Scaling new heights in the fight against heart disease

January 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 2024 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; the timing of initial dosing for 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," "believe," "expected," "plan," "potential," "may," "future," "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 a number of risks, uncertainties and assumptions described in our filings with the SEC, including, but not limited to the section titled "Risk Factors" in our Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2024, and other documents we have, or will file with the SEC. These filings, filed, are 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.

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

Unparalleled cardiology, genetics and rare disease expertise

Foundational capabilities fueling innovation and early-stage research

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 MyClimb 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 RIDGE™ 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

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 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

Initial MyPEAK-1 Cohort 1 data derisks safety; reaffirms AAV9 as capsid of choice

1. **Safety: TN-201 well tolerated; safety profile is consistent with other gene therapies**
   - No cardiotoxicities
   - Liver enzyme elevations manageable and reversible
   - DSMB endorsed dose escalation

2. **Biopsy: TN-201 reaches heart cells and achieves expression**
   - Robust cardiac transduction that exceeds expectations
   - Durable and increasing mRNA expression over time
   - Protein levels modestly higher from 8 to 52 weeks

3. **Clinical Endpoints: Encouraging, but early**
   - Stability—and improvement—seen in certain parameters; further follow-up needed

AAV9 = adeno-associated virus serotype 9 | DSMB = data safety and Monitoring Board | mRNA = messenger ribonucleic acid |

Significant clinical progress in 2025 and beyond

	1H'25	2H'25	2026+
TN-201			
MyPEAK-1	• **Present addl Cohort 1 data** • Complete Cohort 2 enrollment	• **Provide Cohort 1 & 2 data update**	• Present longer-term Cohort 1 & 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 2 enrollment • **Cohort 1 initial data**	• Present longer-term Cohort 1 & 2 data • Pursue regulatory alignment on pivotal study
RIDGE	• Present additional 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

"Accelerated approval will be 'the norm' for gene therapies, FDA's Peter Marks says"
- Endpoints(4)

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1. FDA Draft Guidance for heart failure; for cell and gene therapies
2. Tufts NEWDIGS FoCUS Project
3. FDA; EMA
4. Endpoints News, Feb. 27, 2024

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





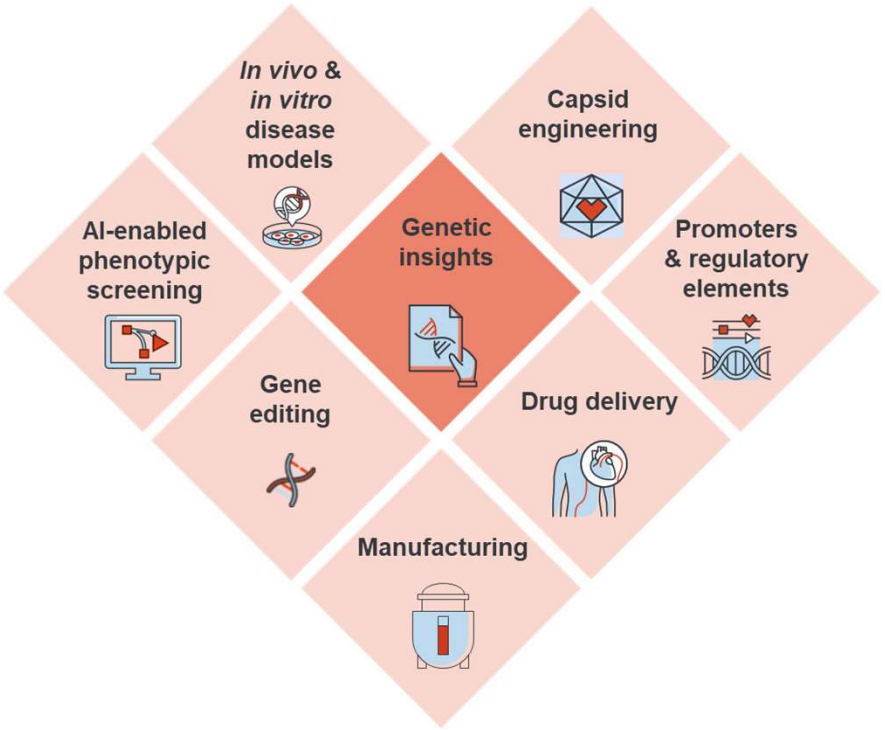


	HCM	ARVC	HFpEF	DCM	MI	HFrEF	DCM
Underlying problem	*MYBPC3* mutation	*PKP2* mutation	Multi-factorial	*PLN*^{R14del} mutation	Loss of heart cells	Decrease in SERCA2a	Unknown mutation(s)
Tenaya approach	Gene transfer	Gene transfer	Small molecule	Gene editing	Cellular regeneration	DWORF addition	Target ID via AI-enabled screens of heart cells
Tenaya programs	TN-201	TN-401	TN-301	← Preclinical efforts →			

MI = myocardial infarction | PLN delR14 = phosolambam deletion of arginine at amino acid residue 14 | SERCA2a = sarcoplasmic reticulum (SR) calcium-ATPase
DWORF= dwarf open reading frame | DCM = dilated cardiomyopathy | MI = myocardial infarction | AI = artificial intelligence

Proprietary capabilities fuel deep modality agnostic pipeline addressing rare and prevalent conditions

Internalization and integration of capabilities have generated rich collection of differentiated assets



~9 Early-stage programs addressing rare & prevalent conditions with gene therapy or gene editing

>1B Novel cardiac tropic AAV capsids and 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™ THERAPEUTICS

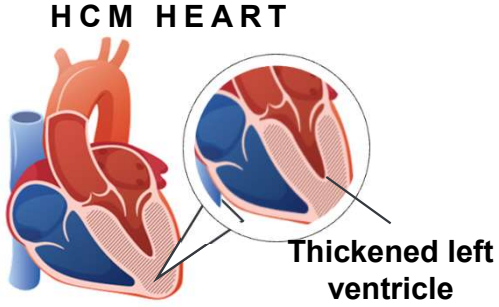
TN-201 for *MYBPC3*-associated HCM

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

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

~57% of identified genetic variants underlying familial HCM are *MYBPC3* mutations (1)

>30% of genetic variants underlying childhood-onset HCM are *MYBPC3* mutations (2)

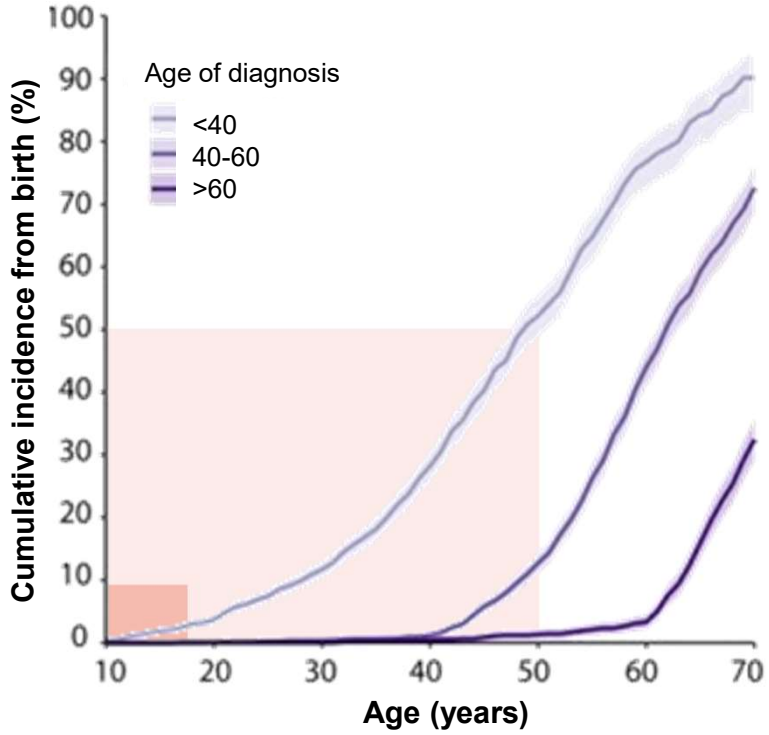


- Significant functional impairment
- Social and psychological impacts
- Symptoms include shortness of breath, fainting, chest pain, fatigue, palpitations, arrhythmias
- Elevated risk of sudden cardiac death and heart failure

1. Ho, et al, *Circulation* 2018
2. Marston, et al, *Eur Heart Jrnl* 2021

Patients with genetic forms of HCM are at higher risk for serious cardiac events(1)

Younger onset correlates with higher risk of morbidity and mortality



39 vs. 51 **Media age of diagnosis** for genetic forms of HCM vs. non-genetic forms (1)

2x **Greater risk of adverse outcomes** with sarcomeric mutations such as *MYBPC3* (1)

