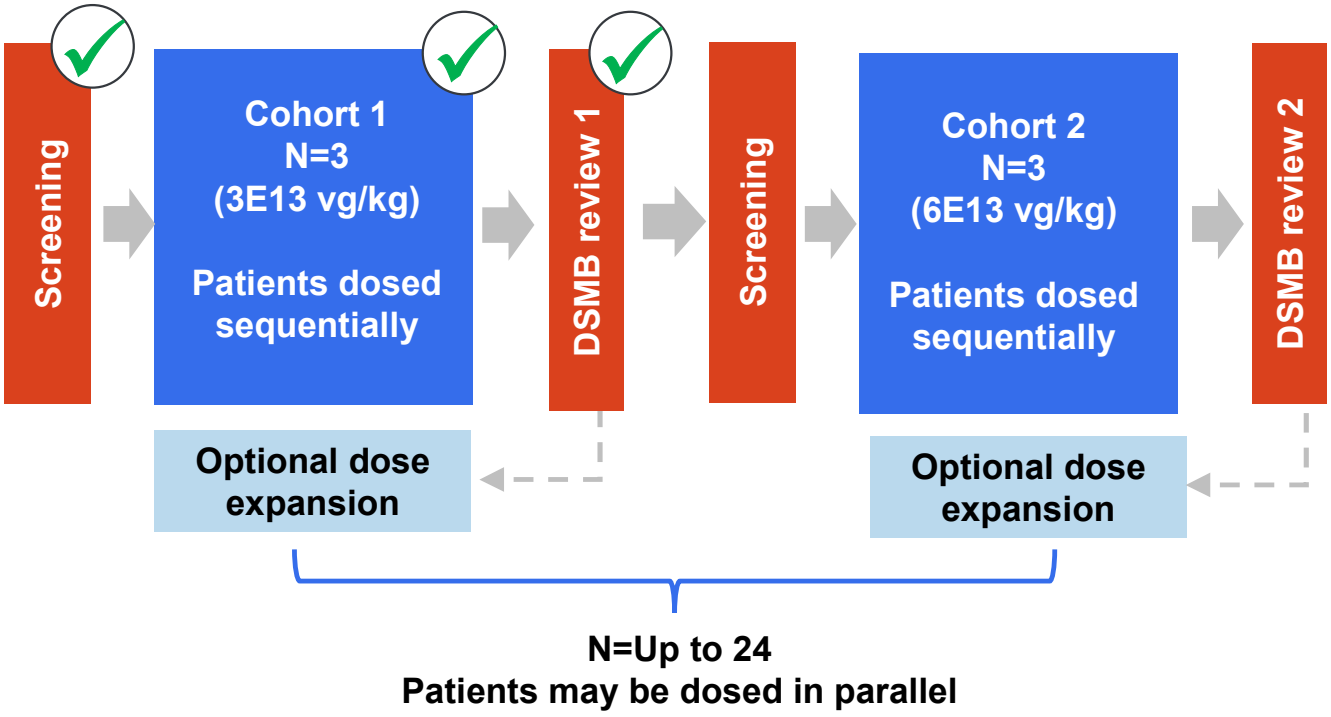
Initial Cohort 2 + additional Cohort 1 data in 2H'25

Study Objectives

- Safety, tolerability
- Dose-finding
- Pharmacodynamics

Design

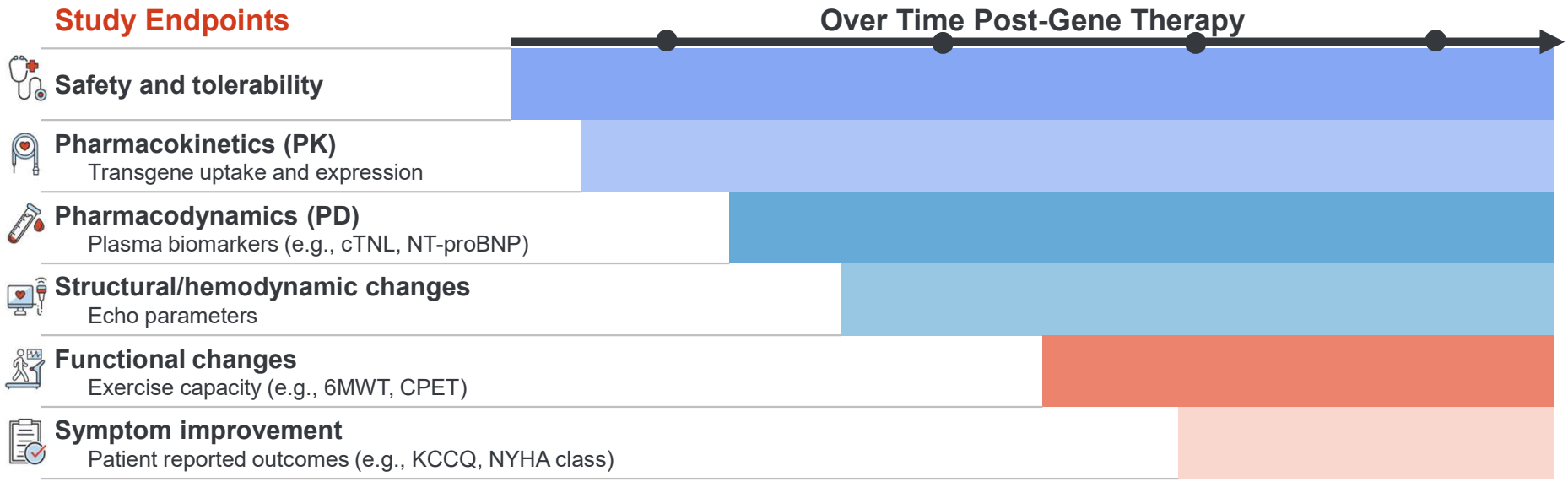
- Open-label, multi-center, dose-escalation and dose-expansion
- 52-week trial period with four-year safety and efficacy follow-up
- Cardiac biopsies at baseline, post-dose and ~52 weeks (effective with Cohort 1, patient 3)



DSMB: Data Safety Monitoring Board
vg/kg: vector genomes per kilogram

MyPEAK-1 Phase 1b/2 clinical endpoints

Seeking directional consistency across multiple parameters over time with the goal of halting or even reversing steady disease progression



cTnI = cardiac troponin
NT-proBNP = N-terminal pro–B-type natriuretic peptide
CPET = Cardiopulmonary exercise testing
6MWT = 6-minute walk test
KCCQ = Kansas City Cardiomyopathy Questionnaire

Interim MyPEAK-1 Data form Cohort 1

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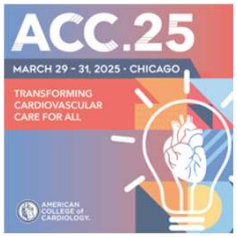
MyPEAK-1 Cohort 1 patients younger and more severe compared to average HCM patient



	Average HCM	Patient 1	Patient 2	Patient 3
Length of Follow-Up	-	12 months	12 months	6 months
Gender	Male (63%)[1]	Female	Female	Male
Phenotype	Nonobstructive (72%)[1]	Nonobstructive	Nonobstructive	Nonobstructive
Current Age	50y[1]	27	43	47
LVMI (g/m^2)	F: 89 | M: 104[3]	174	105	177
NYHA Class	50% ≥ Class II[4]	II	III	II
% Myectomy & Age	18%[5] | Mean = 54y[6]	24	30	39
% ICD & Age	21%[1] | Mean = 38y[2]	27	37	36
NT proBNP (pg/ml)	563[7]	1836	351	1229
Troponin I (ng/L)	27[8]	46	34	53

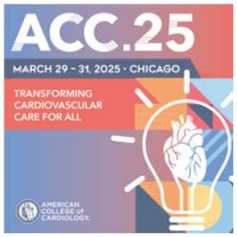
Typical for HCM	Abnormal for HCM	Very abnormal for HCM

LVMI = left ventricular mass index

1. Ho, et al; *Circulation* 2018
2. Rowin, et al; *Circ Arrhytm EP* 2020
3. Olivotto, et al; *JACC* 2008
4. Maron, et al; *JACC* Heart Fail 2018
5. Maurizi, et al; *Circulation* 2024
6. Cui, et al; *JACC* 2019
7. Neubauer, et al; *JACC* 2019
8. Okamoto, et al; *Int Heart J* 2013

TN-201 was generally well tolerated at 3E13 vg/kg dose

Reported AEs consistent with other AAV gene therapies and known effects of immunosuppression



IS regimen effectively managed response to TN-201

- ✓ Patients initiated prophylactic IS of prednisone and sirolimus pre-dose
- ✓ Reversible elevated liver enzymes occurred in all patients, normalized in response to steroid treatment
  - o One mild adverse event classified as an SAE with inpatient steroids
- ✓ All 3 patients tapered off IS

TN-201 safety findings

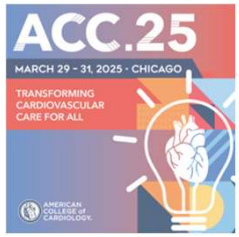
- ✓ No thrombotic microangiopathy TMA) or thrombocytopenia
- ✓ No signs of cardiotoxicities
  - o No signs of myocarditis
  - o No arrythmia-related adverse events
  - o Stable ejection fraction

