Scaling new heights in the fight against heart disease

Corporate Presentation

March 2026

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 2026 milestones; 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; goals, responsibilities and financial terms associated with the Alnylam collaboration; expectations regarding enrollment for MyPEAK™-1 and RIDGE™-1; and plans to pursue regulatory alignment on pivotal trials plans for TN-201 and TN-401, 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," "expected," 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-Q for quarter ended September 30, 2025, 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; the potential for the FDA or other regulatory agencies to conclude at any time that our product candidates may not have an appropriate risk/benefit profile; 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 representation 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

TENAYA™ THERAPEUTICS

Singular focus on the heart

3 clinical-stage programs

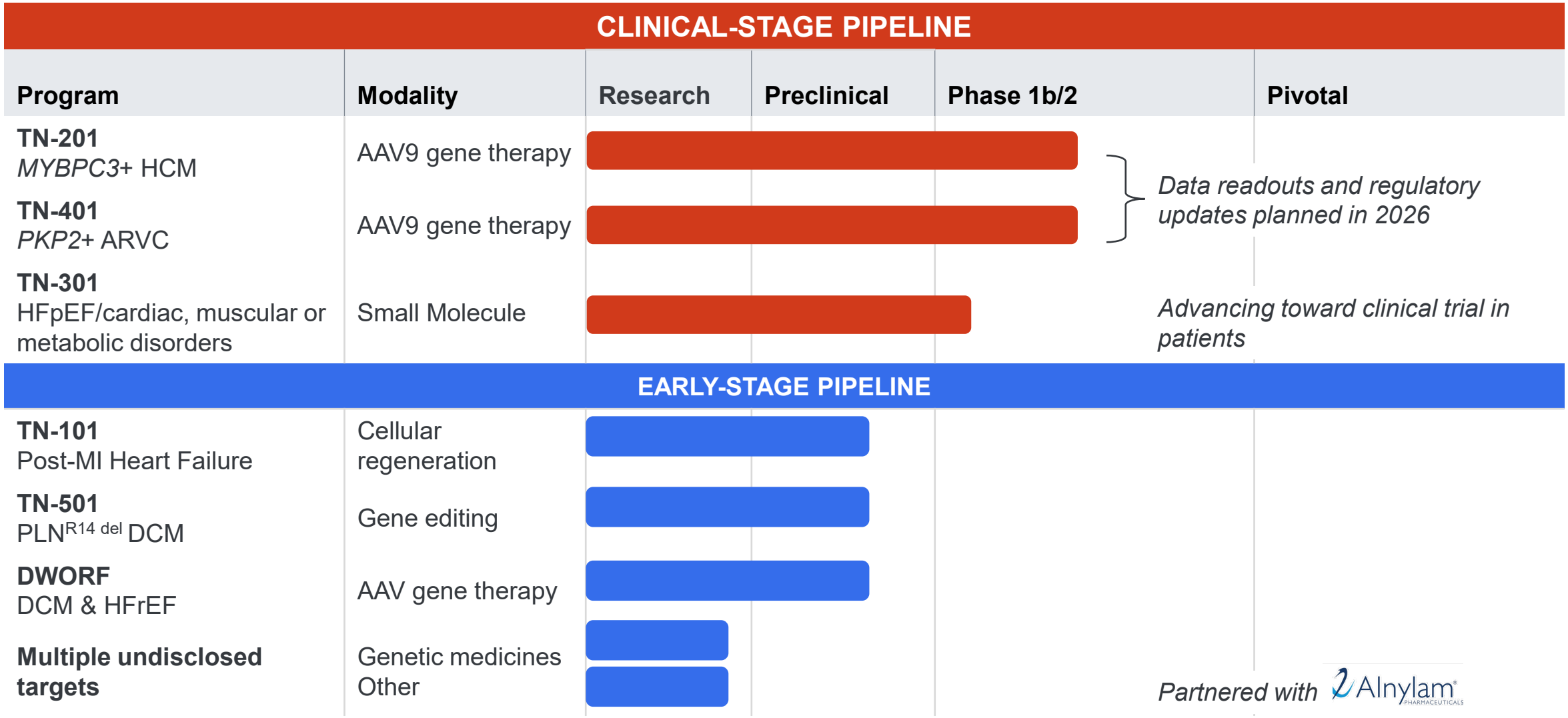
Multiple near-term gene therapy data readouts

Deep expertise in cardiology, genetics and rare disease drug development

Foundational capabilities fuel innovation and first-in-class potential

Track record of execution

Tenaya's pipeline: Focused on clinical-stage catalysts in 2026 backed by continued research innovation



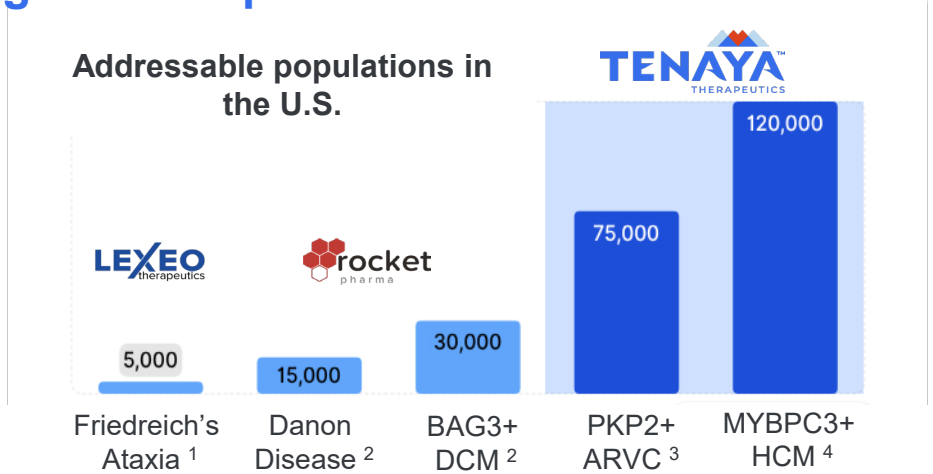
MYBPC3 = Myosin binding protein C3 (gene)
HCM = hypertrophic cardiomyopathy
AAV9 = adeno-associated virus, serotype 9

PKP2 = Plakophilin 2 (gene)
ARVC = arrhythmogenic right ventricular cardiomyopathy
HFpEF = heart failure with preserved ejection fraction
MI = myocardial infarction

PLN = phosolambam. R14del refers to the specific mutation
DCM = dilated cardiomyopathy
HFrEF = heart failure with reduced ejection fraction

Immediate opportunity: Moving TN-201 and TN-401 towards pivotal studies.

Large market potential in rare disease setting



Early evidence of clinically meaningful benefit

TN-201 improved multiple measures of disease (biomarkers, hypertrophy, symptom relief)

TN-401 meaningful improvements in electrical instability (PVCs, NSVTs)

Planned data readouts offer multiple de-risking catalysts in 2026

Increase in protein levels vs. baseline

Decrease in key markers of disease

1H
- My-PEAK™-1 Cohort 2
- RIDGE™-1 Cohort 1 & 2

2H
- MyPEAK-1 Cohort 1 & 2
- RIDGE-1 Cohort 2

Seeking regulatory clarity on approvable endpoints and pivotal trial design.

Updates planned in 2H'26

TENAYA THERAPEUTICS

1. Lexeo presentation, Oct 2025
2. Rocket Pharma presentation, Sep 2025
3. Sedaghat-Hemedani, et al., *Clin Res Cardiol*. 2018
4. Groeneweg, et al, *Circ Cardiovasc Gen 2015* & McKenna, et al, *Nature Rev Cardio* 2021

Next opportunity: Advancing TN-301 towards clinical proof-of-activity to unlock “pipeline-in-a-pill” potential

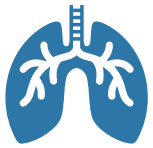
Mechanistic insights into HDAC6 inhibition

DECREASES
- Inflammation
- Oxidative stress
- Fibrosis
- Metabolic dysregulation

INCREASES
- Autophagy
- Lipid metabolism
- Protein quality control
- Mitochondrial metabolism

Pre-clinical studies by Tenaya and others support broad clinical utility in rare and prevalent cardiac disease and cardiac adjacencies

- HFpEF
- (Genetic) DCM



- PH-HFpEF
- PAH

- DMD / DMD-cardiomyopathy (+ other MDs)

Clinical status

Phase 1 trial in healthy volunteers complete
- AEs were mild, similar in profile to placebo across wide range of doses
- Predictable PK supports once-daily dosing

Advancing toward Phase 2 trial to establish proof-of-activity
- Enabling work being conducted within current cash guidance

HDAC6 = Histone deacetylase 6
AEs = adverse events
PAH = Pulmonary Arterial Hypertension
PH = Pulmonary Hypertension
DMD = Duchenne muscular dystrophy
DMD-CM = DMD cardiomyopathy
MDs = Muscular dystrophies