50% of patients with genetic forms of HCM diagnosed **before the age of 50** are likely to experience a **life-threatening** cardiac event(1)

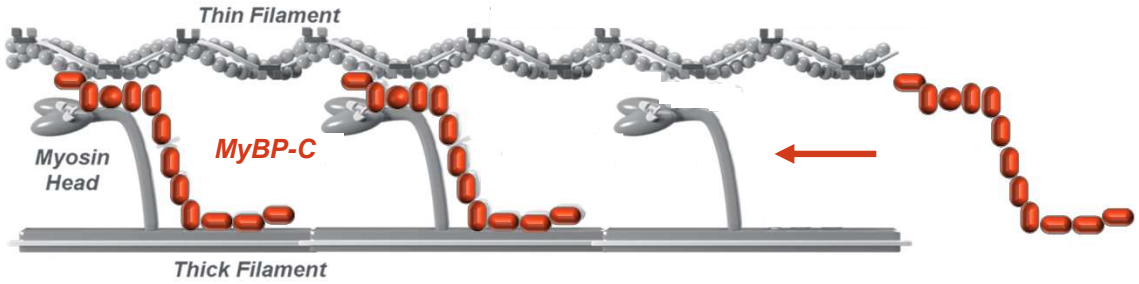
Adverse/life-threatening outcomes include: heart failure, defibrillator implantation, ventricular arrhythmias, atrial fibrillation, transplantation, cardiac arrest/death and stroke

1. Ho, et al, *Circulation* 2018

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

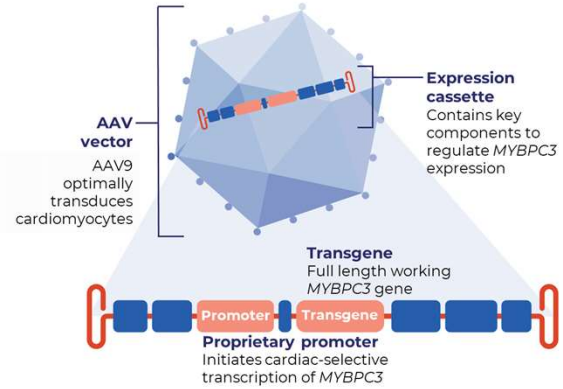
Underlying Problem

- Mutations of the MYBPC3 gene lead to lower levels of myosin-binding protein C (MyBP-C)
- MyBP-C is an essential structural protein required to regulate the binding of myosin and actin in sarcomere
- Lower MyBP-C protein results in increased cardiac contractility (hypertrophy), thickening of left ventricle and impaired diastolic relaxation



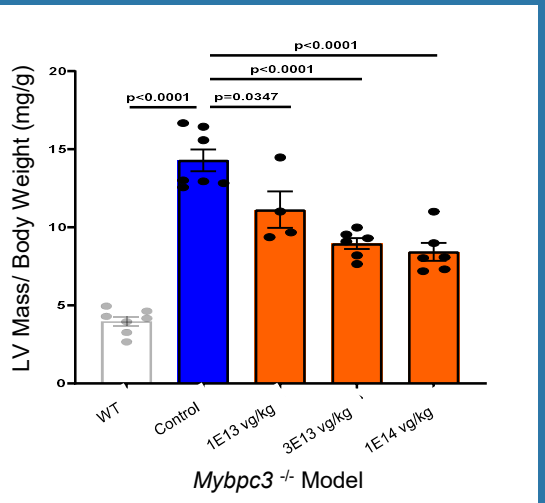
Tenaya Approach

- Target the underlying genetic cause of disease
- Deliver a working *MYBPC3* gene utilizing AAV9 capsid
- Produce functional protein to increase MyBP-C levels
- Potential to halt disease progression, reverse symptoms and improve patient quality of life

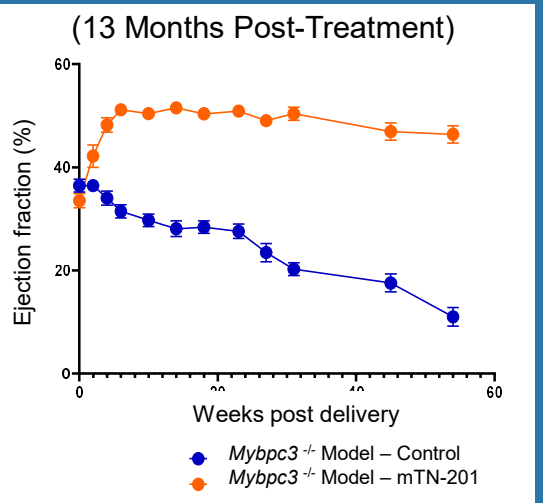


Single 3E13 vg/kg dose of TN-201 in preclinical KO mouse model reversed disease and increased survival

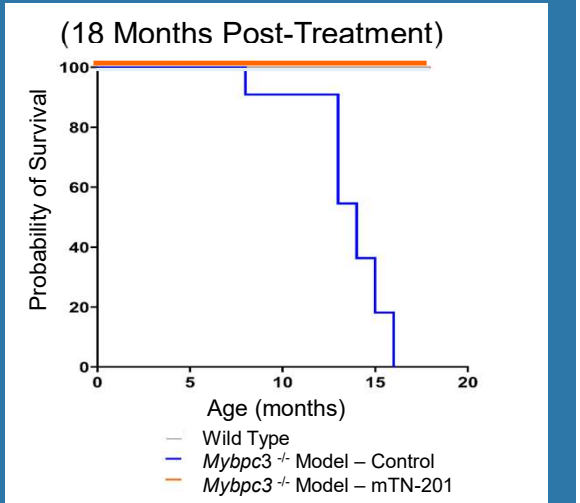
Reduced heart mass



Improved heart function



Extended survival



mTN-201 = mouse analog | LV = left ventricular

Lombardi, et al, ASGCT 2021

MyPEAK-1 Phase 1b/2 clinical trial design

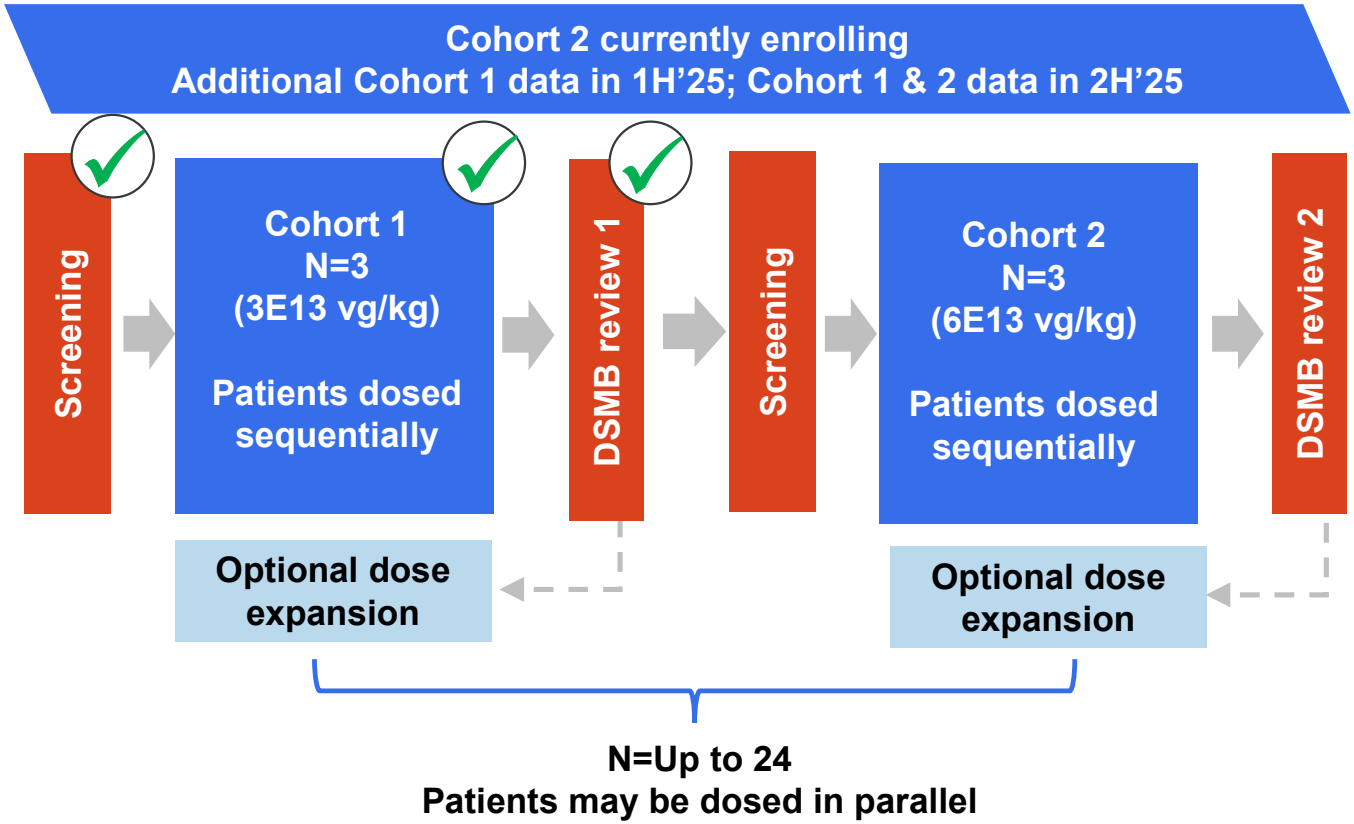
Open-label, multi-center dose escalation and expansion trial