On study events deemed unrelated to TN-201

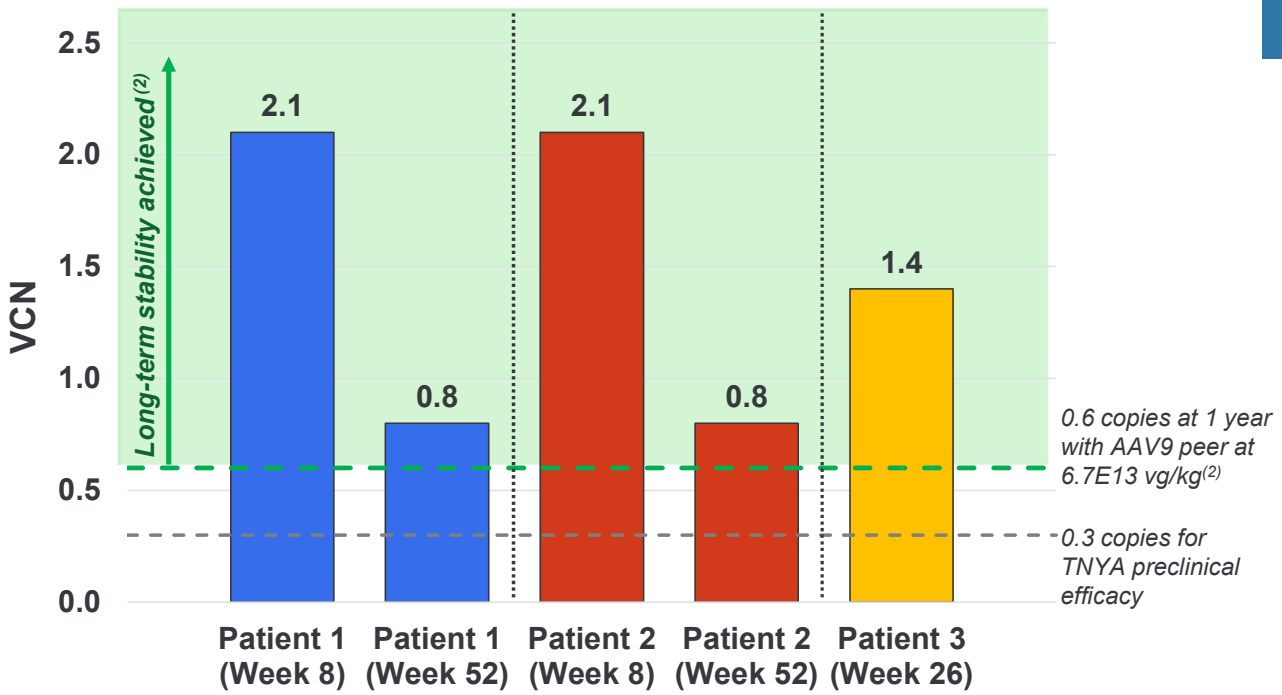
- ✓ Majority of treatment-emergent adverse events were mild, transient or reversible
  - o 2 SAEs unrelated to TN-201 occurred

AE = adverse event
IS = Immunosuppression
SAE = serious adverse event
TMA = thrombotic microangiopathy

TN-201 demonstrates robust and durable cardiac transduction at 3E13 vg/kg dose



TN-201 DNA in Cardiac Biopsy



TN-201 VCN surpasses preclinical efficacy threshold and compares favorably to peer

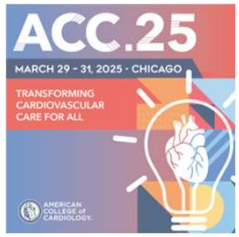
- TN-201 DNA not present at baseline as expected
- Patients 1 & 2 biopsies at Weeks 8 and 52 post-dose
- Patient 3 at Week 26; Week 52 forthcoming
- Consistent levels across patients
- TN-201 DNA remains in cardiomyocytes; cleared from non-cardiomyocytes over time

DNA= Deoxyribonucleic acid
VCN = vector copies/genome number

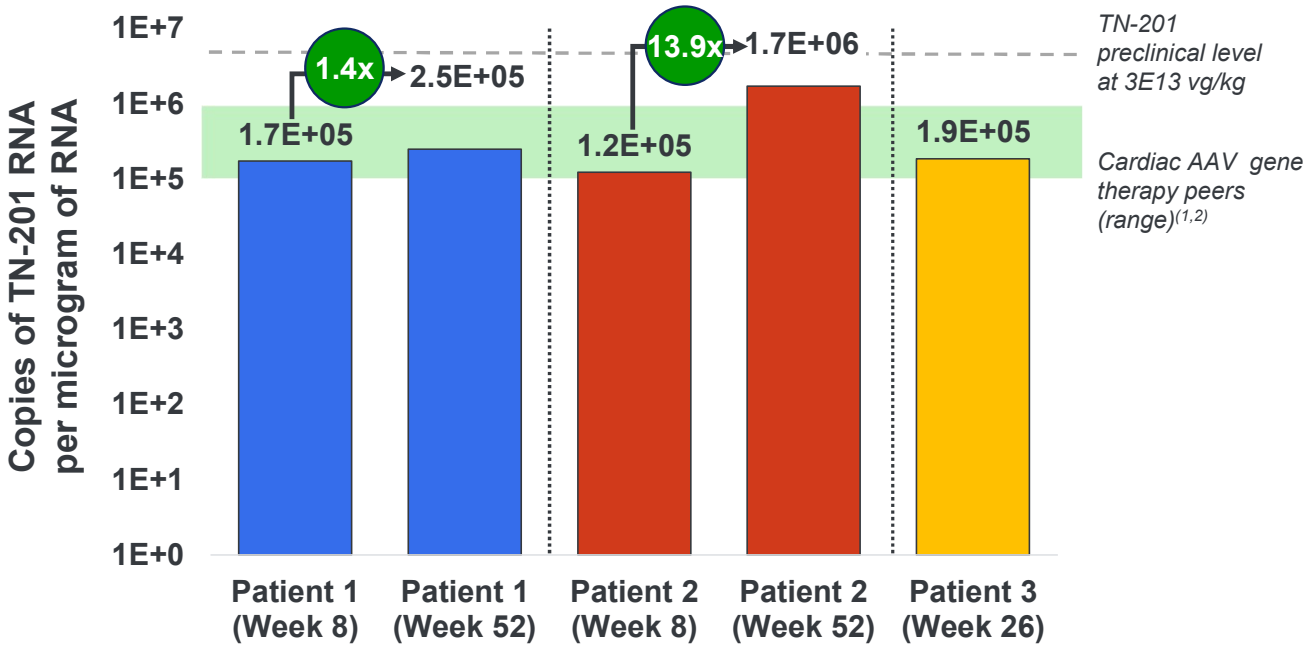
1. Desai, et al, ACC 2025
2. Greenberg, *NEJM* 2024

Comparison with other gene therapy programs is not intended to indicate likelihood of TN-201 clinical benefit

TN-201 RNA expressed in cardiomyocytes and continues to increases over time



TN-201 RNA in Cardiac Biopsy



TN-201 RNA expression increased by as much as 13-fold from week 8 to Week 52

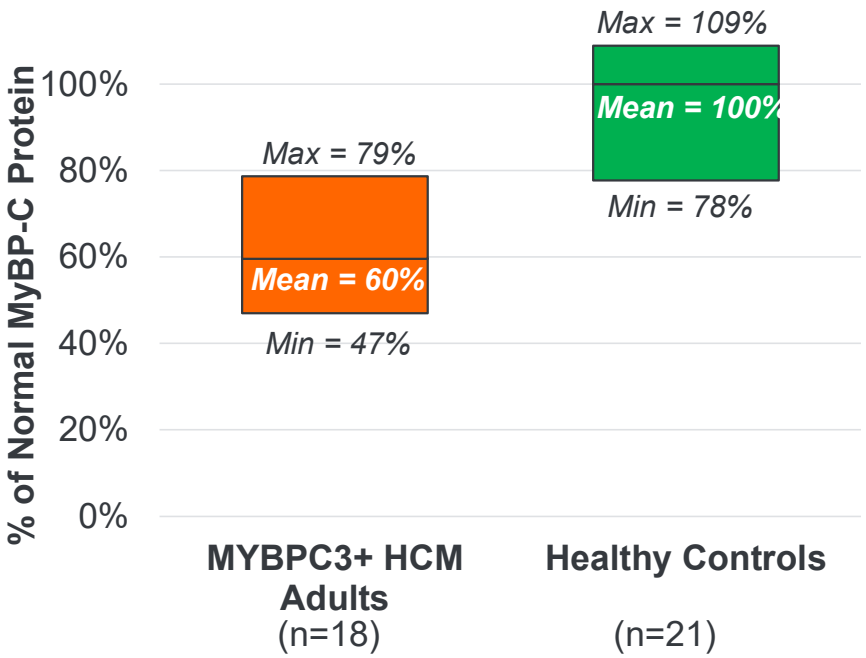
- Highly specific assay for TN-201 RNA
- Early TN-201 RNA expression observed that increases over time
  - May not yet be at steady state
- Within or above ranges observed in AAV cardiac gene therapy trials[1,2]

1. Greenberg, *NEJM* 2024; median number of mRNA transcripts per µg RNA from 6.7E13 vg/kg and 1.1E14 vg/kg patients at latest timepoint
2. Thomas, WORLD Symposium February 2024; n=1 patient at Week 26

Comparison with other gene therapy programs is not intended to indicate likelihood of TN-201 clinical benefit

MyBP-C protein levels vary between healthy and *MYBPC3*+HCM populations and between individuals

Range of MyBP-C protein levels in *MYBPC3*-associated HCM and healthy controls[1]



Treatment goal = Increase MyBP-C levels from patient's own baseline

- *MYBPC3*-associated HCM patients exhibit ~40% lower MyBP-C protein levels on average vs. healthy controls
- No apparent correlation between MyBP-C protein level and markers of disease severity; suggests differing sensitivity to protein levels on an individual basis

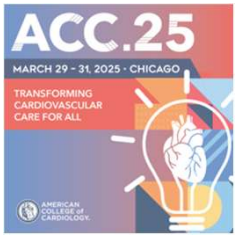
Treatment goal with cardiac gene therapy: Increase each individual's protein levels from their own baseline.