TENAYA™ THERAPEUTICS

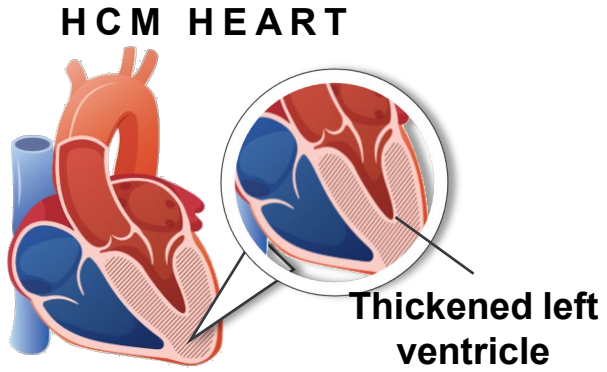
TN-201 for *MYBPC3*-associated HCM

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]

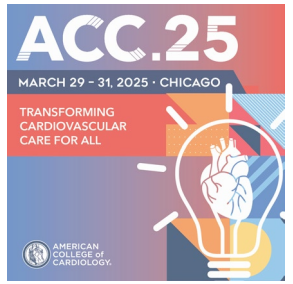
>30% of genetic variants underlying childhood-onset HCM are *MYBPC3* mutations[3]



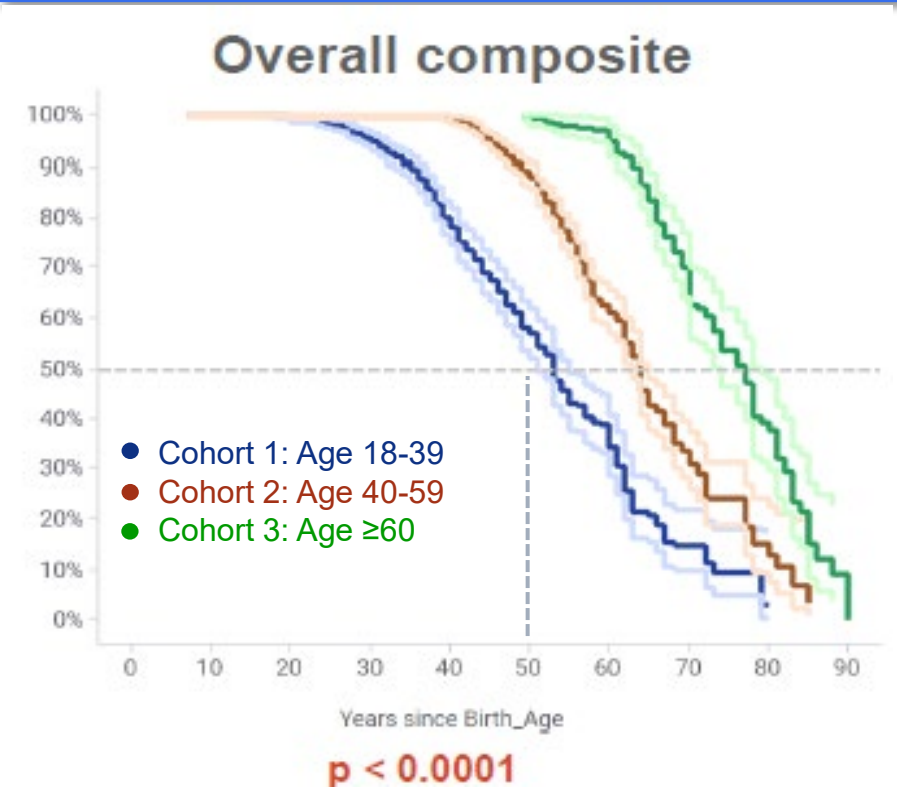
- Significant functional impairment
- Social and psychological impacts
- Symptoms include shortness of breath, fainting, chest pain, fatigue, palpitations, arrhythmias
- Elevated risk of sudden cardiac death and heart failure

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

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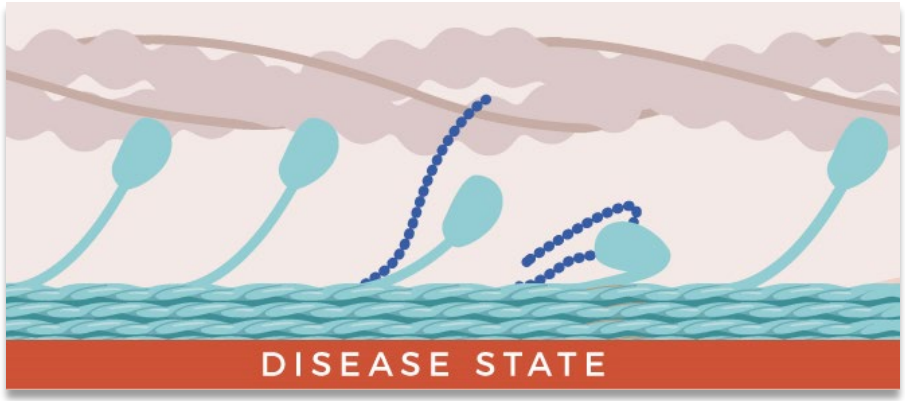
SCD = Sudden cardiac death
ICD = implantable cardio defibrillator

NYHA = New York Heart Association
1. Wang, et al; ACC 2025

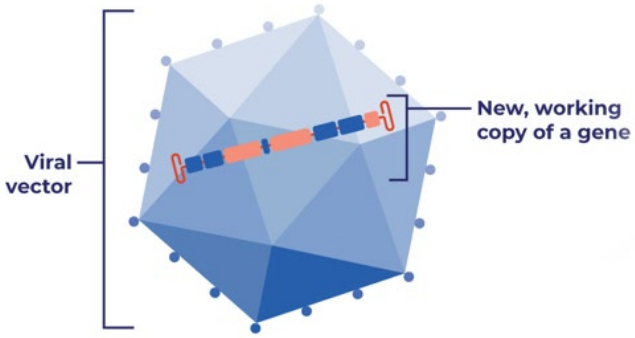
TN-201 is the first gene therapy being developed for *MYBPC3*-associated HCM(1)

MYBPC3 Pathophysiology

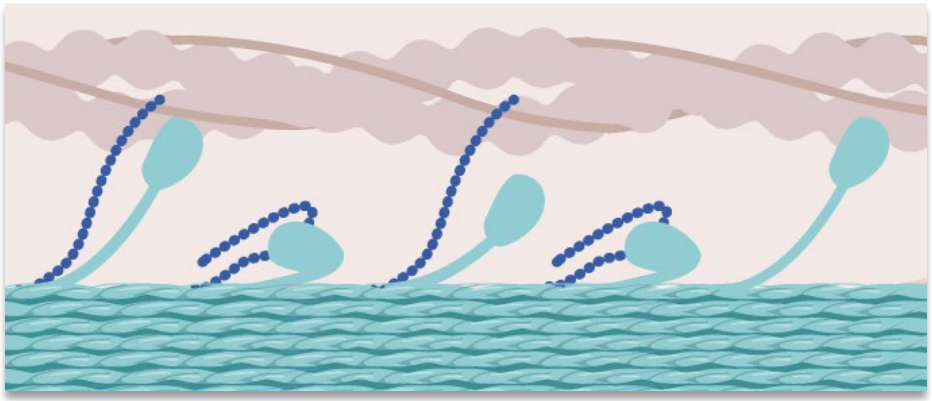


Heterozygous mutations in the *MYBPC3* gene lead to significantly **lower levels of MyBP-C protein** and dysregulated cardiac contractility[1]

TN-201 Mechanism of Action



TN-201 delivers a full-length, functional copy of the *MYBPC3* gene to cardiomyocytes using the most widely dosed capsid, AAV9[2]



Expression of the *MYBPC3* gene increases MyBP-C protein levels and is expected to restore sarcomeric function, reduce hypertrophy, and halt disease progression[3]

MyBP-C protein present in sarcomere

MyBP-C = Myosin-binding protein C

1. O'Leary, et al., *J Mol Cell Cardiol* 2019
2. Byrne, et al., *Mol Ther* 2025
3. Greer-Short, et al., *Nat Commun* 2025