Study Objectives

- Safety, tolerability
- Dose-finding
- Pharmacodynamics

Design

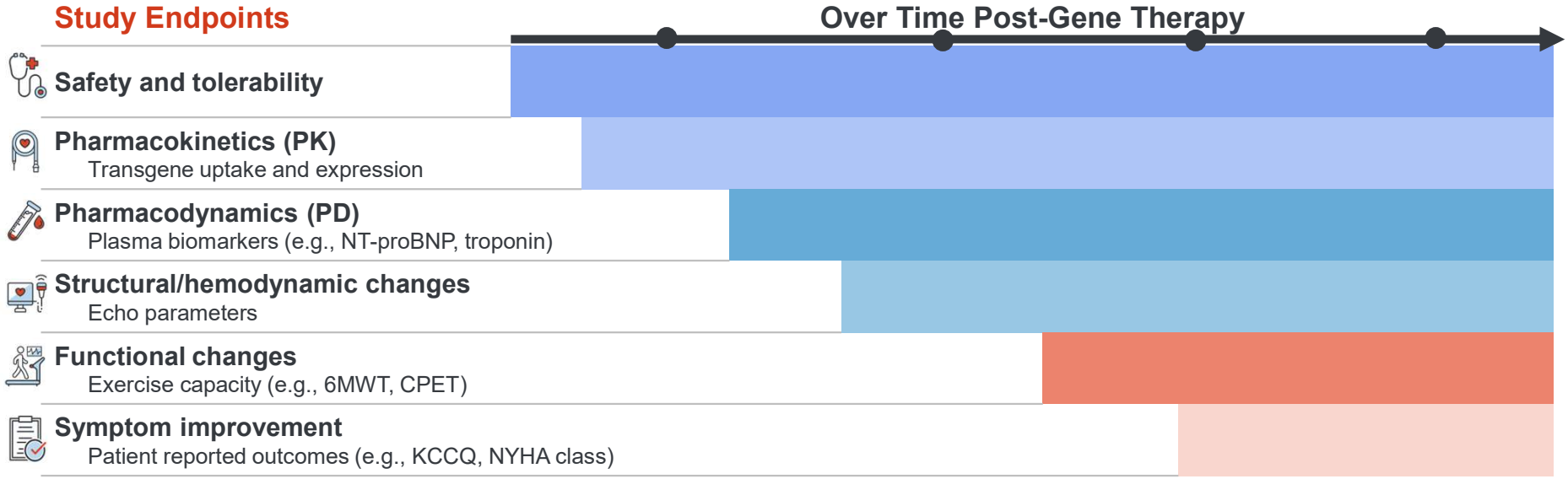
- Open-label, multi-center, dose-escalation and dose-expansion
- 52-week trial period with four-year safety and efficacy follow-up
- Cardiac biopsies at baseline, post-dose and ~52 weeks (effective with Cohort 1, patient 3)



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



mRNA = messenger ribonucleic acid | NT-proBNP = N-terminal pro–B-type natriuretic peptide
CPET = Cardiopulmonary exercise testing | 6MWT = 6-minute walk test | KCCQ = Kansas City Cardiomyopathy Questionnaire

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

Typical for HCM	Abnormal for HCM	Very abnormal for HCM

	Average HCM Patient	Patient 1	Patient 2	Patient 3
Length of Follow-Up	-	12 months Biopsy at 8 & 52 weeks	9 months Biopsy at 8 weeks	3 months Biopsy at baseline
Gender	Male (63%)[1]	Female	Female	Male
Current Age (years)	50[1]	27	43	47
ICD Implantation (years)	21% with ICD[1] Average age 38[2]	27	37	36
Myectomy Age (years)	18% with myectomy[3] Average age 54[4]	24	30	39
NT proBNP (pg/ml)	563[5]	1836	732	1229
Cardiac Troponin I (ng/L)	27[6]	46	34	53
LVMI (g/m^2)	Female: 89 | Male: 104[7]	174	105	177
NYHA Class	50% ≥ Class II[8]	II	III	II

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

ICD = implantable cardio defibrillator | LVMI = left ventricular mass index

TN-201 was generally well tolerated

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

TN-201 related-events

Reversible elevated liver enzymes occurred in all patients, normalized in response to steroid treatment

Patient 1	**Grade 3 AE at Week 15** Mitigated for subsequent patients by increased monitoring throughout IS tapering
Patient 2	**Grade 1 AE at Week 1**
Patient 3	**Grade 1 SAE at Week 2** Mild elevations classified as SAE because steroids administered in hospital
Patients 1 & 2 completed IS regimen; Patent 3 tapering	

Summary of TN-201 safety findings

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

On study events deemed unrelated to TN-201

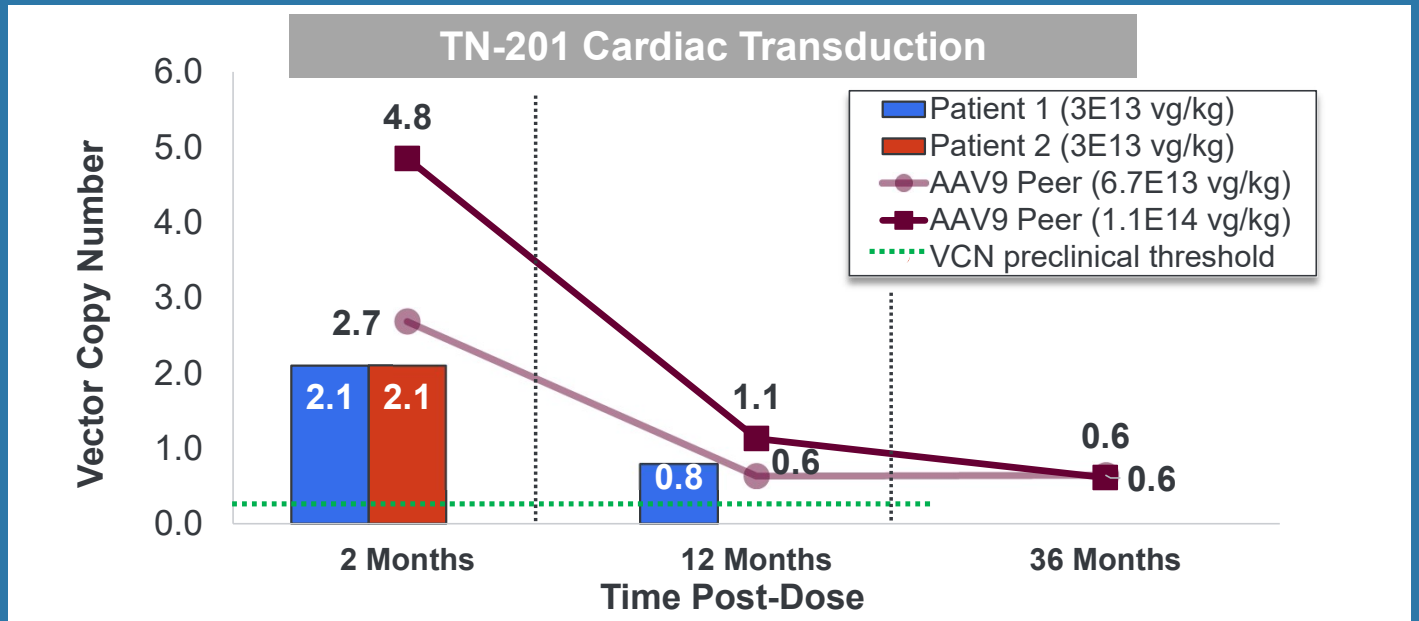
- ✓ Majority of treatment-emergent adverse events (TEAEs) were mild, transient or reversible
  - 2 SAEs unrelated to TN-201 occurred