Modest restoration has achieved measurable benefit in other cardiac gene therapy clinical trials.

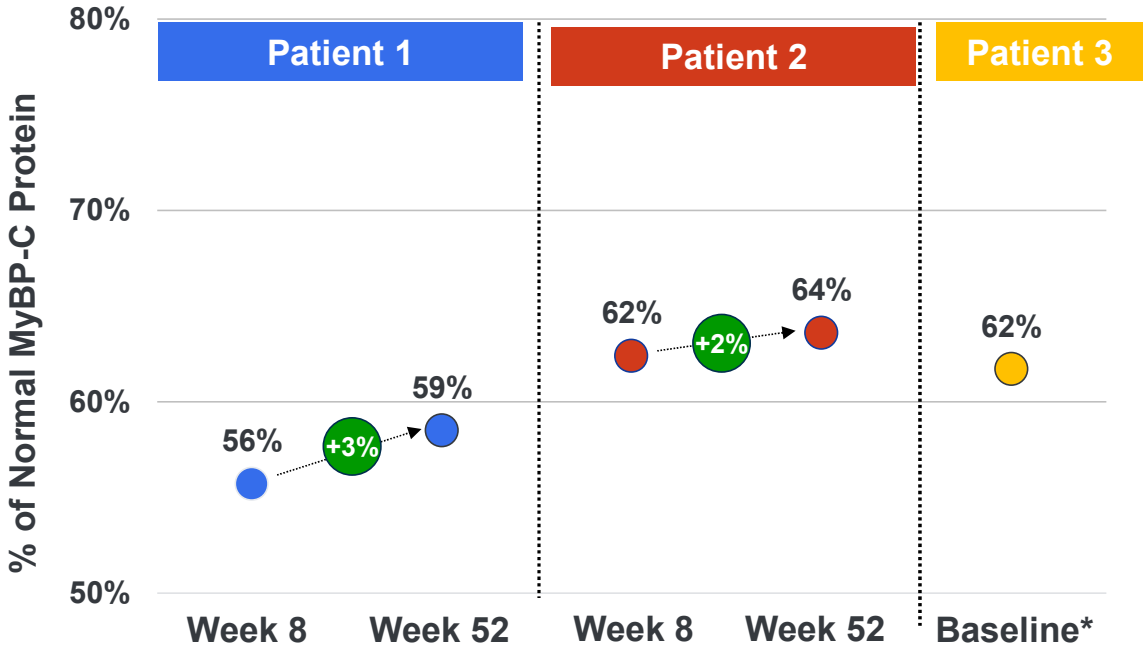
1. O'Leary, et al; *J Mol Cell Cardiol* 2019 (updated)

TN-201 treatment results in modest increase in MyBP-C protein levels

Changes in both mRNA and protein levels suggest TN-201 is being transcribed and expressed



MyBP-C Protein Compared to Healthy Controls



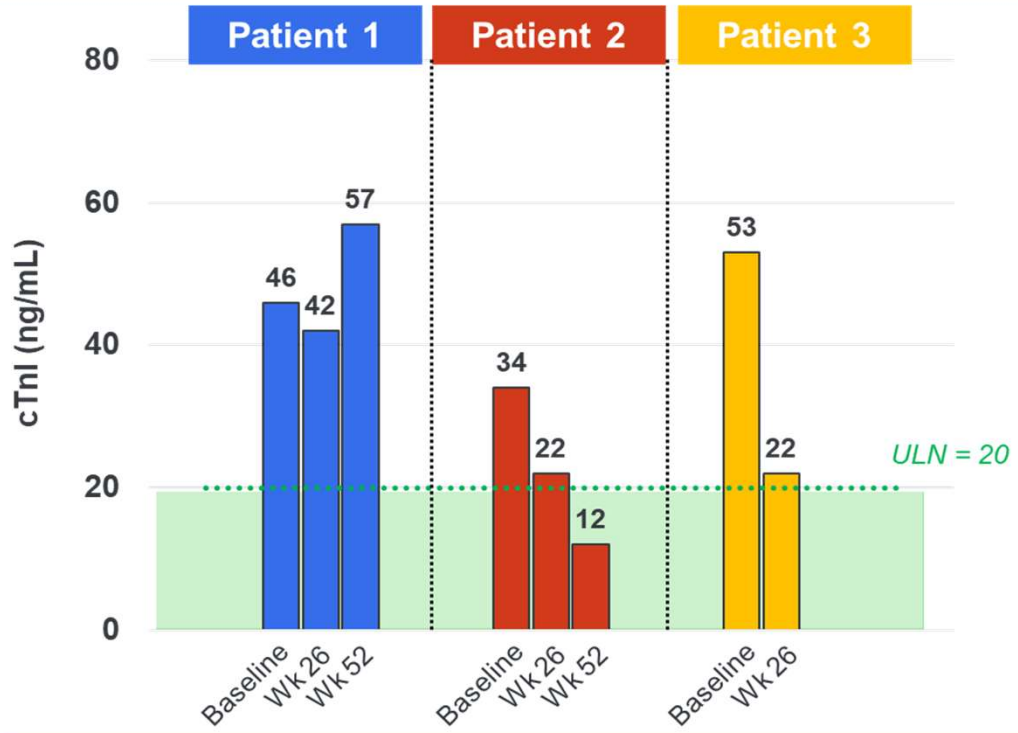
*Patient 3 Week 26 biopsy not evaluable due to low cardiomyocyte content in sample

Protein levels increase over time between 8- and 52-week biopsies

- TN-201-generated protein indistinguishable from endogenous
- Lack of baseline biopsies (per protocol) for Patients 1 & 2 limit ability to infer total MyBP-C increase
- Patient 3 has baseline, but Week 26 sample not evaluable. Will collect Week 52

Cardiac biomarkers improved or stabilized

Cardiac Troponin Levels



Interim Cohort 1 TN-201 Biomarker Results

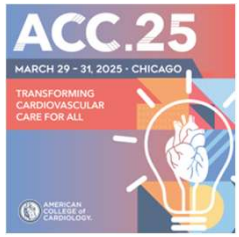
Cardiac troponin is a biomarker in the blood that indicates injury to heart cells; associated with increased risk of adverse events

- Cardiac troponin improved by ≥60%, to normal or near normal levels, in Patient 2 and Patient 3

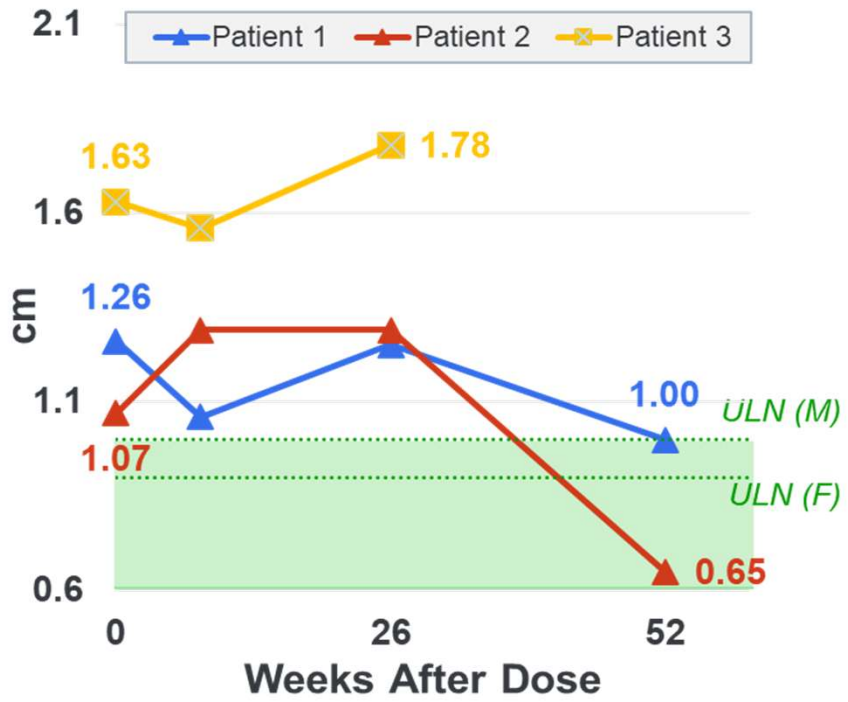
NT-proBNP (not shown) is a biomarker that indicates strain of the heart muscle