MyPEAK-1 Phase 1b/2 clinical trial design

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

Study Objectives

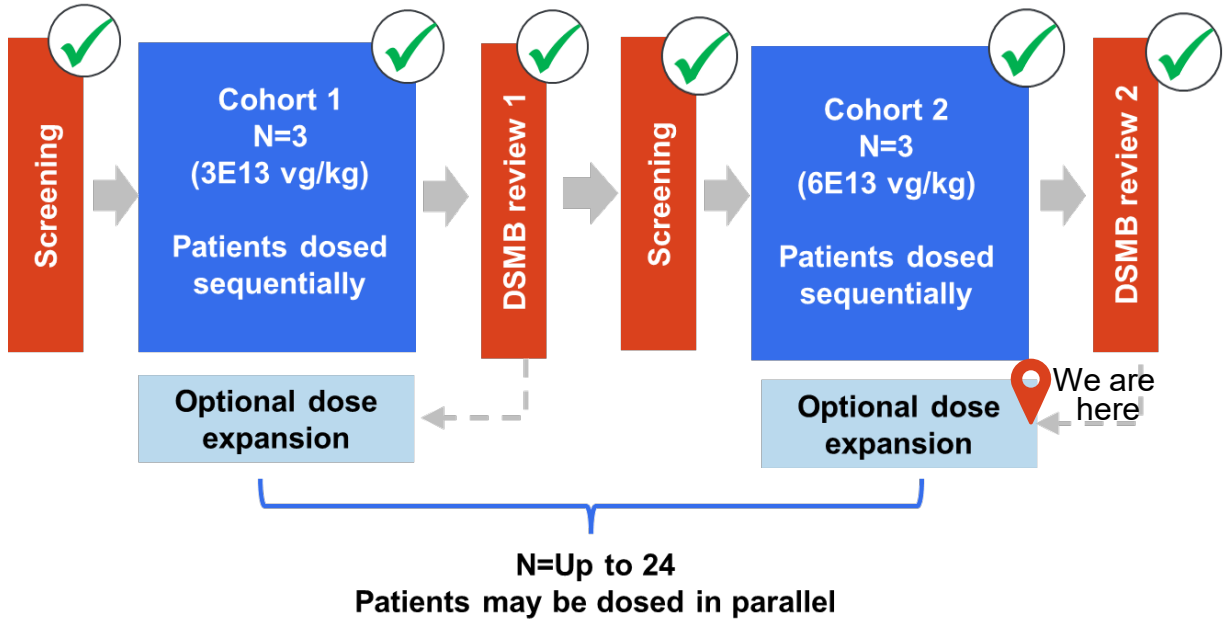
- Safety, tolerability
- Dose-finding
- Pharmacodynamics

Endpoints

- Safety and tolerability
- Transgene uptake and expression
- Plasma biomarkers
- Structural/hemodynamic changes
- Functional changes
- Symptom improvement

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)



Patients in both cohorts have more severe disease burden vs. average HCM patient

	Average / % of HCM	Cohort 1			Cohort 2		
		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Gender	Male (63%)[1]	Female	Female	Male	Female	Female	Female
Phenotype	nHCM (72%)[1]	nHCM	nHCM	nHCM	nHCM	nHCM	nHCM
Age at Dose	50y[1]	27	43	47	60	48	63
LVMI (g/m^2)	F: 89 | M: 104[3]	174	105	178	110	143	138
Myectomy	18%[5]	Yes	Yes	Yes	-	Yes	-
ICD	21%[1]	Yes	Yes	Yes	Yes	Yes	Yes
NT proBNP	563 pg/mL[7]	1884	351	913	337	1013	465
Troponin I	27 ng/L[8]	46	34	53	10	27	8
NYHA Class	50% ≥ II[4]	II	III	II	II	II	II

Baseline Characteristics

- Substantial hypertrophy
- All high-risk with ICD
- Majority with history of myectomy
- All symptomatic
- Anti-AAV9 neutralizing antibody titers ≤1:40

LEGEND
Typical for HCM
Abnormal for HCM
Very abnormal for HCM

Data presented at the American Heart Association Scientific Session in November 2025 reflect a July 2025 data cut

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

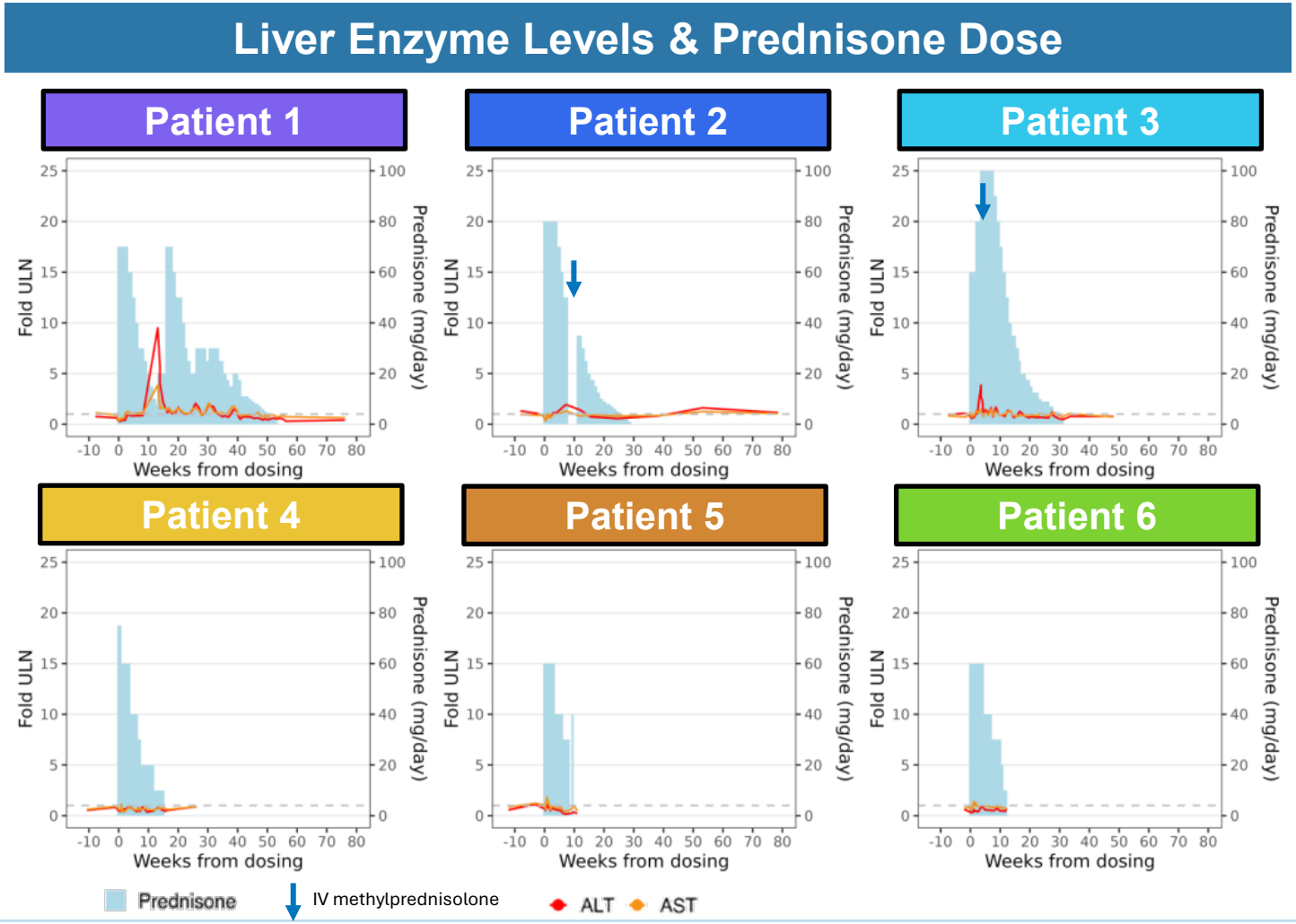
nHCM = nonobstructive HCM
LVMI = left ventricular mass index
ICD = implantable cardiac defibrillator
NT proBNP = N-terminal pro-B-type natriuretic peptide
NYHA = New York Heart Association

TN-201 has been well tolerated at both doses

- Majority of treatment-emergent **adverse events** were **mild, transient and/or reversible**
  - Nausea (n=5) was the most common treatment-emergent adverse event
  - Two treatment-related serious adverse events (SAEs) occurred
    - One SAE of moderate (Grade 2) transaminase elevations, treated with IV steroid in hospital
    - One SAE of mild (Grade 1) complement elevation monitored in hospital
- Four of six patients experienced **reversible elevations in liver enzymes**
  - Elevations normalized after additional steroid treatment
  - All transaminase elevations asymptomatic, with no change in bilirubin or liver synthetic function
- Two Cohort 2 patients experienced **lab abnormalities, including complement elevation, related to innate immune response** within 1 week of dosing
  - Abnormalities **resolved in days without additional treatment or organ involvement**
- **All six patients have tapered off** prophylactic immunosuppression with prednisone and sirolimus
- **No signs of cardiotoxicity**, including **no declines in left ventricular ejection fraction (LVEF)**

Data cut as of July 2025

MyPEAK-1: Optimized immunosuppression successfully reduced steroid requirements in Cohort 2



IS Adjustments During Cohort 1

- Reduced maximum starting dose of prednisone dose from 80mg to 60mg
- Sirolimus initiated earlier (Day -7)
- Weekly monitoring during taper