DSMB cleared dose escalation to 6E13 vg/kg | All patients remain on study

AE = adverse event | SAE = serious adverse event | IS = immunosuppression

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

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

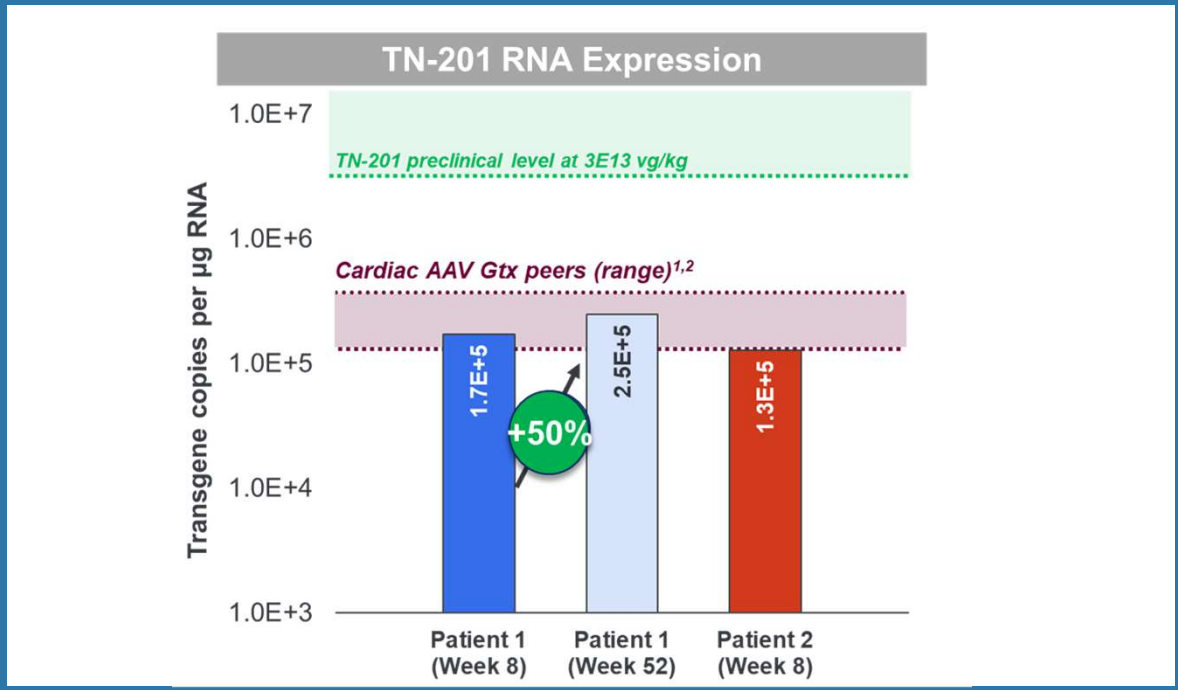


Greenberg, NEJM 2024; Peer values represented as means for given timepoint

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

TN-201 RNA expression confirmed in cardiomyocytes

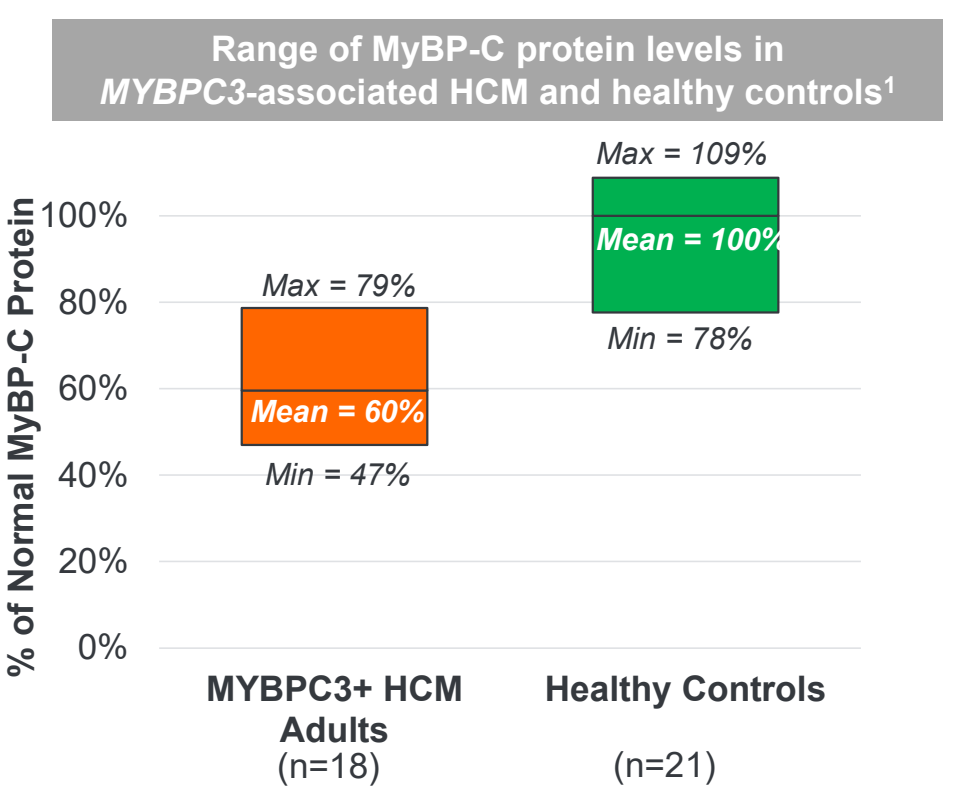
TN-201 RNA expression increases over time and performs similarly to other sponsors



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 GTx 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



MyBP-C protein in *MYBPC3*-associated HCM

- *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.

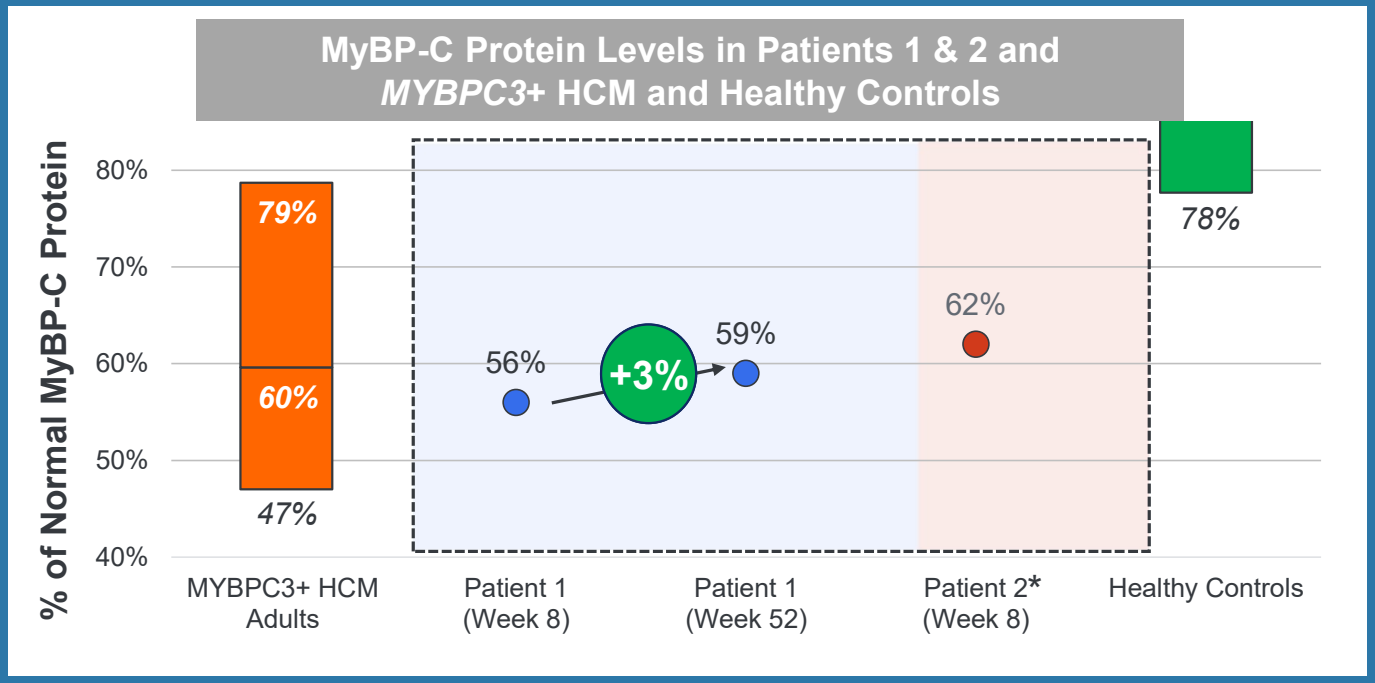
[1]O'Leary, et al; *J Mol Cell Cardiol* 2019 (updated)

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

Increase in MyBP-C protein levels observed in Patient 1

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

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



- 3% increase may not represent total change in protein levels due to lack of baseline
- Baseline biopsies (plus post-dose and Week 52) are now in protocol starting with Patient 3
- Clinical endpoint changes anticipated to coincide with changes in protein over time

* Patient 2 52-week biopsy not yet taken

Encouraging early clinical signals

Up next: More follow-up, more patients, and data from higher-dose cohort

		Clinical Snapshot	
Domain		**Patient 1 at Week 52**	**Patient 2 at Week 40**
Biomarker	NT-proBNP		
	Troponin I		
Imaging	Hypertrophy		
	Diastolic Function		
Functional Capacity		*	
Symptoms	NYHA		
	KCCQ		*

Improved | Stable | Mixed/Declined

* Unavailable or confounded due to AEs unrelated to study drug

- Initial improvement and/or stabilization observed across several domains
- Seeking directional improvement in multiple parameters over time

Next planned readout to include

- Additional safety
- Patient 2 52-week biopsy and assessments
- Patient 3 baseline and post-dose biopsies, plus clinical assessments

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%)

- 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 NHx study serves as a run-in study and control arm for potential future Ph1/2/3 pivotal study. > 220 patients have been enrolled across 29 sites.