- NT-proBNP levels increased with IS, but stabilized to baseline or below as steroids were discontinued

Improvements observed in measures of hypertrophy



Posterior Wall Thickness

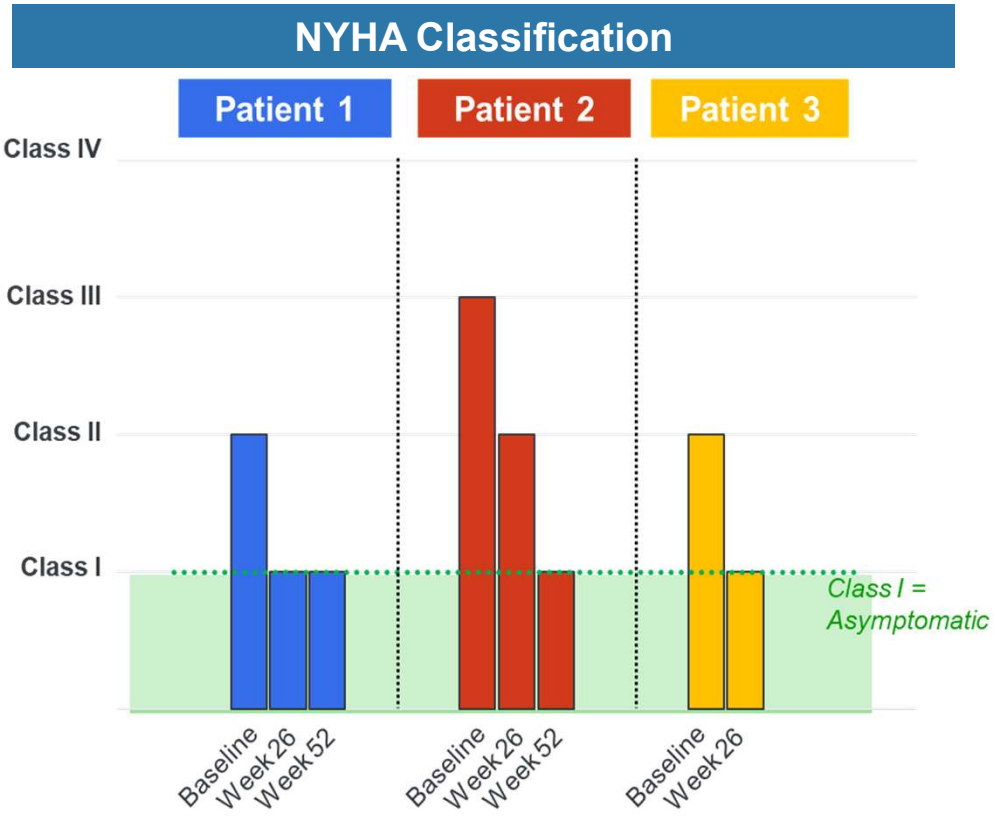


Interim Cohort 1 TN-201 Hypertrophy Results

Echo measurements of heart mass and thickness were taken to assess changes

- 2 of 3 patients saw improvements in one or more measures of hypertrophy
- Left ventricular posterior wall thickness decreased for Patient 1 and Patient 2 at 52 weeks
- Left ventricular mass index (not shown) decreased by >10% in Patient 2
- Other measures of hypertrophy, as well as diastolic function, remain largely stable

Symptoms of heart failure improved in all Cohort 1 patients

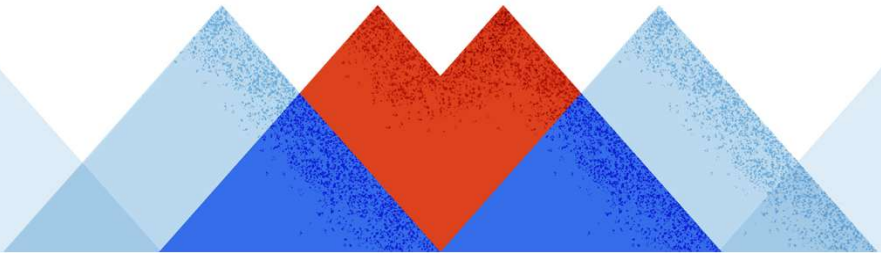


Interim Cohort 1 TN-201 NYHA Results

NYHA classification is used to categorize the severity of heart failure based on symptoms and physical activity

- Before treatment, all patients were symptomatic during ordinary physical activities (NYHA II-III)
- All patients improved to NYHA Class I by Week 26, indicating no limitation of physical activity

Future directions



TENAYA™ THERAPEUTICS

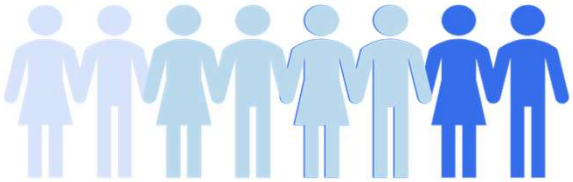
Plan to explore TN-201 in the full spectrum of patient presentation caused by *MYBPC3* mutations

Adults | **Adolescents** | **Peds** | **Infants**

Heterozygotes → **Homozygotes**

Non-Obstructive Phenotype (70%)

Obstructive Phenotype (30%)



TENAYA · GENE THERAPY · MyPEAK™-1

- Adults (18-65) with *MYBPC3* mutation
- Nonobstructive or obstructive HCM
- NYHA class II or III
- With or without ICD present
- NT-proBNP elevated
- Low AAV9 NAbs

Potential future expansion

MyClimb Natural History Study

- **MyPEAK-1 Cohort 1 enrolled nonobstructive HCM adult patients w/ ICDs**
- **Cohort 2+ expands population to obstructive or nonobstructive adults, with or without ICD**

- **MyClimb natural history study may serve as a run-in study and control arm for potential future Ph1/2/3 pediatric pivotal study**
- **> 220 patients have been enrolled across 29 sites**

TENAYA THERAPEUTICS

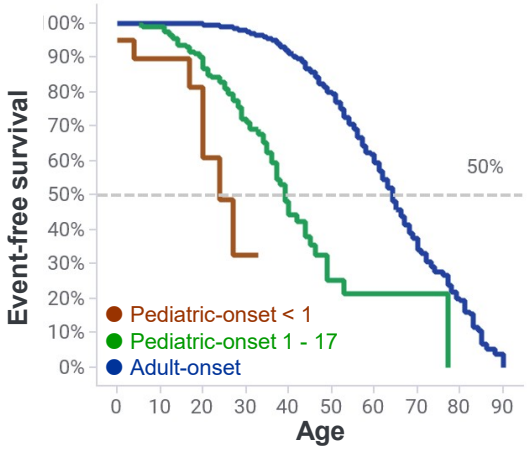
MYBPC3-associated pediatric patients represents sizable severe population lacking therapeutic options

Pediatric-onset patients experience a markedly greater disease progression and cumulative disease burden vs. adult-onset patients (1)

36% more likely to develop life-threatening ventricular arrhythmias(2)

2x more likely to require transplant or ventricular assist device (2)

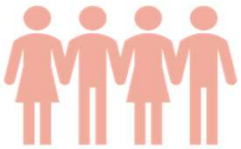
Time to event* since birth



* Event-free survival composite endpoint includes NYHA class III/IV, transplant, sudden cardiac arrest, atrial fibrillation, ICD firing, heart failure, stroke, death

TN-201 granted FDA **Rare Pediatric Disease Designation** for the treatment of *MYBPC3*-associated HCM in children, adolescents, and young adults

~3,000(3)
diagnosed < age 18
and currently < age 18



~13,000(3)
diagnosed < age 18
and currently ≥ age 18

~104,000(3)
diagnosed > age 18

TENAYA THERAPEUTICS

1. Meisner, et al, HCMS 2024
2. Marston, et al, *Eur Heart Journal* 2021
3. SHaRe registry; Data on file

TN-401 for *PKP2*-associated ARVC

PKP2-associated ARVC is estimated to affect >70,000 people in the U.S.[1]

A severe and progressive genetic heart disease lacking therapeutic treatment options

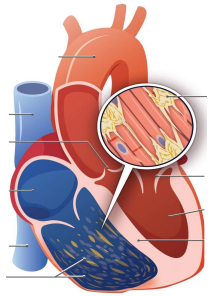
>15% of heart-related deaths in patients < 35 are due to ARVC[2]

23% of ARVC patients present with sudden cardiac death[2]

40% of ARVC patients carry pathogenic *PKP2* mutations[3]

- Early symptoms include palpitations, lightheadedness, fainting [1]
- Significant impact on quality of life due to arrhythmias, ICD shocks and restrictions on physical exertion [4]