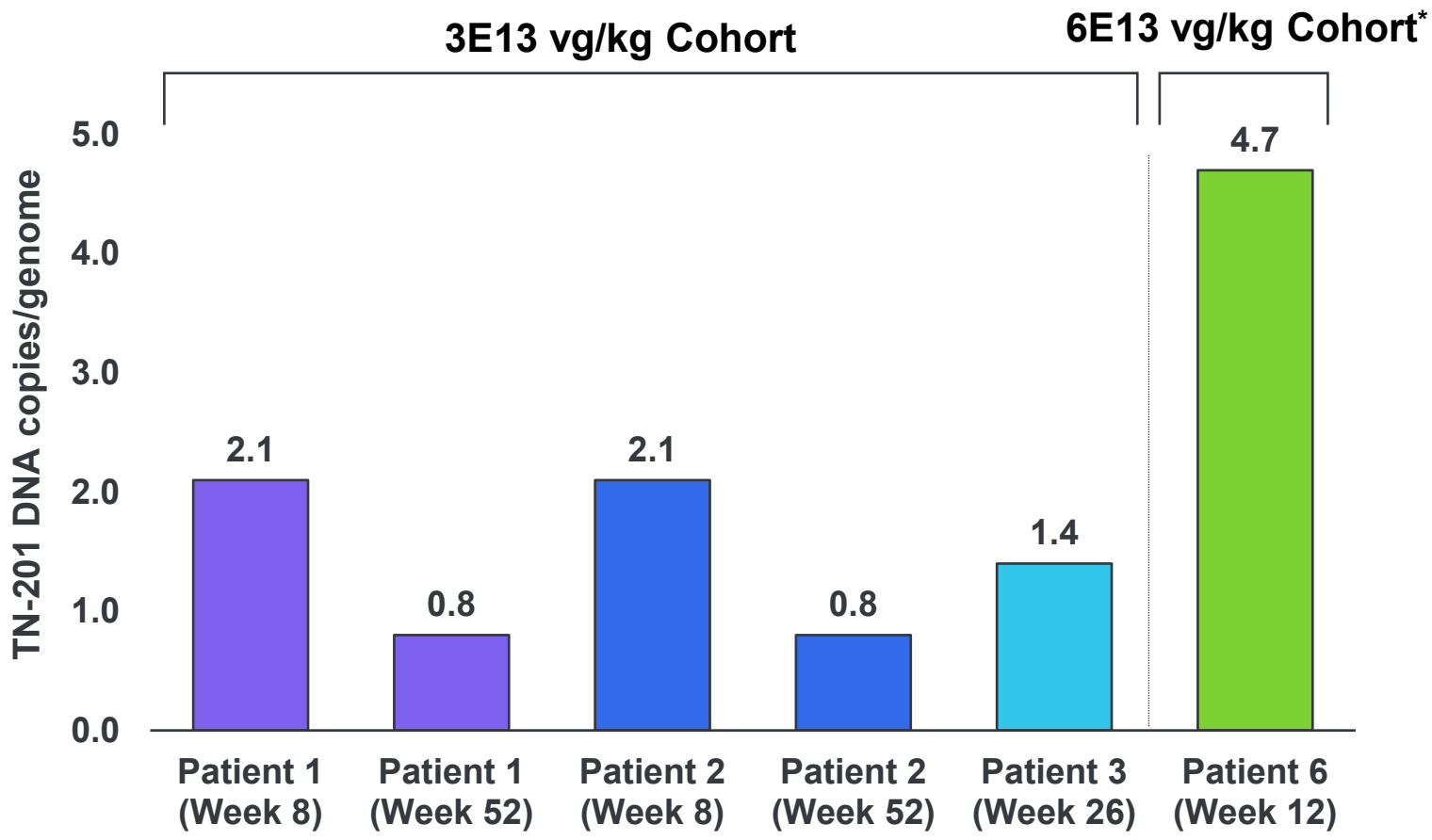
Cohort 2 Results

- Despite higher dose of TN-201, Cohort 2 had fewer, lower elevations in AST/ALT
- Prednisone taper shorter for Cohort 2 (82±23 days) vs. Cohort 1 (262±98 days)

Data cut as of July 2025
AST = aspartate aminotransferase
ALT = alanine aminotransferase

MyPEAK-1: TN-201 DNA and RNA levels across doses and over time

TN-201 DNA in Cardiac Biopsy*



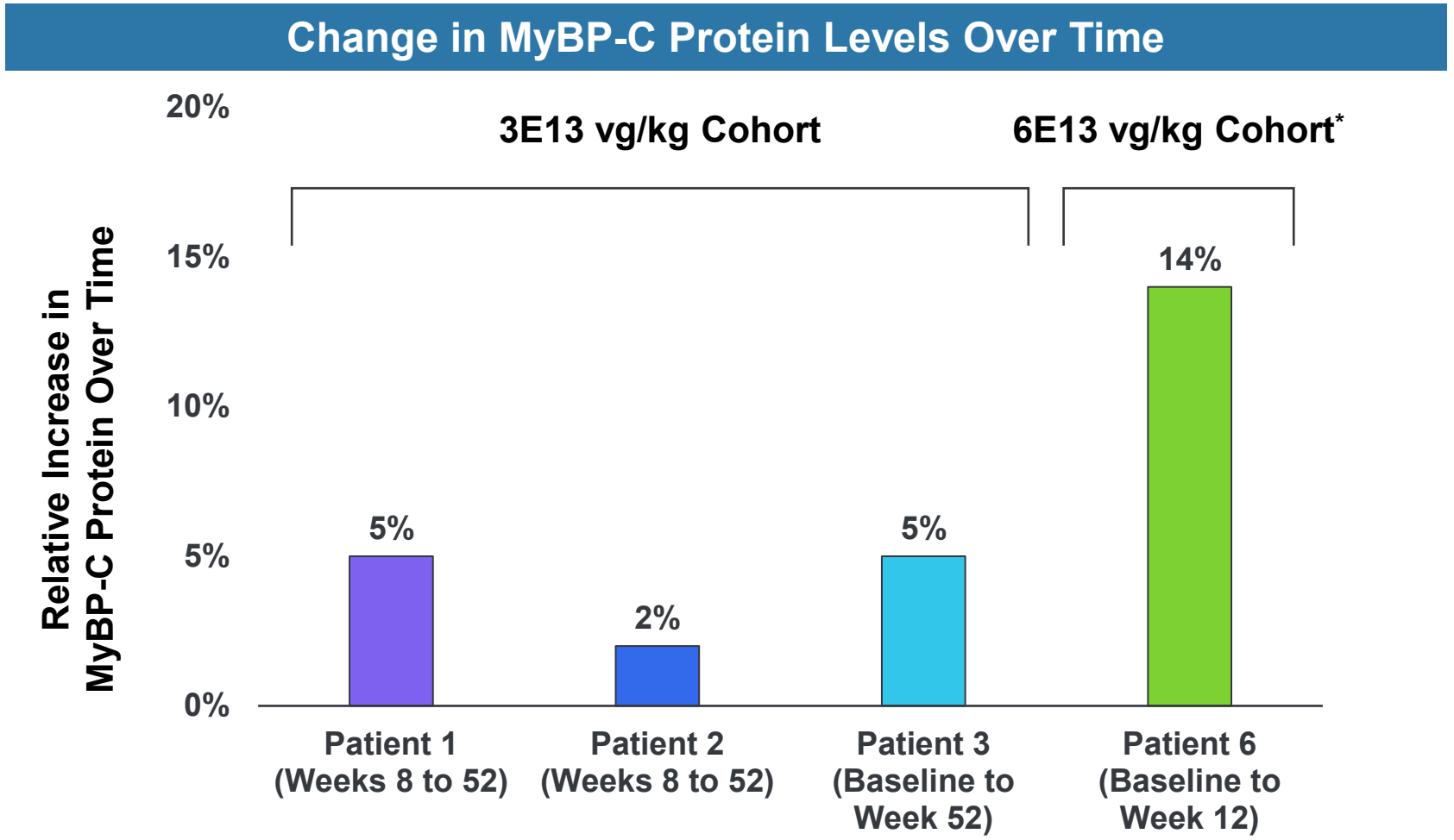
*Patients 4 and 5 had not yet provided post-dose biopsy at time of the July 2025 data cut off

TN-201 DNA & RNA Levels

- Assays specific for TN-201 DNA & TN-201 mRNA
- Patient 6 had a >2x increase in TN-201 DNA levels following 2x increase in dose
- Levels across both cohorts exceed threshold necessary for efficacy in preclinical studies
- TN-201 mRNA expression clearly detected at first post-dose biopsy and increases over time; initial Cohort 2 mRNA level higher than Cohort 1
- Increasing TN-201 mRNA expression consistent with simultaneous increase in MyBP-C protein levels

Data cut as of July 2025

MyPEAK-1: Higher dose resulted in greater increase in MyBP-C protein levels



*Patients 4 and 5 had not yet provided post-dose biopsy at time of the July 2025 data cut off