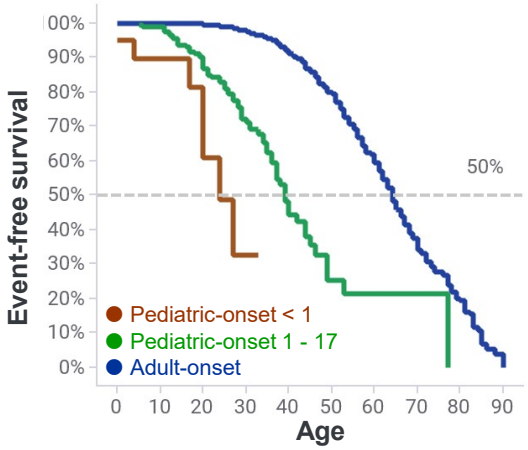
MYBPC3-associated pediatric patients represents sizable severe population lacking therapeutic options

Pediatric-onset patients experience a markedly greater disease progression and cumulative disease burden vs. adult-onset patients (2)

36% more likely to develop life-threatening ventricular arrhythmias(1)

2x more likely to require transplant or ventricular assist device (1)

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
diagnosed < age 18
and currently < age 18

~13,000
diagnosed < age 18
and currently ≥ age 18

~104,000
diagnosed > age 18

1. Marston, et al, *Eur Heart Journal* 2021
2. Meisner, et al, HCMS 2024

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

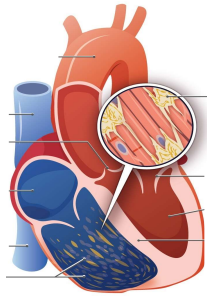
>15% of heart-related deaths in patients < 35 are due to ARVC (2)

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



Enlarged right ventricle with fat and scar tissue

Scar tissue leads to electrical misfiring between cells

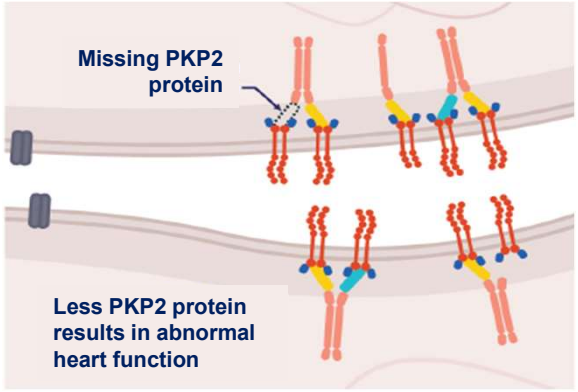
1. Peters, et a, Int J Cardiol 2004; McKenna, Nat Rev Card, 2021
2. Dalal, et al, Circ, 2005
3. Hemida, et al, Eur J Heart Failure, 2018
4. SADS Foundation

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

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

Underlying problem

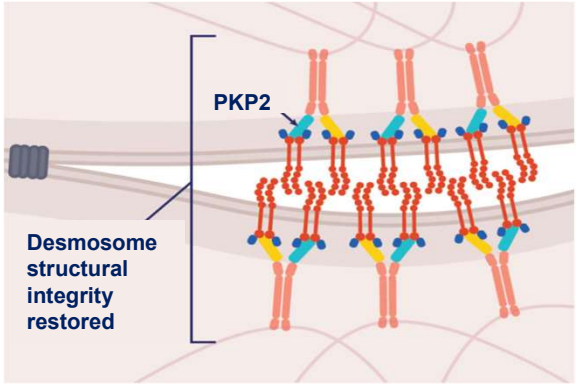
- Mutations of the *PKP2* gene lead to lower levels of Plakophilin-2 (PKP2) protein [1]
- PKP2 is an essential structural protein in the desmosomes, connecting cardiomyocytes supporting electrical and mechanical signaling and overall tissue strength



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

TN-401 use of AAV9 capsid comes with robust validation from preclinical efficacy and clinical studies

Human

- ✓ **Most well-established safety record of any capsid.** Zolgensma is an approved product using AAV9 and has been used in >3700 patients in >51 countries, with >9 years follow-up (1)
- ✓ **Only capsid with validation from human hearts** for biodistribution, transduction, and durable gene expression (2)
- ✓ **Only capsid endemic to humans being used in *PKP2* clinical studies** as compared to AAVrh74 and AAVrh10 discovered in rhesus monkeys (8)

Non-Human Primates

- ✓ **Proven to achieve significantly higher gene expression in cardiomyocytes** vs other capsids in several preclinical studies, include head-to-head comparisons in NHPs (and mice) (3)

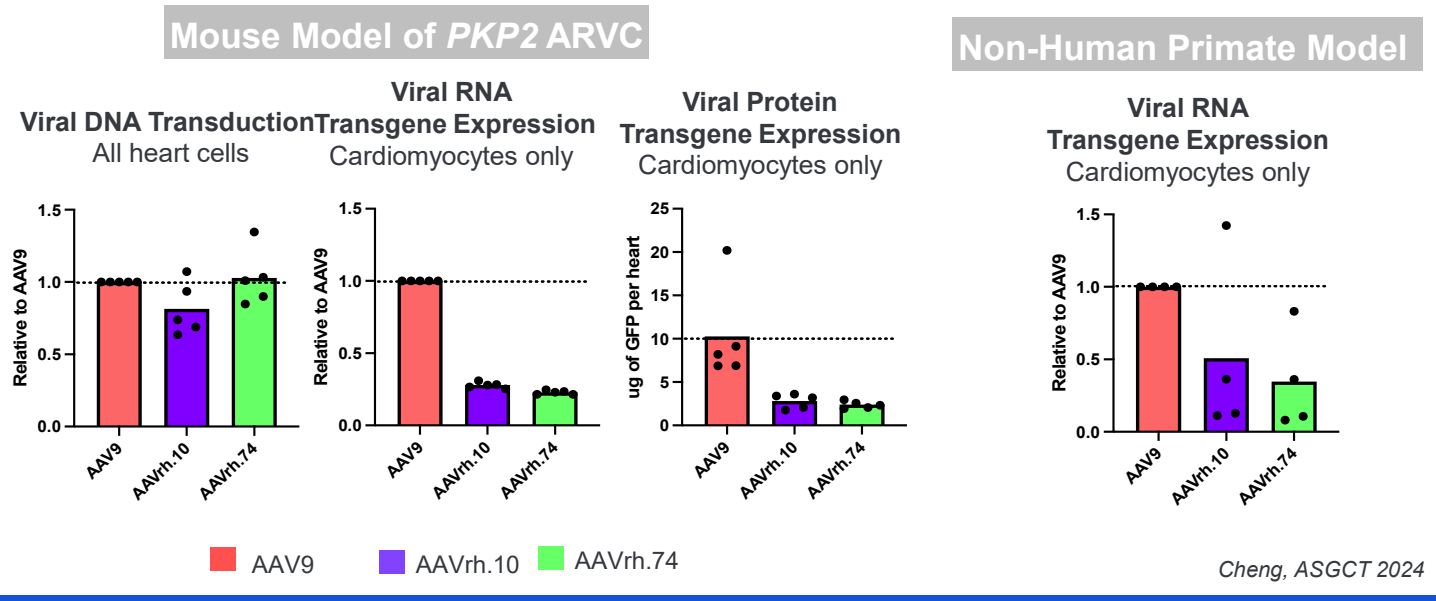
Mice

- ✓ **Most extensive body of preclinical evidence in *PKP2* disease models** from three independently published studies (5,6,7)
- ✓ **Outperformed AAVrh74 in a head-to-head preclinical comparison in *PKP2* models** plus in other disease models (3,4)