ARVC HEART



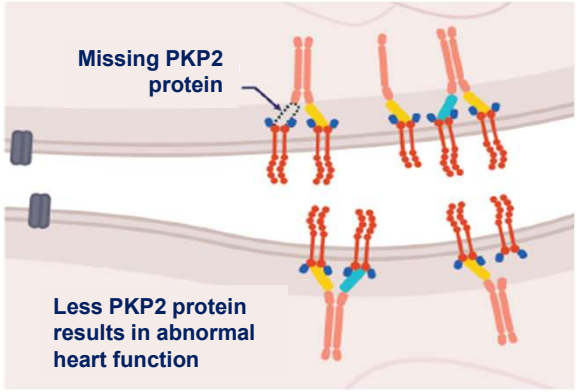
1. Peters, et a, Int J Cardiol 2004; McKenna, Nat Rev Card, 2021
2. Dalal, et al, Circ, 2005
3. Hemida, et al, Eur J Heart Failure, 2018
4. SADS Foundation

SCD= sudden cardiac death
RV = right ventricle
LV = left ventricle
ICD = implantable cardiodefibrillator

TN-401 gene therapy for *PKP2*-associated ARVC

Underlying problem

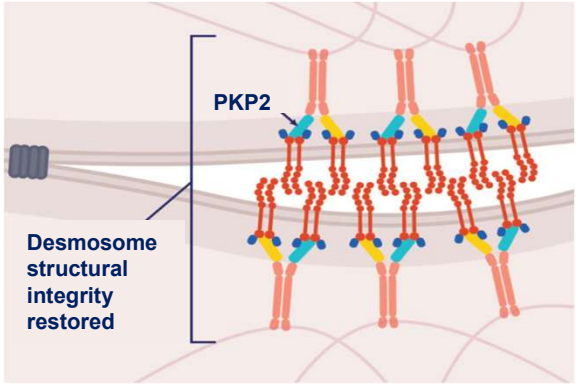
- Mutations of the *PKP2* gene lead to lower levels of Plakophilin-2 (PKP2) protein[1]
- PKP2 is an essential structural protein in the desmosomes, connecting cardiomyocytes supporting electrical and mechanical signaling and overall tissue strength



Desmosome and Gap Junctions in *PKP2*-associated HCM Heart

Tenaya Approach

- Target the underlying genetic cause of disease
- Deliver a working *PKP2* gene utilizing AAV9 capsid
- Increase PKP2 protein levels
- Potential to halt disease progression, reverse symptoms and improve patient quality of life



Treated with TN-401

1. McKenna, et al, Nature Rev Cardio 2021

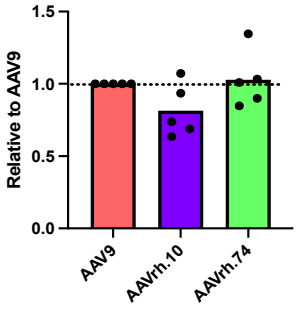
AAV9 capsid comes with robust validation from preclinical efficacy and clinical studies

Outperforms other serotypes in head-to-head preclinical models of mice and NHPs

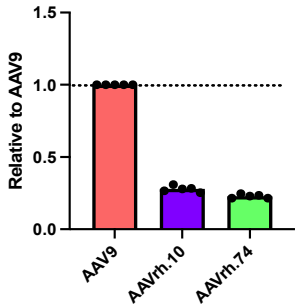
Mouse Model

Non-Human Primate Model

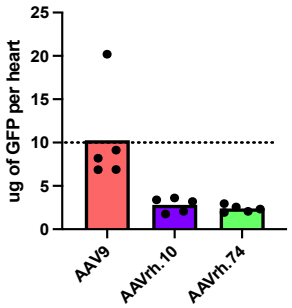
Viral DNA Transduction
All heart cells



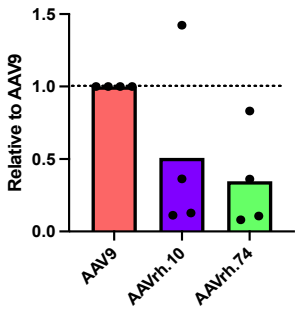
Viral RNA Transgene Expression
Cardiomyocytes only



Viral Protein Transgene Expression
Cardiomyocytes only



Viral RNA Transgene Expression
Cardiomyocytes only



AAV9 AAVrh.10 AAVrh.74

Cheng, ASGCT 2024

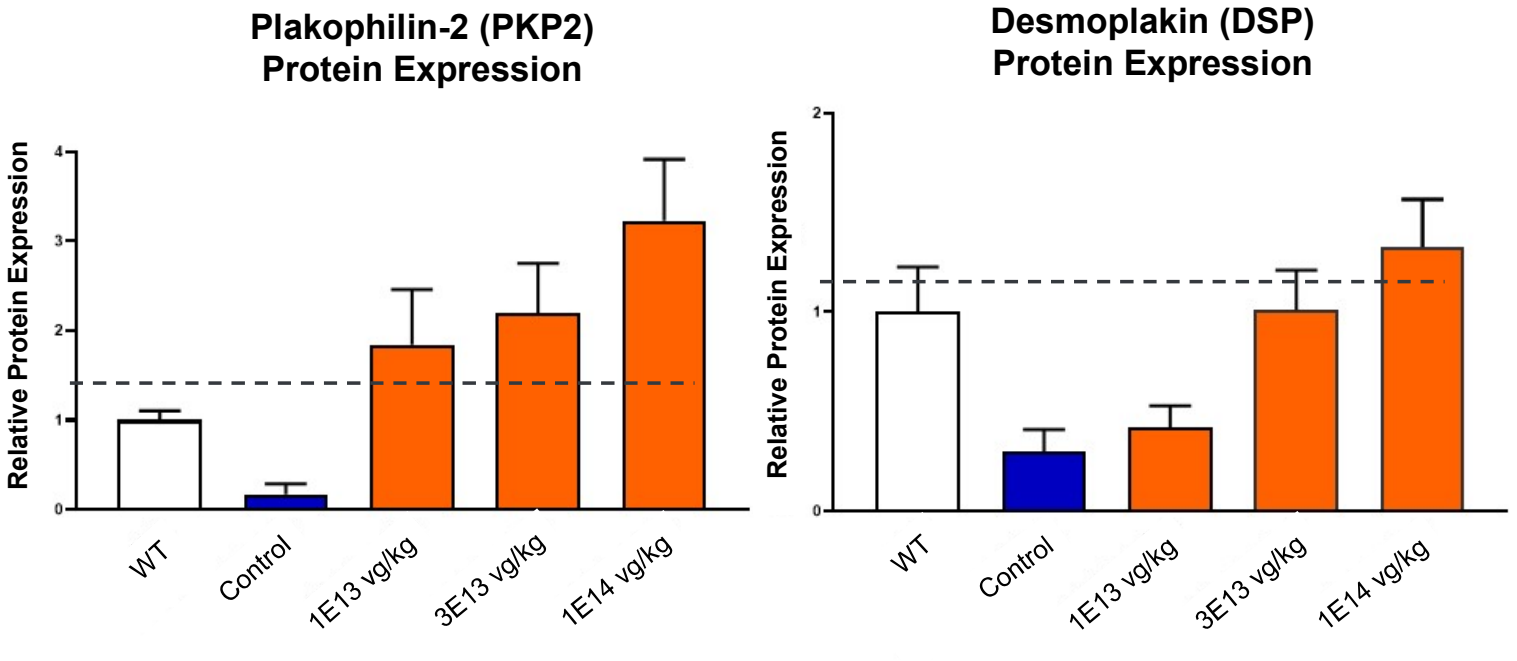
Most established clincial safety record of any capsid

AAV9 has been used in >4000 patients in >51 countries, with >9 years follow-up[1]

1. Novartis

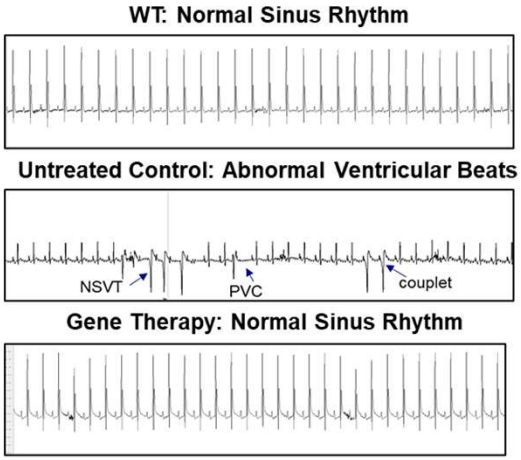
3E13vg/kg dose restored PKP2 and other desmosomal proteins to normal levels

***Pkp2*-cKO Mice**

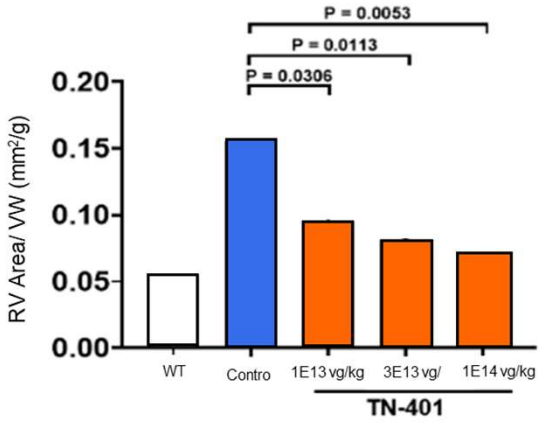


Single 3E13 vg/kg dose of TN-401 in preclinical KO mouse model reverses hallmarks of disease and extends survival