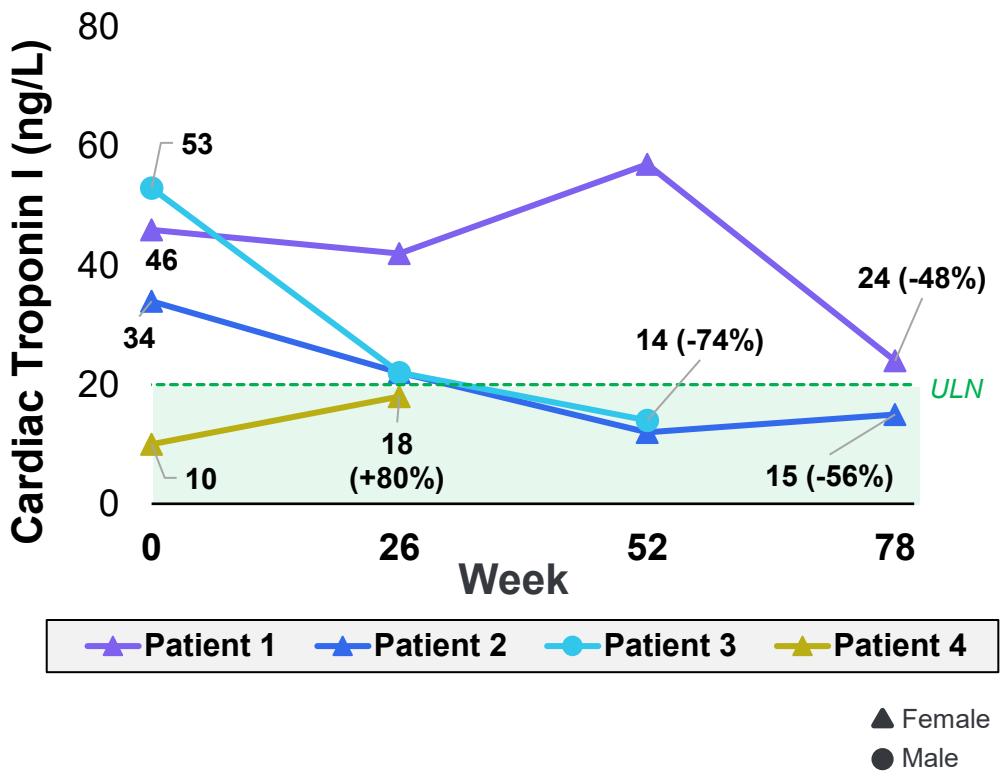
Interim MyBP-C Protein Levels

- Quantitative assay sensitive, but need baseline to quantify full amount of TN-201-derived MyBP-C protein
- Cohort 1 MyBP-C protein levels increased simultaneous with increase in RNA
- First patient from Cohort 2 shows dramatic increase only 12 weeks post-dose
- DNA and RNA similarly follow dose response in Cohort 2

Data cut as of July 2025

MyPEAK-1: Cardiac biomarkers improved or remained stable 52-78 weeks after dosing

Cardiac Troponin I Levels Over Time (Change)



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 declined 48-74% to normal or near-normal levels at most recent visit in all patients with abnormal levels at baseline

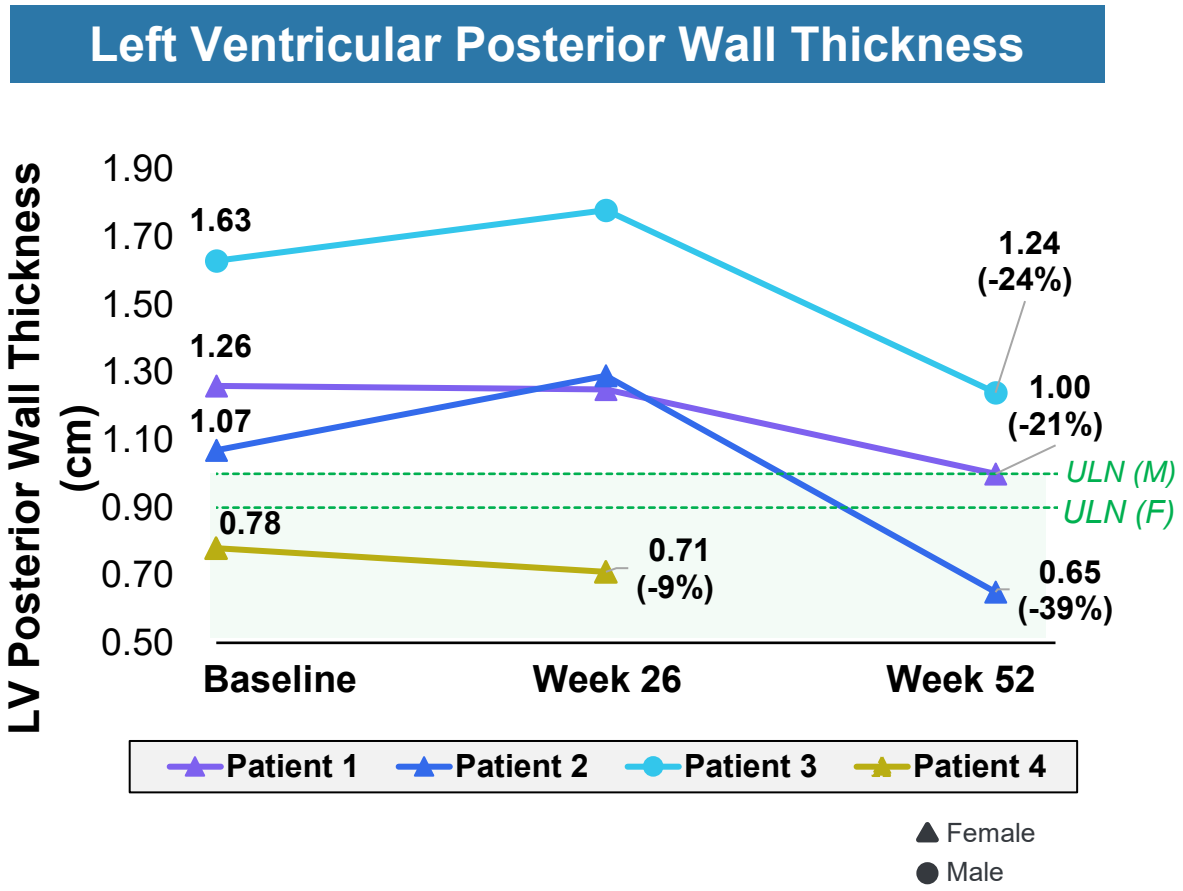
NT-proBNP (not shown) is a biomarker that indicates strain of the heart muscle

- NT-proBNP increased with IS, but declined from or returned to baseline after IS in 2 of 3 patients from Cohort 1

Data cut as of July 2025

ULN = upper limit of normal

Reductions in hypertrophy moving toward normal and deepening over time



Hypertrophy Results

Echo measurements of heart mass and thickness were taken to assess changes; greater LVPWT is a risk factor for reduced post-myectomy survival

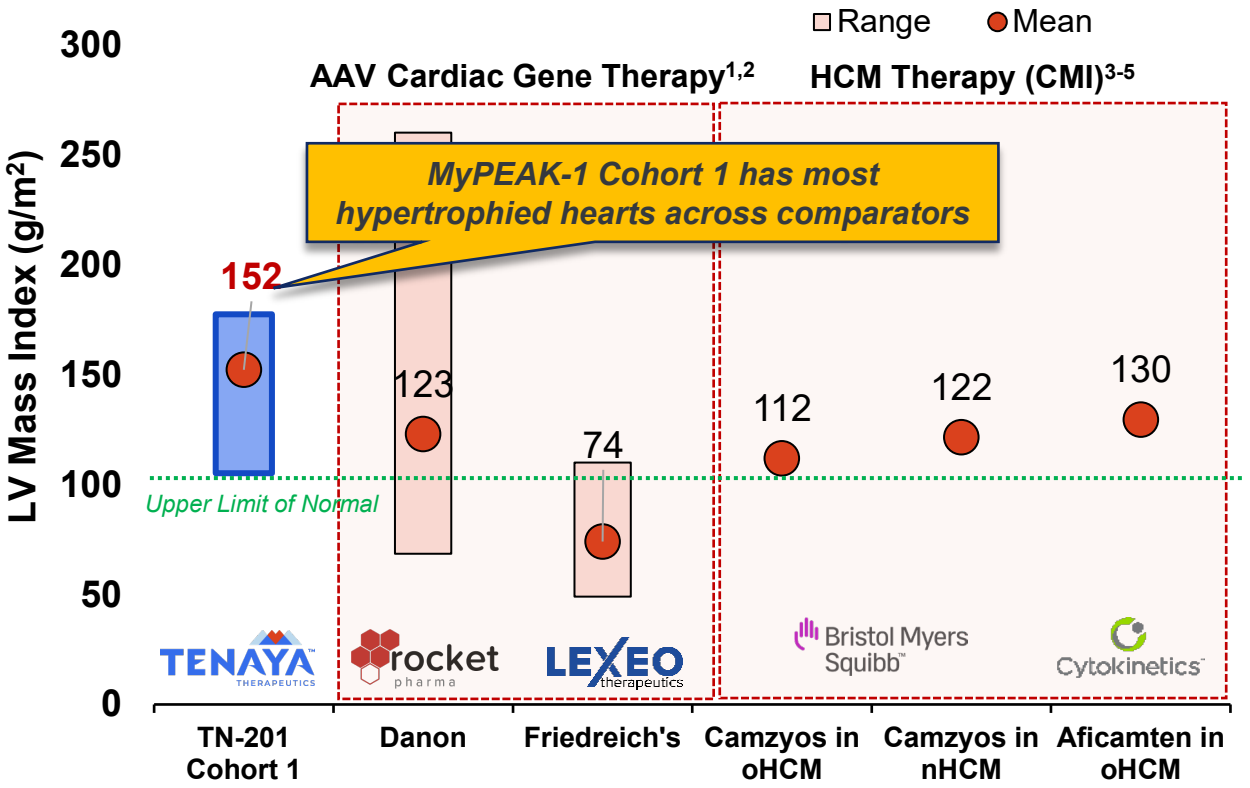
- At 52 Weeks, Cohort 1 patients saw improvements in one or more measures of hypertrophy
- Left ventricular posterior wall thickness decreased in all Cohort 1 patients by 21%-39%
- Left ventricular mass index (not shown) decreased by 12% and 22% in patients 2 & 3
- Other measures of hypertrophy and diastolic function remain largely stable