1. Novartis March 2024 PR
2. Rocket corporate presentation
3. Ze, et al. ASGCT 2023
4. Herzog, et al, US PTO US 2022/0168446 A1
5. 5 Bradford et al, Nature CV Res, 2023
6 Kyriakopoulou et al, Nature CV Res, 2023
7 (In press) Yang, et al, Communications Medicine
AAVrh = Adeno-associated virus rhesus isolate
8 Wang, Nat Rev Drug Discov. 2019

AAV9 outperforms other serotypes in preclinical models of mice and NHPs

AAV9 achieved significantly higher gene expression in cardiomyocytes in a head-to-head preclinical comparisons of AAV9, AAVrh10, and AAVrh74

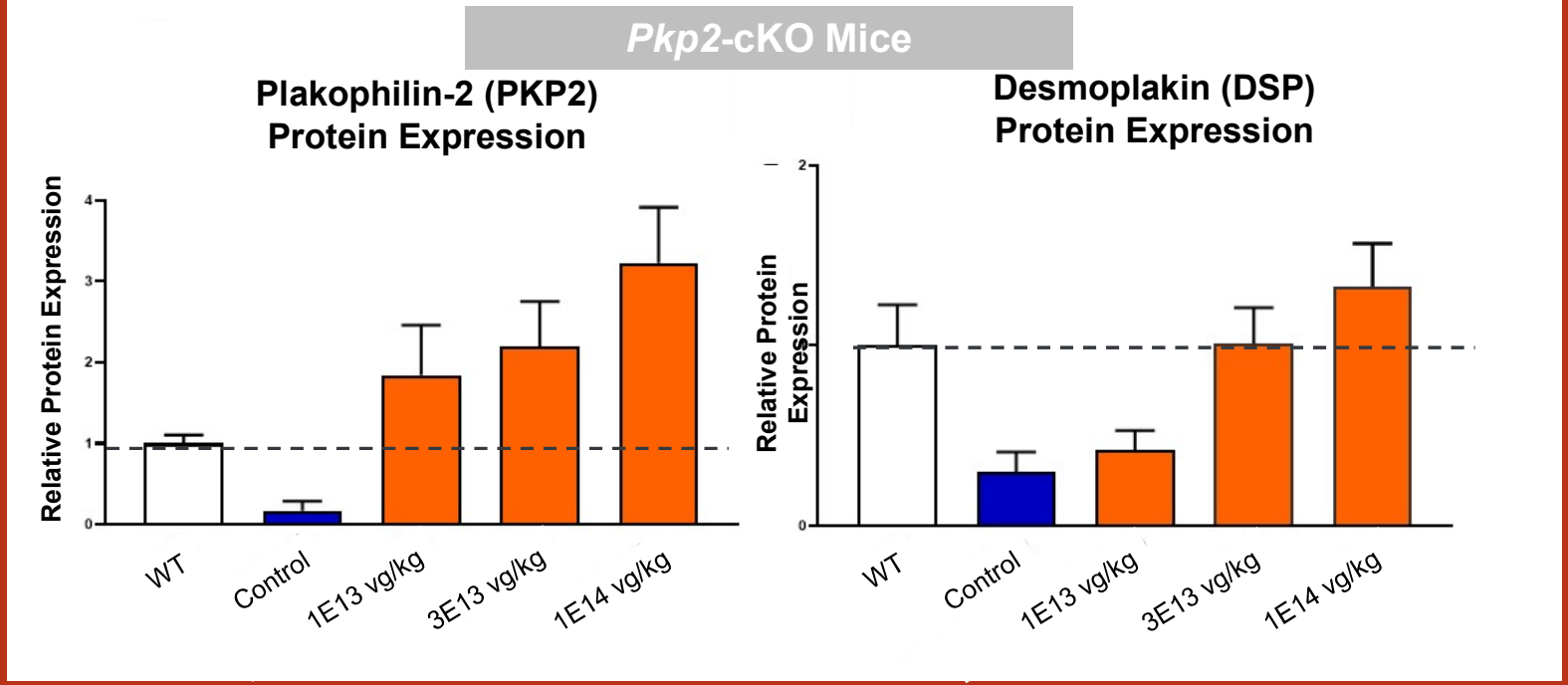


✓ **AAV9 outperformed AAVrh74 in a head-to-head preclinical comparison in *PKP2* and other disease models** in studies conducted by others [1,2]

1. Ze, et al. ASGCT 2023
2. Herzog, et al, US PTO US 2022/0168446 A1

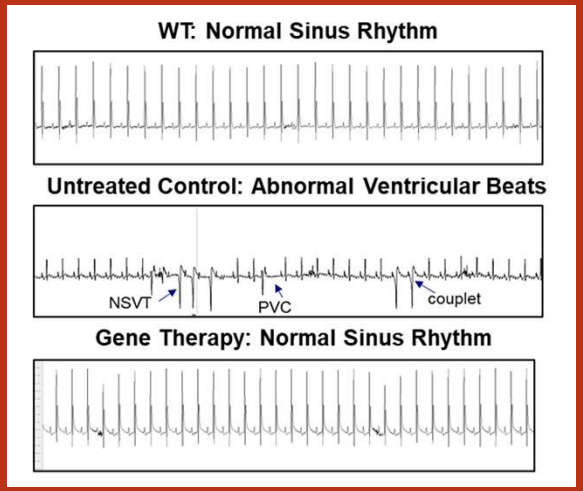
3E13vg/kg dose restored PKP2 protein to normal levels

PKP2 and other desmosomal proteins restored to normal levels in animal model

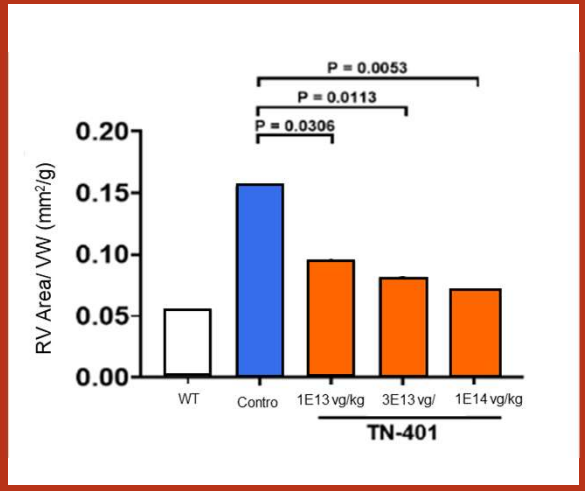


Single 3E13 vg/kg dose of TN-401 in preclinical KO mouse model reverses hallmarks of disease and extends survival