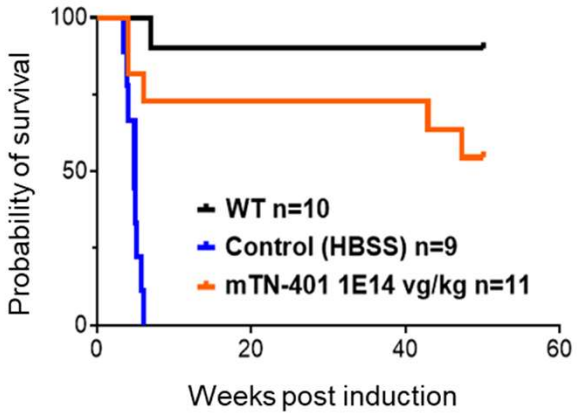
Reversal of arrhythmia



Reduction of RV enlargement



Improved survival



Yang, et al, ASGCT 2022

RIDGE-1 Phase 1b clinical trial for *PKP2*-associated ARVC

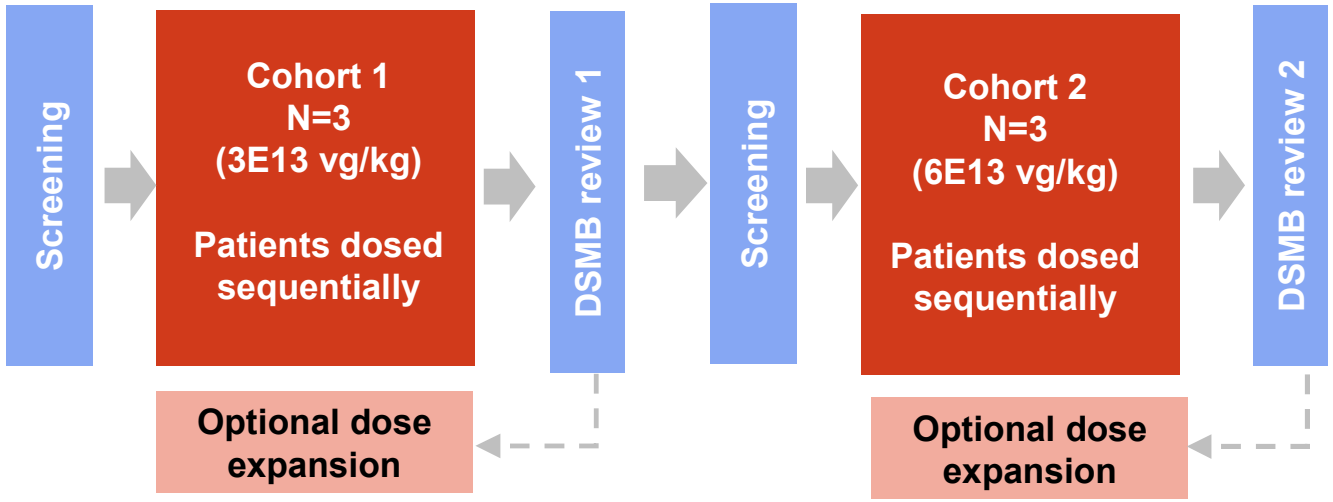
Initial Cohort 1 data anticipated in 2H'25

Study Objectives

- Safety and tolerability
- Dose-finding
- Pharmacodynamics

Design

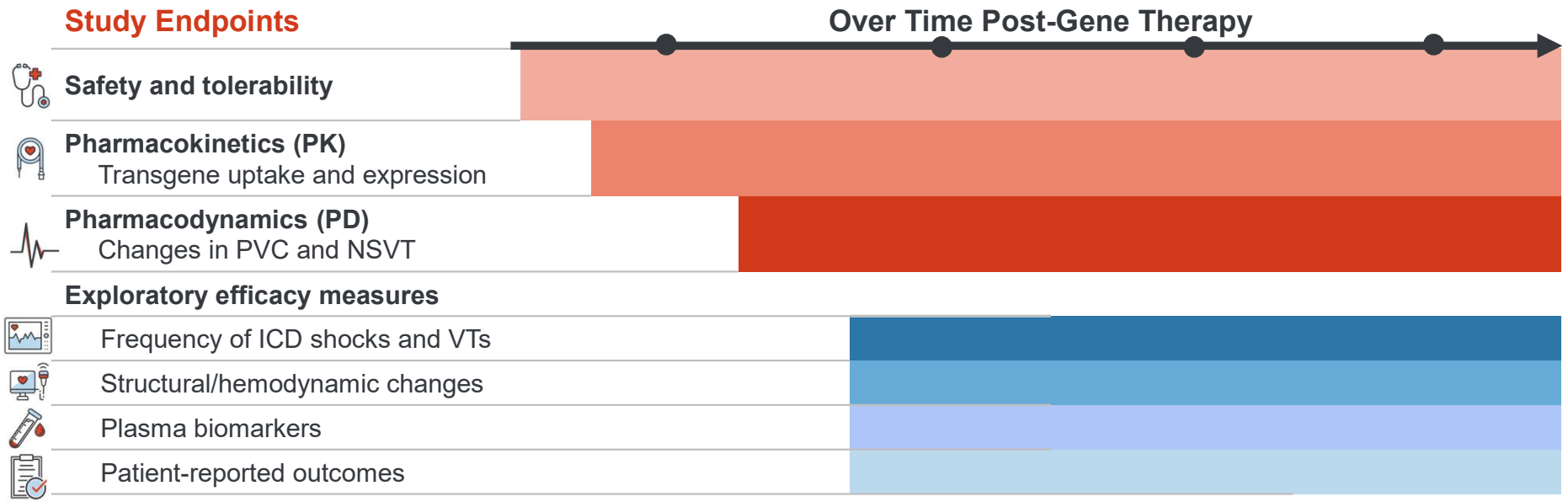
- Open-label, multi-center dose-escalation and dose-expansion
- 52-week study period with four-year follow-up
- Cardiac biopsies at baseline, post-dose and week 52



LVEF = left ventricular ejection fraction
PVCs = premature ventricular contractions

RIDGE-1 Phase 1b endpoints

Treatment goal: demonstrate reduction in arrhythmic events
Initial data in 2025 to include safety and biopsy results at low-dose



NSVT = non-sustained ventricular tachycardia
VT = Ventricular tachycardia

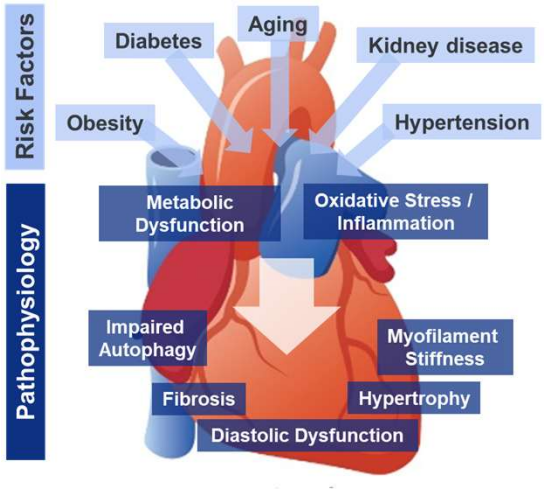
TN-301 HDAC6 inhibitor for HFpEF

TN-301 small molecule HDAC6 inhibitor for HFpEF

HFpEF remains the largest unmet need in heart disease estimated to affect >3M in the U.S. alone[1, 2]

- Characterized by diastolic dysfunction driven by stiffening of heart ventricles
- Initial presentation includes shortness of breath, edema, fatigue, coughing, wheezing, dizziness
- Co-morbidities include obesity, metabolic syndrome, diabetes hypertension, atrial fibrillation, pulmonary disease, and renal dysfunction[3]
- 75% of people hospitalized with HFpEF die within 5 years[4]

- Multiple contributing risk factors resulting in complex pathophysiology



HDAC6 = histone deacetylase 6

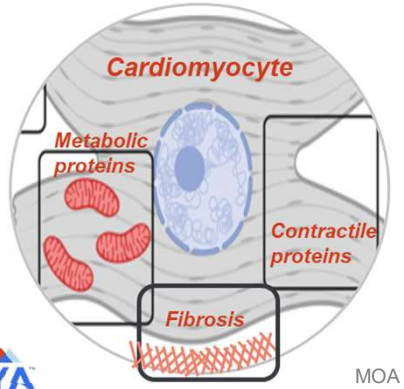
1. Cilia et al, *Am J Lifestyle Med* 2019
2. Tsao, et al *Circulation* 2023
3. Van Heerebeek, et al. *Neth Heart Jour* 2016
4.Shah, et al, *JACC* 2017