Data cut as of July 2025

ULN (M) or (F) = upper limit of normal male / female

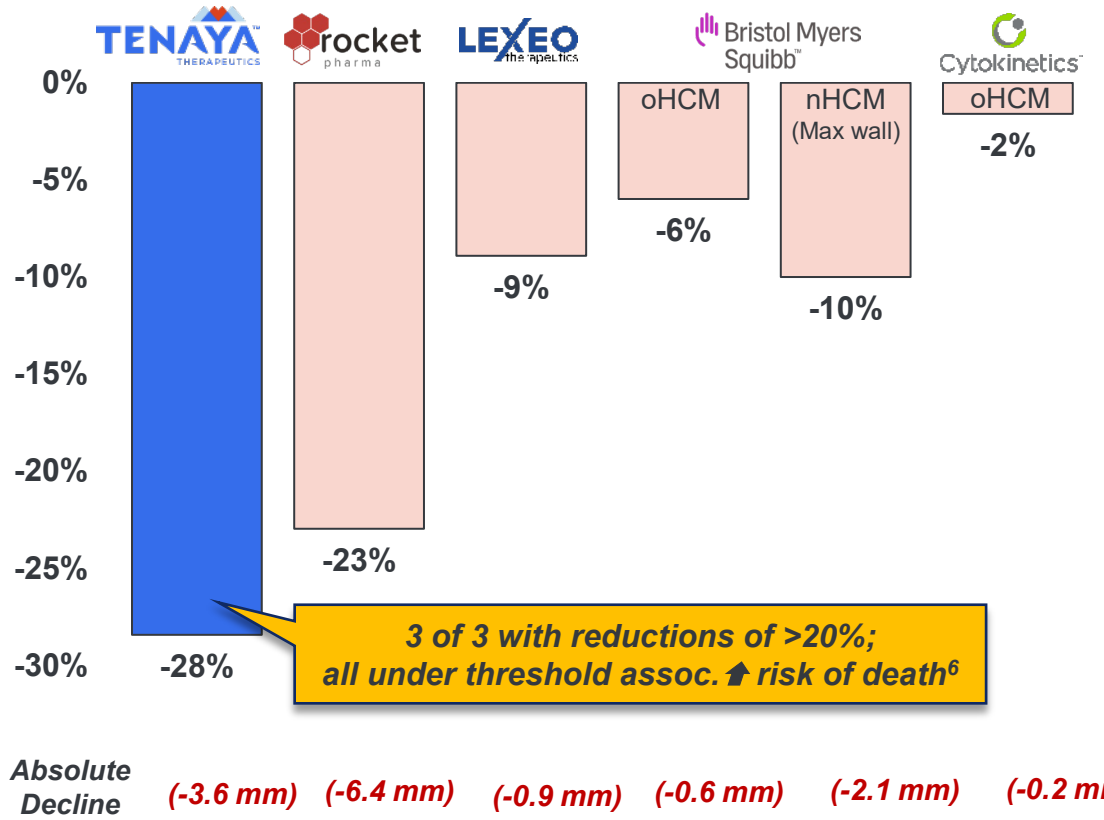
Despite level of severity, TN-201 reductions in hypertrophy compare favorably to others

Baseline LVMI Values of Relevant HCM Trials



These trials are not head-to-head and caution should be used in drawing any conclusions from these comparisons. Comparisons with peer programs are not intended to indicate likelihood of TN-201 clinical benefit.

Change in LVPWT from Baseline to 12 Months/MRV*[1-5]



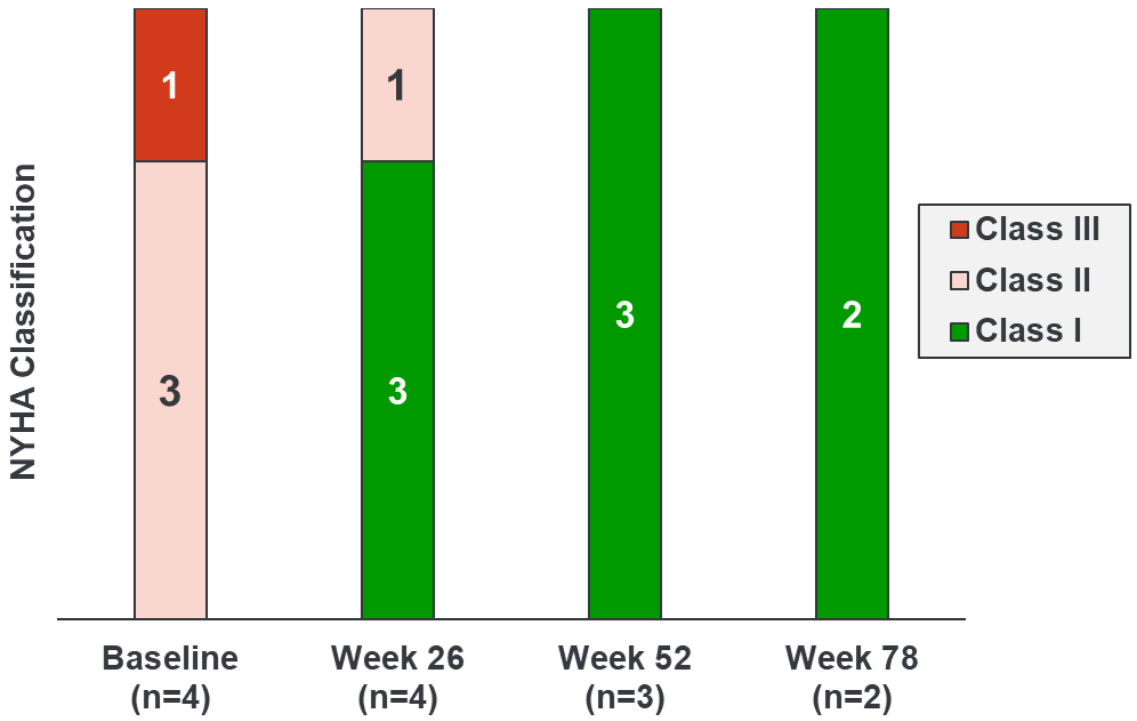
*Lexeo most proximal visit to 12mo. Rocket most recent vist. BMS oHCM & nHCM 30 and 48wk, respectively. Cytokinetics oHCM at 24wk

1. Greenberg, et al., *NEJM* 2024
2. Lexeo Apr&Oct'25 Corp Updates
3. Hegde, et al., *JACC* 2021
4. Desai, et al., *JACC* 2025
5. Hegde, et al., *JACC* 2024
6. Sun, et al. *JACC* 2022

oHCM = obstructive HCM
CMI = cardiac myosin inhibitor
MRV = most recent visit
LVPWT = left ventricular posterior wall thickness

Cohort 1 patients were free of heart failure symptoms at Week 52 and remain asymptomatic

NYHA Classification



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)
- Heart failure symptoms improved by at least one class in all patients at Week 26
- Changes in NYHA class coincide with positive changes in cardiac biomarkers and measures of hypertrophy

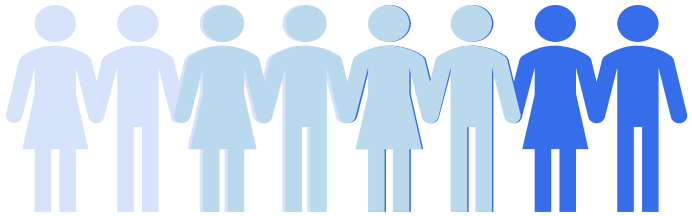
Data cut as of July 2025

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

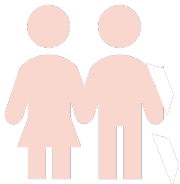
Adults | **Adolescents** | **Peds** | **Infants**