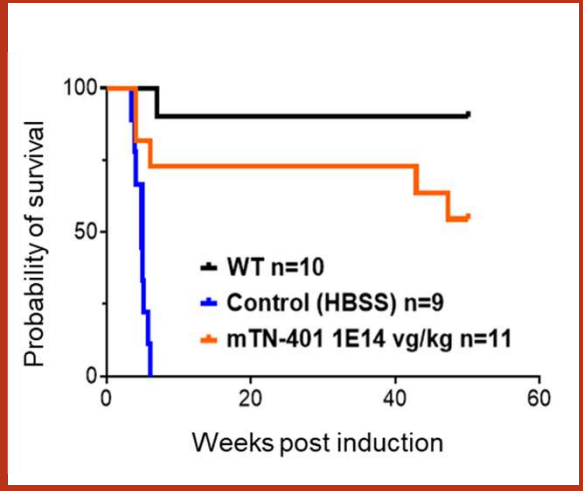
Reversal of arrhythmia



Reduction of RV enlargement



Improved survival



Yang, et al, ASGCT 2022

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

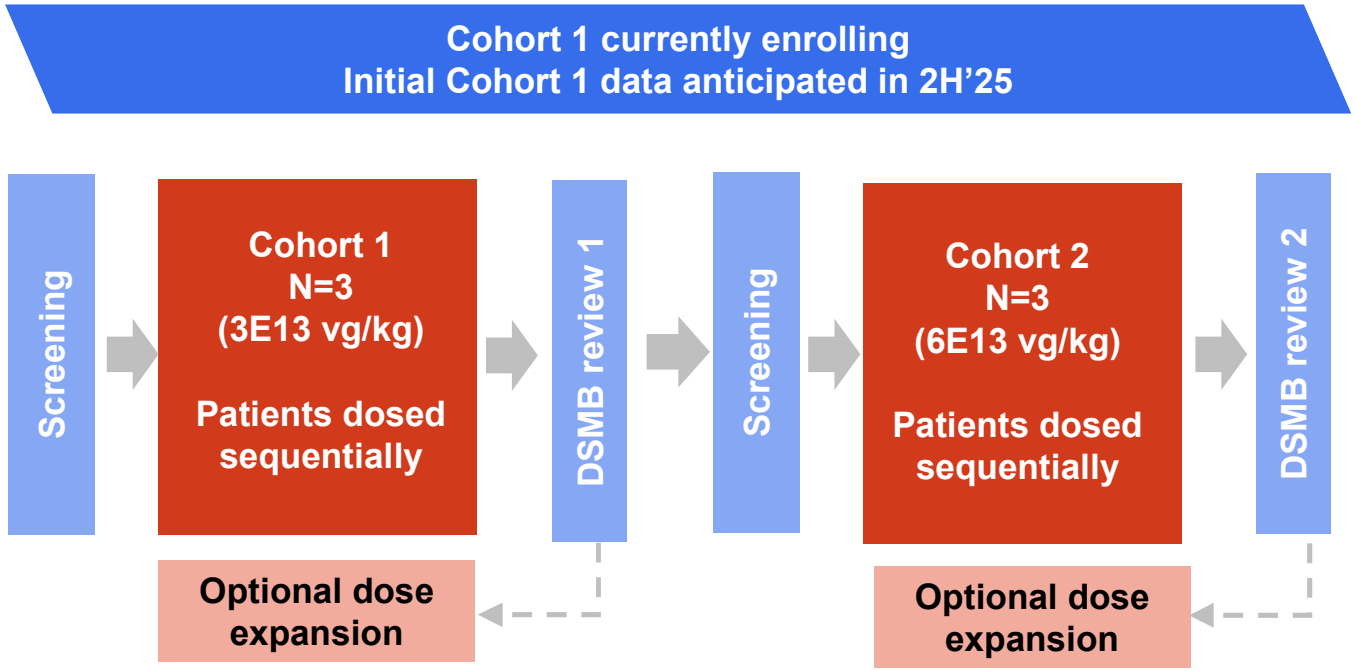
Patient dosing commenced November 2024

Study Objectives

- Safety and tolerability
- Dose-finding
- Pharmacodynamics

Design

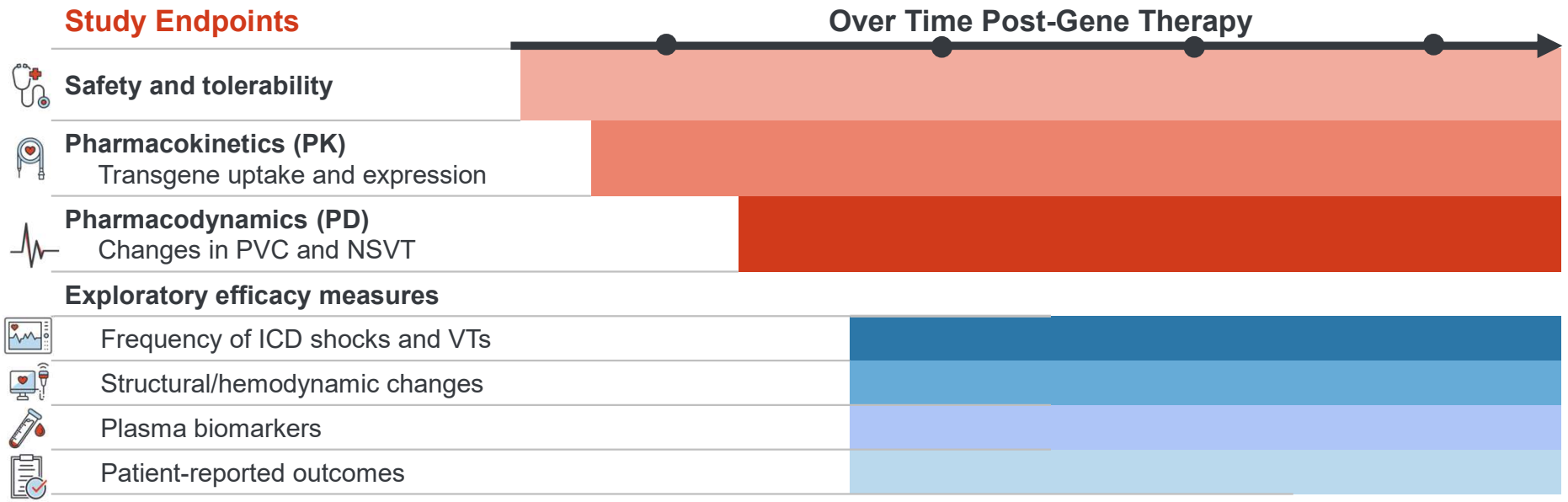
- Open-label, multi-center dose-escalation and dose-expansion
- 52-week study period with four-year follow-up
- Cardiac biopsies at baseline, post-dose and week 52



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 on safety and biopsy results at low-dose



NSVT = non-sustained ventricular tachycardia
Ventricular tachycardia

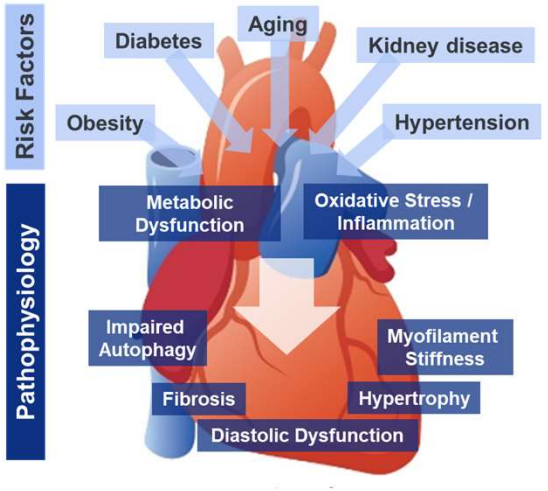
TN-301 HDAC6 inhibitor for HFpEF

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

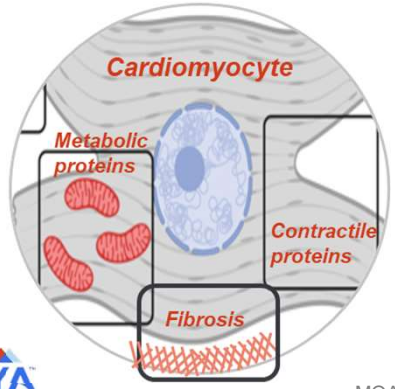
1. Cilia et al, Am J Lifestyle Med 2019
2. Tsao, et al Circulation 2023
3. Van Heerebeek, et al. Neth Heart Jour 2016
4.Shah, et al, JACC 2017

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

TENAYA THERAPEUTICS

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

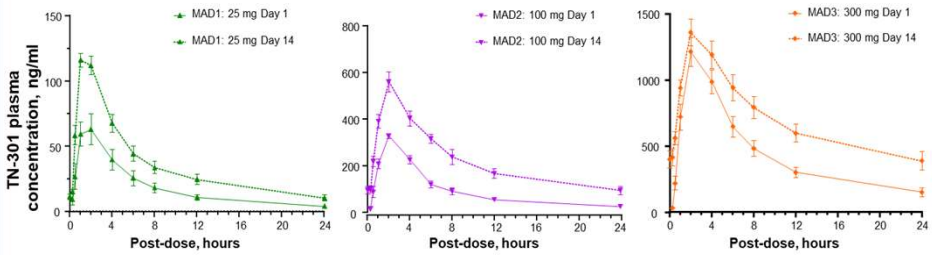
Completed Phase 1 trial of TN-301 in healthy participants

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

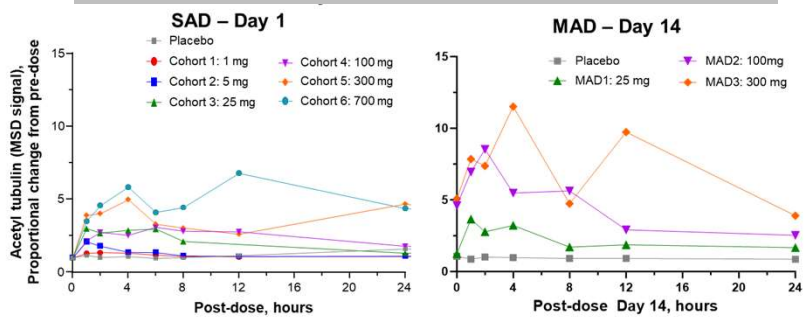
Mean (SEM) plasma TN-301 concentration over time (MAD)



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)