TN-301 small molecule HDAC6 inhibitor for HFpEF

Phase 1 complete; Optimally suited for development by/with a partner

About HFpEF

- Disease driven by multi-factorial processes involving many cell types and cellular structures:
  - Inside heart: cardiomyocytes, fibroblasts, mitochondria, sarcomeres, arterial walls
  - Outside heart: systemic inflammation, oxidative stress, metabolic dysregulation



Tenaya Approach

- Designed to specifically inhibit HDAC6 in the cytoplasm of heart cells
- Multi-modal MOA addresses diverse HFpEF pathophysiological processes
- Preclinical evidence of robust direct (e.g., hypertrophy, stiffness) and systemic benefits (e.g., inflammation, metabolic)

Key Advantages

- High selectivity (1000x fold) offers potential safety advantage vs. partially selective HDAC6 inhibitors
- MOA is orthogonal to other heart medicines (e.g. SGLT2 inhibitors) and may yield additive benefits
- PD marker of target engagement conveniently measurable in human plasma
- Small molecule cost of goods appropriate for large indications

HDAC6 is a cytoplasmic enzyme that regulates diverse cellular processes in many different types of cells of the body

MOA = mechanism of action
SGLT2 =sodium glucose cotransporter-2

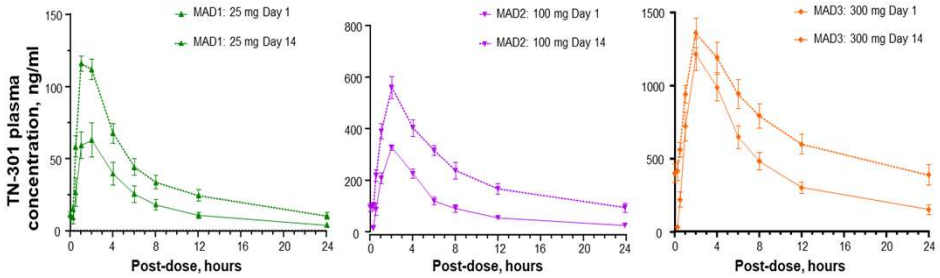
Completed Phase 1 trial of TN-301 in healthy participants

TN-301 was generally well tolerated across broad dose ranges

- SAD (1mg – 700mg) and MAD (25mg, 100 mg, 300 mg for 14 days)
- Most AEs were GI related; occurred with similar frequency in placebo group and did not increase with dose

Potential for once-daily dosing

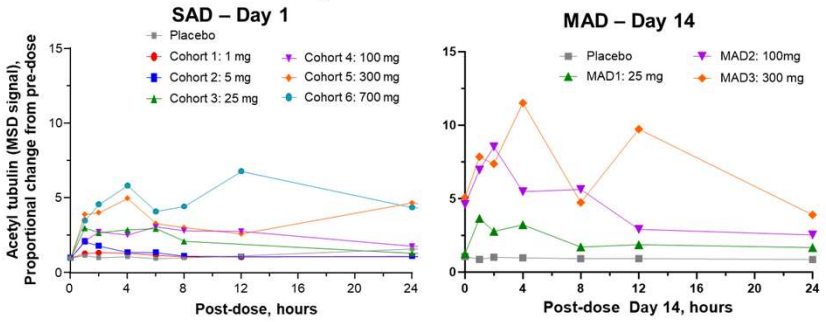
Mean (SEM) plasma TN-301 concentration over time (MAD)



Plasma exposure increased proportionally with TN-301 dose across ranges evaluated

Target engagement seen at low doses

Mean acetylated tubulin levels over time



Variability (SEM) in acetylated tubulin levels ranged from 0.038 to 1.410 (SAD results); and 0.067 to 4.050 (MAD results)

Increasing TN-301 exposure correlated with PD effect

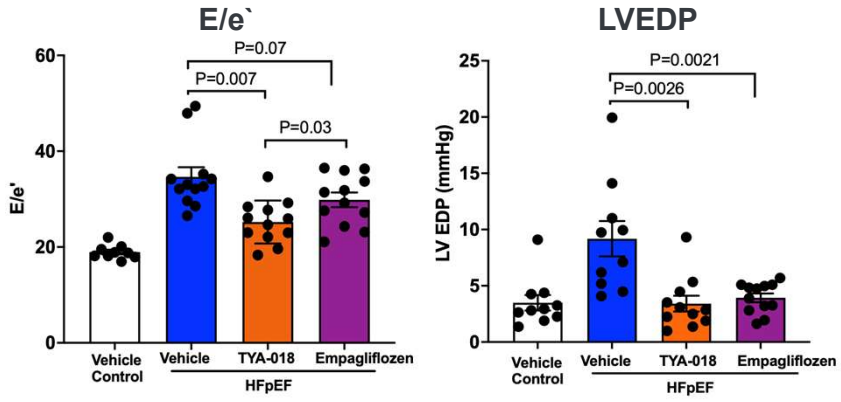
SAD= Single ascending dose
MAD = Multiple ascending dose
AEs = Adverse events
GI = gastrointestinal

HDAC6 inhibitor demonstrates preclinical potential for use as single-agent or in combination with SGLT2 inhibitor

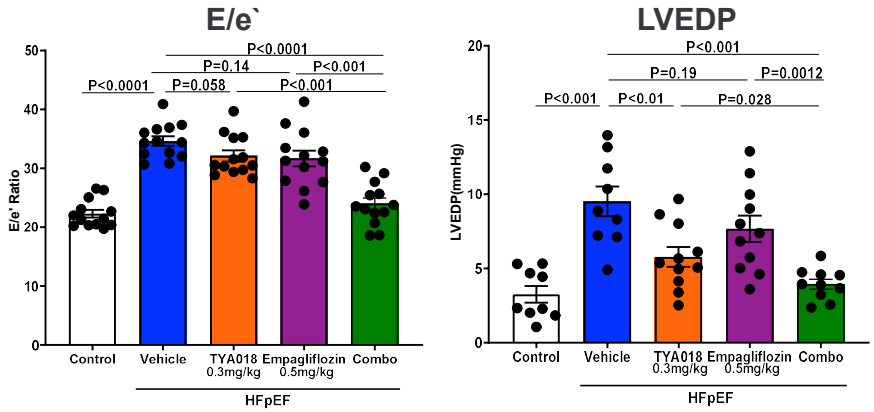
Comparable efficacy as a single agent

Additive efficacy in combination

HDAC6 vs. SGLT2[1]



HDAC6 + SGLT2[2]



HDAC6 inhibitor demonstrates greater impact vs. SGLT2 inhibitor on improving metabolism, oxidative stress and inflammation

E/e' = measure of diastolic function
LVEDP = left ventricular end diastolic pressure

1. Yang, et al; ESC-HF 2022
2. Farshidfar, et al; HFSA 2023

TENAYA™ THERAPEUTICS

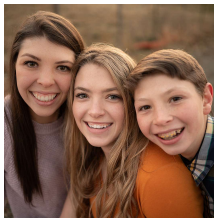
Capabilities

Modality-agnostic target and drug discovery that aims to address the underlying problem







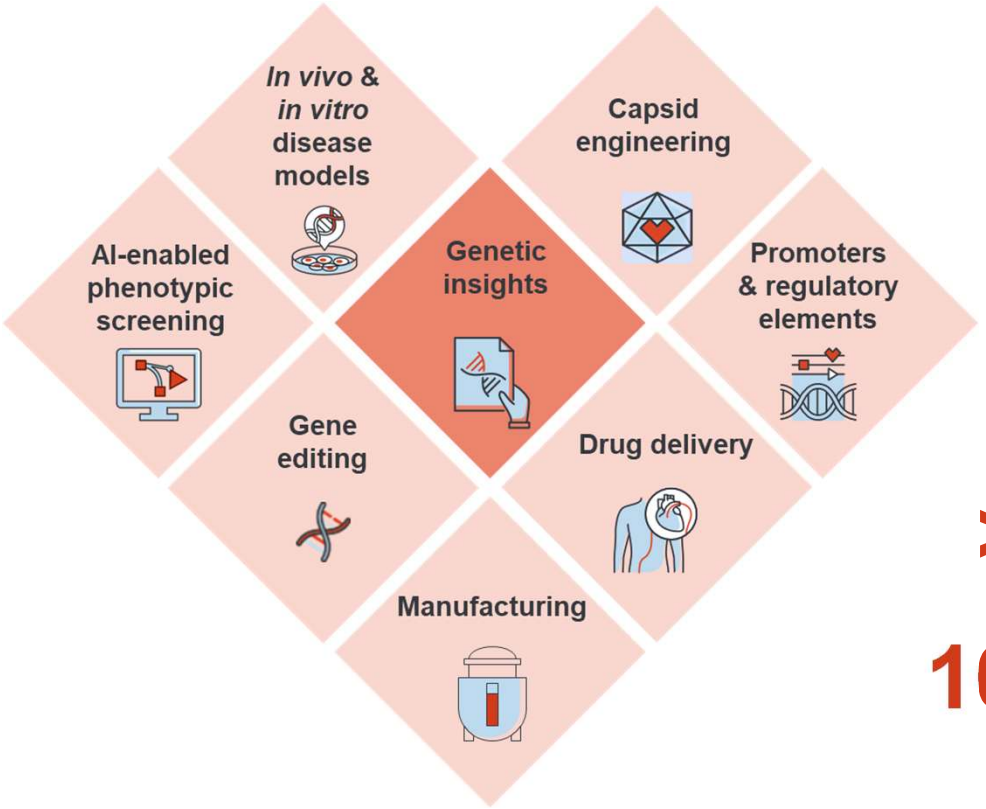


	HCM	ARVC	HFpEF	DCM	MI	HFrEF	DCM
Underlying problem	*MYBPC3* mutation	*PKP2* mutation	Multi-factorial	*PLN*^{R14del} mutation	Loss of heart cells	Decrease in SERCA2a	Unknown mutation(s)
Tenaya approach	Gene transfer	Gene transfer	Small molecule	Gene editing	Cellular regeneration	DWORF addition	Target identification using AI and iPSCs
	TN-201	TN-401	TN-301				