Heterozygotes — **Homozygotes**

Non-Obstructive Phenotype (70%)



Obstructive Phenotype (30%)



MyPEAK-1 started in nHCM patients with ICDs, now includes all symptomatic adults, with/without ICD

Potential future expansion

Pediatric *MYBPC3*-associated HCM pathway supported by MyClimb natural history study

MyClimb Natural History Study

- **> 220 patients have been enrolled across 29 sites**
- **May serve as run-in study and control arm for potential future pediatric pivotal trial**

Seeking regulatory alignment on pivotal trial plans in 2026

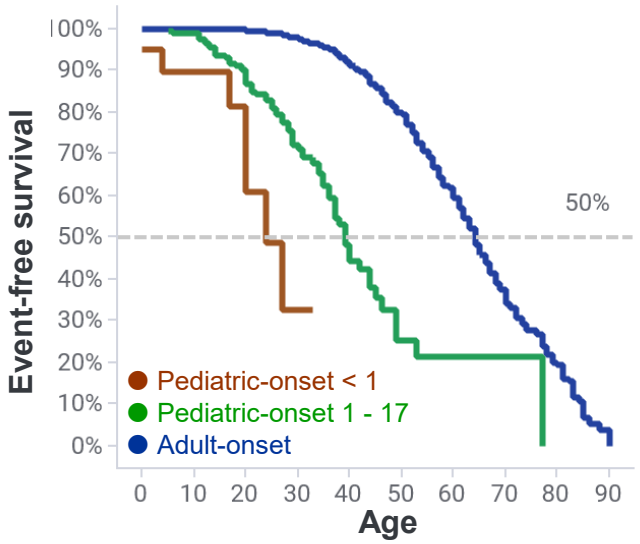
MYBPC3-associated pediatric patients represents sizable severe population lacking therapeutic options

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)

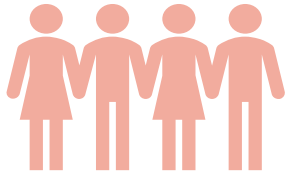
Time to event* since birth



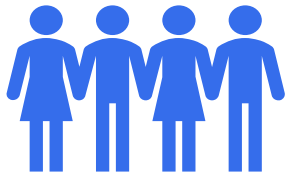
* Event-free survival composite endpoint includes NYHA class III/IV, transplant, sudden cardiac arrest, atrial fibrillation, ICD firing, heart failure, stroke, death

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

TENAYA™ THERAPEUTICS

TN-401 for *PKP2*-associated ARVC

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

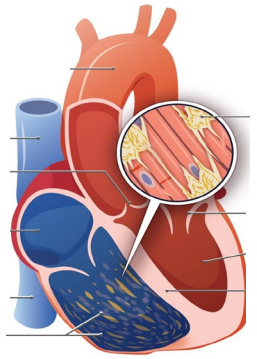
ARVC is a severe and progressive genetic heart disease lacking therapeutic treatment options

>15% of heart-related deaths in patients < 35 are due to ARVC[1]

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

~40% Of those diagnosed with ARVC carry pathogenic *PKP2* mutations [3]

ARVC HEART



Enlarged right ventricle with fat and scar tissue

Unstable connections and scar tissue between cells lead to electrical misfiring

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

1. SADS Foundation
2. Dalal, et al., Circulation 2005
3. Hermida, et al, Eur J Heart Failure, 2019

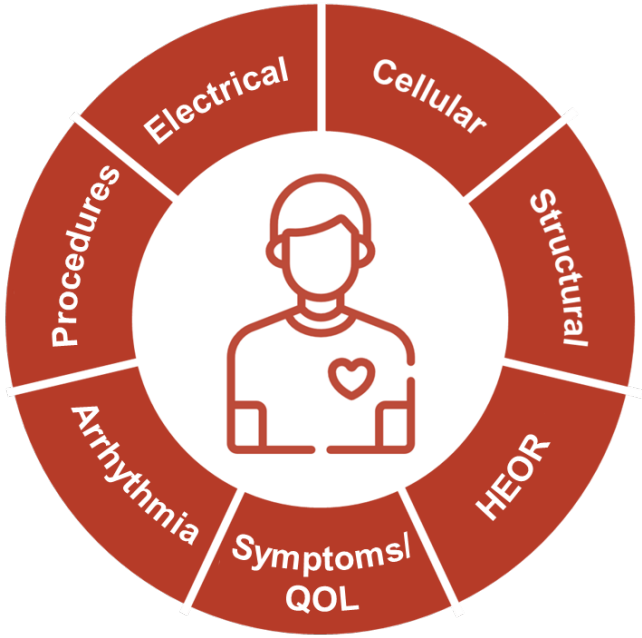
Gathering unique disease insights from RIDGE, the largest natural history study for *PKP2*-associated ARVC

Largest *PKP2*+ ARVC Study Ever…

RIDGE™

>185 Patients	**>2,500** Years of Follow-Up
21 Sites	**6** Countries

…Collecting Data Across Domains…



…Directly Feeding RIDGE-1 Trial

RIDGE™-1

- All RIDGE-1 participants to date were identified through RIDGE
- RIDGE informed RIDGE-1 design, including eligibility criteria and endpoints
- Complements trial results by demonstrating natural history without gene therapy
- Supports potential pivotal trial & BLA

~70% of RIDGE patients eligible for RIDGE-1

BLA = Biologics license application

Genetic subtypes in ARVC influence prognosis

RIDGE Natural History Study provides distinct insights into *PKP2*-specific disease

Stages of *PKP2*-associated ARVC Progression[1, 2]

Concealed Stage → **Overt Electrical Instability Stage** → **Structural Dysfunction Stage**

60%
of patients with cardiac arrest had no prior symptoms[2]

>80%
of patients have had >500 PVCs per day despite standard of care

49%
have history of ventricular tachycardia

51%
have RV dysfunction

36%
have LV involvement; fewer report HF symptoms

Insights*[3] *from RIDGE™

PKP2-specific finding

***PKP2*+ patients are more likely to experience consequences of electrical instability than HF[3,4]**

Risk of Sudden Cardiac Arrest / Death At Any Stage

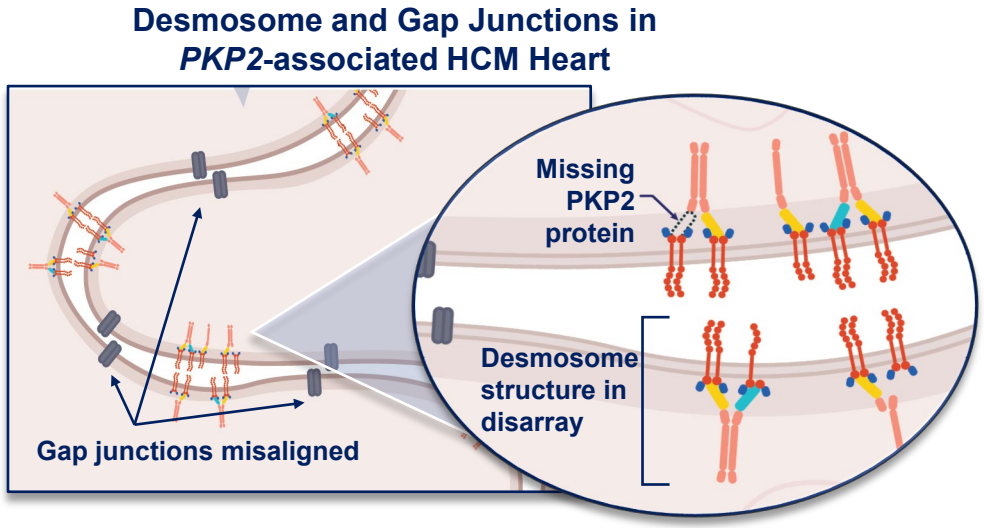
TENAYA THERAPEUTICS

1. Adapted from Tadros, App of Clinical Genetics 2023
2. Shah, et al, Statpearls 2024
3. Calkins, HRS 2025
4. Biernacka, et al, J. Applied Genetics 2021