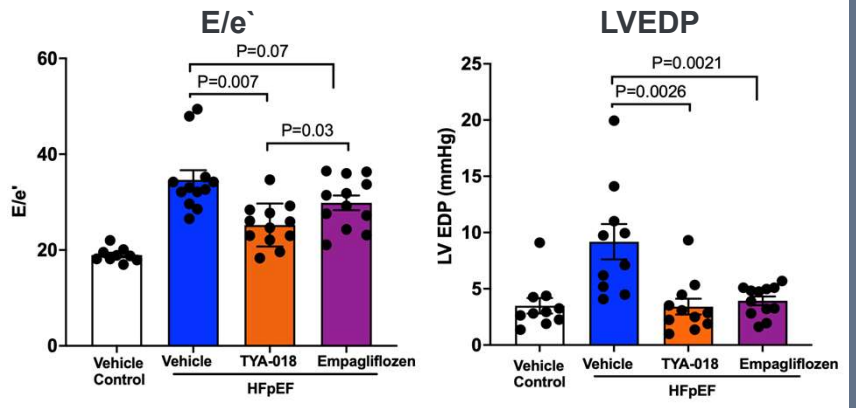
Increasing TN-301 exposure correlated with PD effect

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

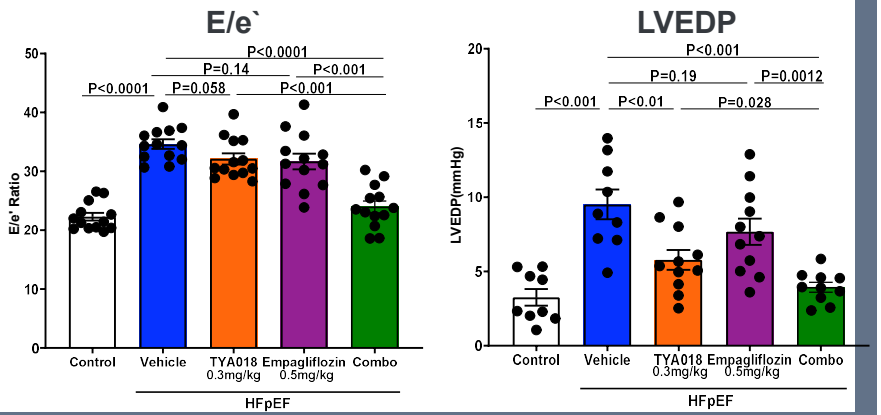
Comparable efficacy as a single agent

HDAC6 vs. SGLT2[1]



Additive efficacy in combination

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

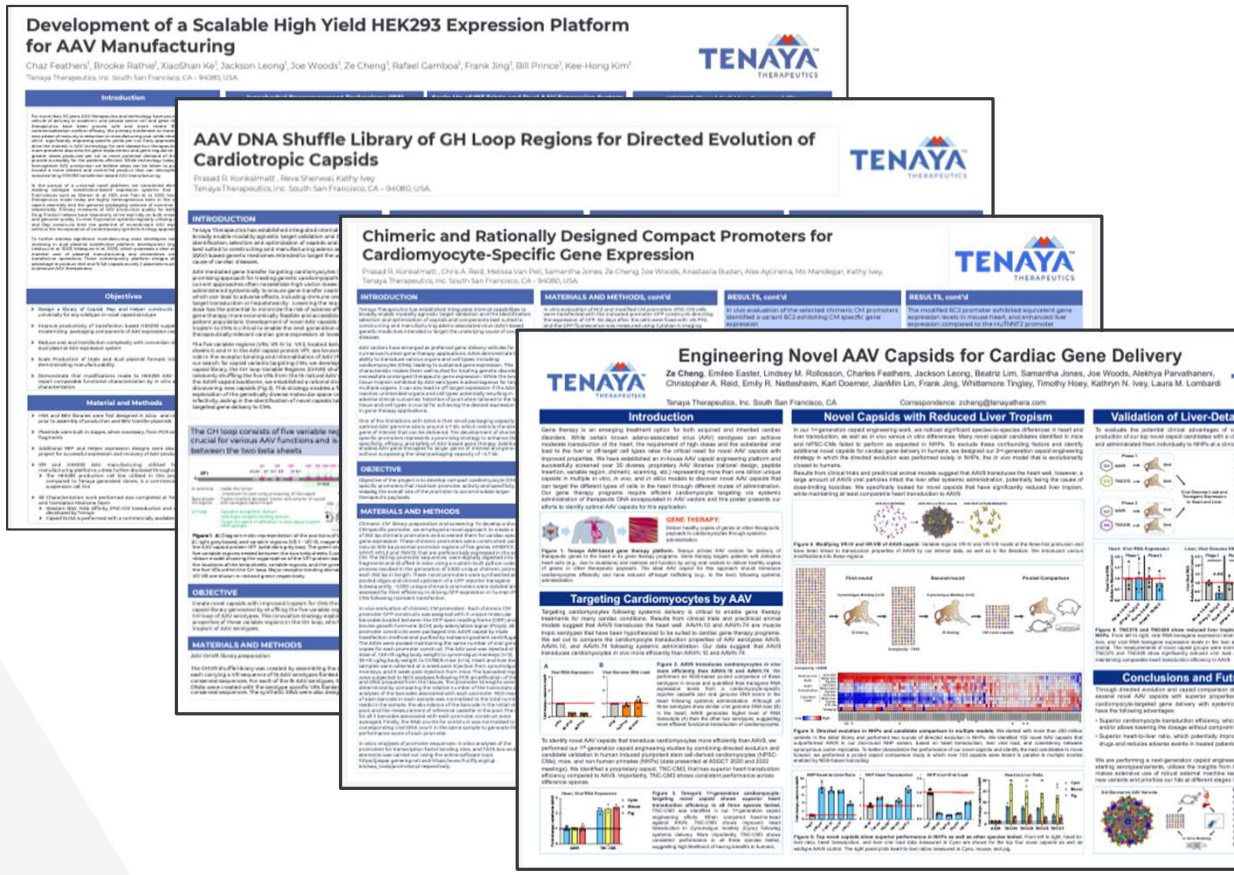
1. *Yang, et al; ESC-HF 2022*
2. *Farshidfar, et al; HFSA 2023*

TENAYA™ THERAPEUTICS

Focus on capsids

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



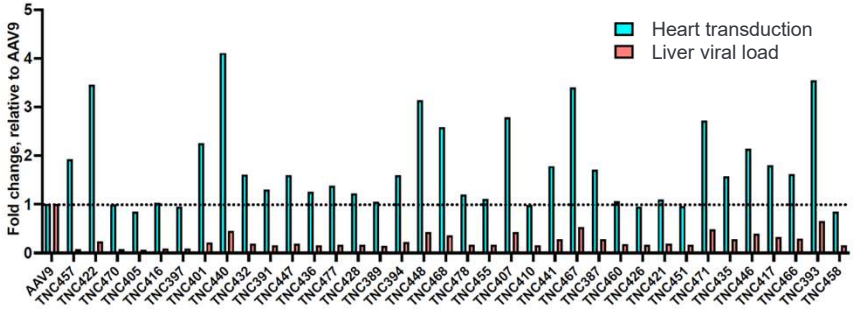
Next generation AAV capsid engineering efforts aimed at enhanced efficacy and safety

Focused AAV Screening Efforts Using Multiple Strategies

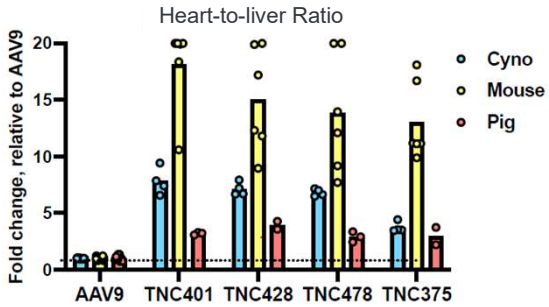
- Screened > 1B variants from ~30 diverse libraries
- Validated *in silico, in vitro* and *in vivo* (4 species)
- Multiple criteria
  - ↑ heart transduction
  - ↓ liver transduction
  - ↔ antigenicity
  - ↔ manufacturability

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

2025 Milestones

Anticipated 2025 milestones

	1H'25	2H'25
TN-201		
MyPEAK-1	• Present Cohort 1 additional data • Complete Cohort 2 enrollment	• Provide Cohort 1 & 2 data update
MyClimb	Present initial data	
TN-401		
RIDGE-1	• Complete Cohort 1 enrollment • Ex-US expansion	• Cohort 2 enrollment
RIDGE	Cohort 1 initial data Present additional data	
Research and Manufacturing		
	Present data from early-stage research efforts and platform enhancement innovations	

Cash and equivalents of $79.5* million as of September 30, 2024
Planned operations funded into 2H 2025

* Tenaya has not drawn on the $45M credit facility put in place in Q3'24

Thank you