Clinical-stage programs → ← **Select early-stage programs** →

MI = myocardial infarction
PLNR14del = phosolambam deletion of arginine at amino acid residue 14
SERCA2a = sarcoplasmic reticulum (SR) calcium-ATPase
DWORF= dwarf open reading frame
DCM = dilated cardiomyopathy
AI = artificial intelligence

Proprietary internal capabilities and know-how generating differentiated, next-gen assets



>1B Novel cardiac-tropic AAV capsids, cardiac-specific promoters and regulatory elements screened to identify components that meaningfully out-perform existing options

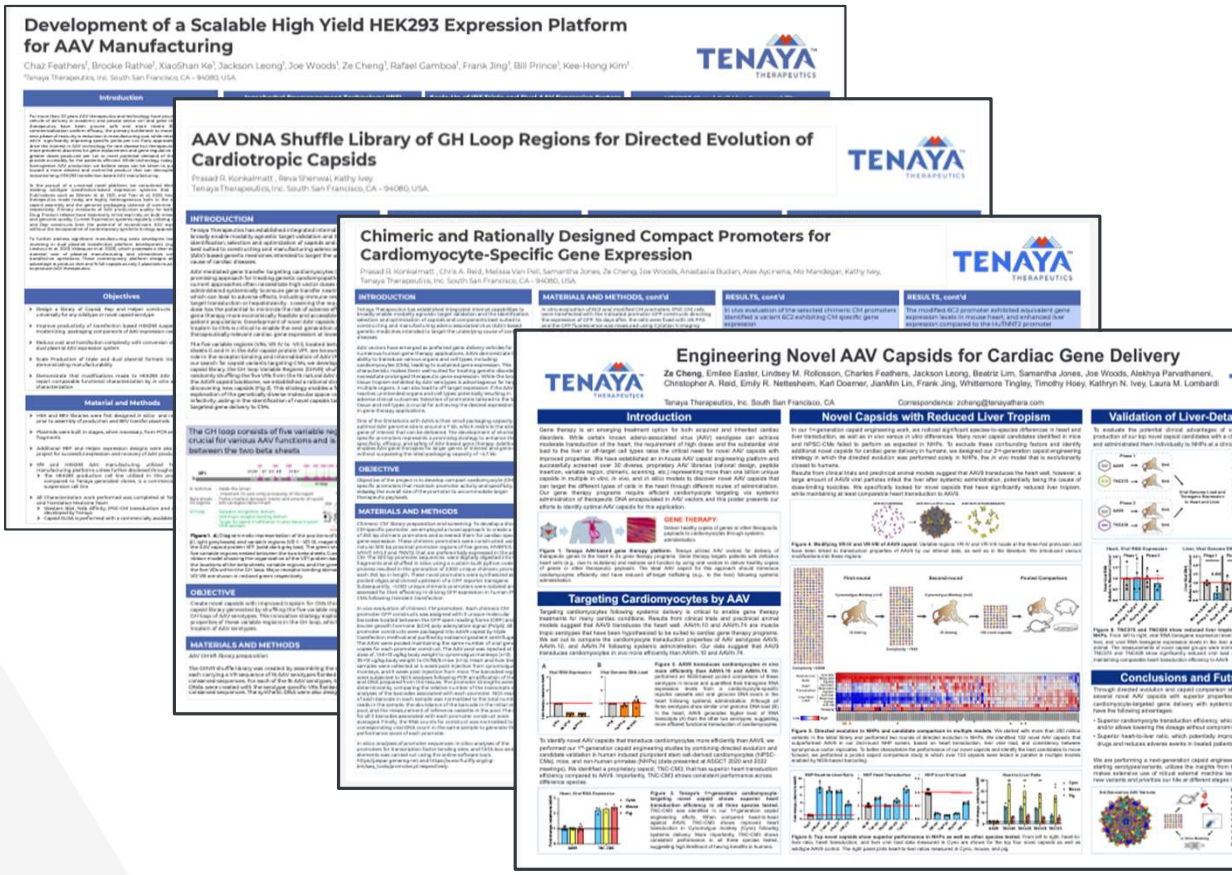
>50 In-house *in vivo* and *in vitro* models to support rapid drug discovery

>140 Genetically validated leads generated from target identification and validation engine

1000L cGMP AAV manufacturing scale achieved; clinical supply for TN-201 and TN-401 ready

Tenaya's capsid engineering and manufacturing know-how are building on AAV's success

- Capsid engineering efforts resulting in novel capsids with improved heart:liver tropism
- Cardiac-specific promoters and regulatory elements enable robust expression of target gene in the heart
- AAV manufacturing processes that scale from shake flask to 1000L



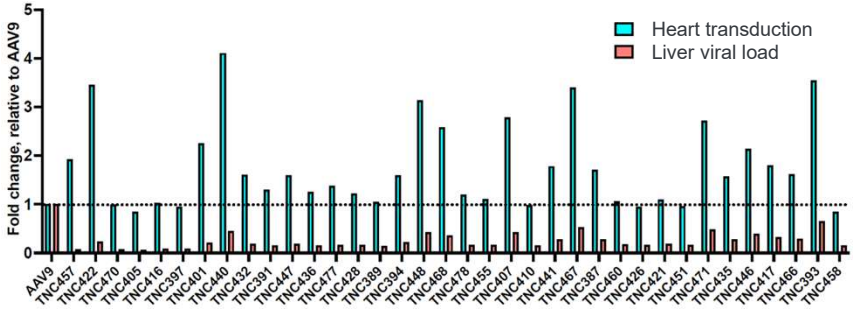
Next generation AAV capsid engineering efforts aimed at enhanced efficacy and safety

Focused AAV Screening Efforts Using Multiple Strategies

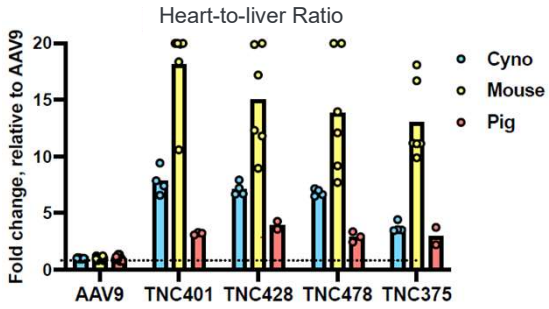
- Screened > 1B variants from ~30 diverse libraries
- Validated *in silico, in vitro* and *in vivo* (4 species)
- Multiple criteria
  - ↑ heart transduction
  - ↓ liver transduction
  - ↔ antigenicity
  - ↔ manufacturability

Novel AAV Capsids for Heart that **Outperform** Parental Vectors

2nd generation novel capsids demonstrate reduced trafficking to the liver in NHPs vs. AAV9



Top novel capsids show improved heart-to-liver ratio across 3 species



Chen, et al; ESGCT 2022

2nd Generation Capsid Characteristics

- ☑ Superior heart transduction → may lead to **more efficacious therapy**
- ☑ Superior liver de-targeting → may **improve the safety profile**
- ☑ Superior NAb evasion → may enable treatment of a **greater number of patients**

NHP = Non-Human Primate | NAb = neutralizing antibodies

TENAYA™ THERAPEUTICS

2025 Milestones

Anticipated 2025 milestones

	1H'25	2H'25	2026+
TN-201			
MyPEAK-1	✓ **Present additional Cohort 1 data** • Complete Cohort 2 enrollment	• **Provide Cohort 1 data update & present initial Cohort 2 data**	• **1H'26: Present two-year Cohort 1 and one-year Cohort 2 data** • Pursue regulatory alignment on pivotal studies • Initiate pediatric pivotal study
MyClimb	• Present initial data		
TN-401			
RIDGE-1	• Complete Cohort 1 enrollment • Ex-US expansion	• **Cohort 1 initial data** • Cohort 2 and/or expansion cohort enrollment	• **1H'26: Present one-year Cohort 1 data and early Cohort 2 data** • Pursue regulatory alignment on pivotal study
RIDGE	• Present additional data		

Cash and equivalents sufficient to fund operations into 2H'26 – beyond longer-term data readouts for MyPEAK-1 and RIDGE-1 trials

Based on $61.4M* as of YE'24 + $49M financing in March'25
*Tenaya has not drawn on the $45M credit facility put in place in Q3'24

Thank you