RV = right ventricular
LV = left ventricular
HF = heart failure

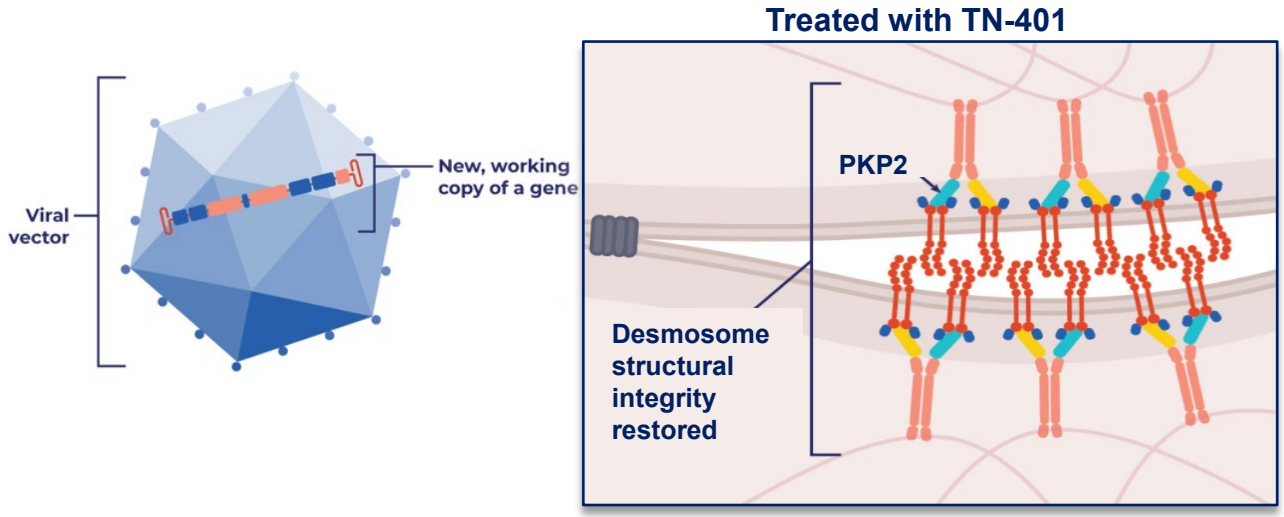
TN-401 gene therapy for *PKP2*-associated ARVC

PKP2+ Pathophysiology



- Mutations of the *PKP2* gene lead to lower levels of PKP2 protein[1] resulting in
  - Weakened cell-to-cell adhesion
  - Abnormal electrical activity

TN-401 Mechanism of Action



- TN-401 targets the underlying genetic cause of disease by delivering a full-length *PKP2* gene to cardiomyocytes via an AAV9 capsid
- An increase in PKP2 protein levels is expected to restore desmosome function, with the potential to halt disease progression, reverse symptoms, improve patient quality of life and prevent SCA

1. van Tintelen, et al, Circulation 2006

SCA = Sudden cardiac arrest

RIDGE-1 Phase 1b/2 clinical trial for *PKP2*-associated ARVC

Treatment goal: demonstrate reduction in arrhythmic events

Study Objectives

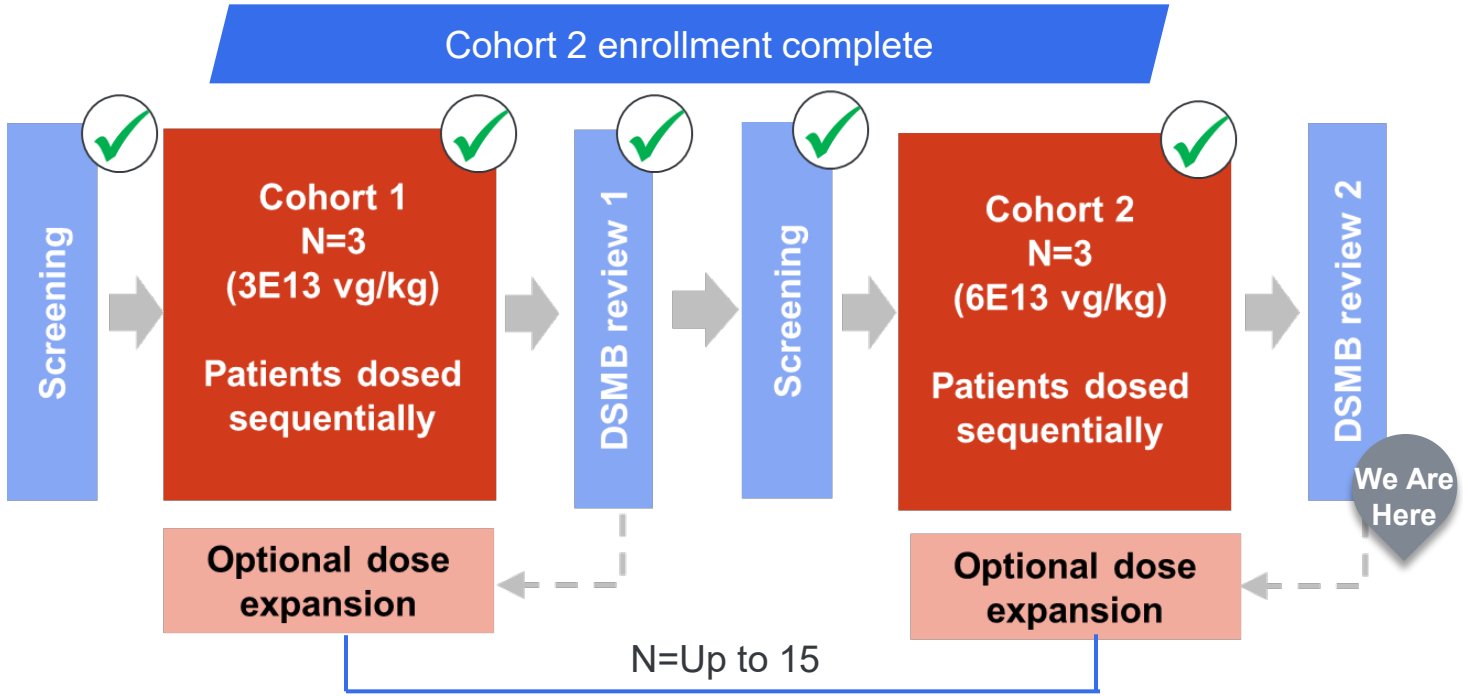
- Safety and tolerability
- Dose-finding
- Pharmacodynamics

Endpoints

- Safety and tolerability
- Transgene uptake and expression
- Changes in PVC and NSVT counts
- ICD shock and VT frequency
- Structural/hemodynamic changes
- Plasma biomarkers
- Patient-reported outcomes

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



NSVT = Non-sustained ventricular tachycardia

VT = ventricular tachycardia

Cohort 1 patients all show signs of electrical instability resistant to SoC at baseline

RIDGE-1 Cohort 1 Screening Characteristics

	Average Patient from RIDGE*	Patient 1	Patient 2	Patient 3
Follow-Up	-	40 weeks	32 weeks	20 weeks
Gender	Male (62%)	Male	Male	Male
Age at Dosing (y)	-	41	36	56
Age of ARVC Dx (y)	34	26	16	49
PVC Count (#/24h)	2,480	2,462	618	2,666
NYHA Class	Class I (74%)	Class I	Class I	Class I
% ICD & Age (y)	100%, 35	25	20	53
Severe VA**	39%	Yes; ≥4x	Yes; ≥6x	-***
VT Ablation	46%	Yes; twice	Yes	Yes
Background meds	≥65%	Yes	Yes	Yes

* Data from RIDGE as of September 2025

** Severe ventricular arrythmias include sustained VT, VF, and appropriate ICD therapy

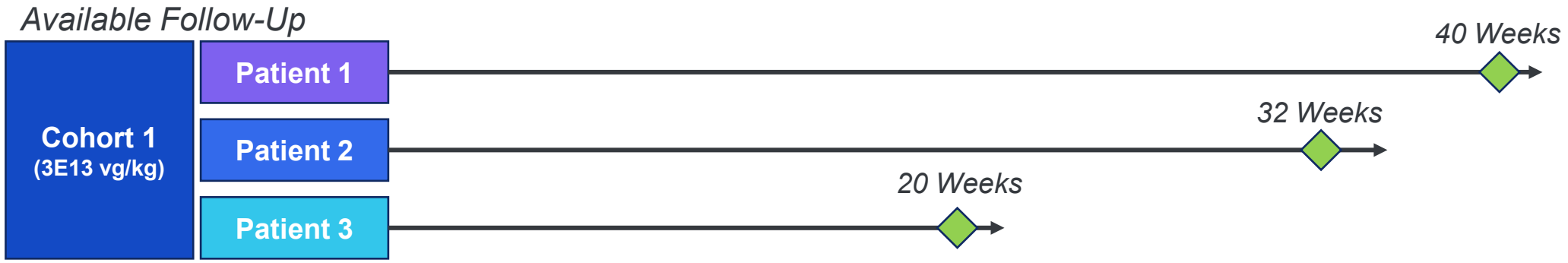
*** Patient 3 likely had prior VT, given history of VT ablation

Data cut as of October 2025

SoC = standard of care

VF = ventricular fibrillations

Cohort 1 safety: 3E13vg/kg dose has been well tolerated



- ✓ Majority of TN-401-related AEs have been **mild, asymptomatic, and manageable**
  - Most frequent AEs were transient elevations of transaminases or troponin requiring no additional treatment and with no sequelae
  - 1 Grade 1 SAE of troponin elevation (classified as "SAE" due to inpatient monitoring)
- ✓ **No TMA**
- ✓ **No cardiotoxicities**
  - No arrhythmias deemed related to treatment
  - No signs of myocarditis on echo, electrocardiography, histology or cardiac MRI
  - No ICD shocks or arrhythmias associated with TN-401 to date
- ✓ All patients **have tapered off immunosuppressive** medicines

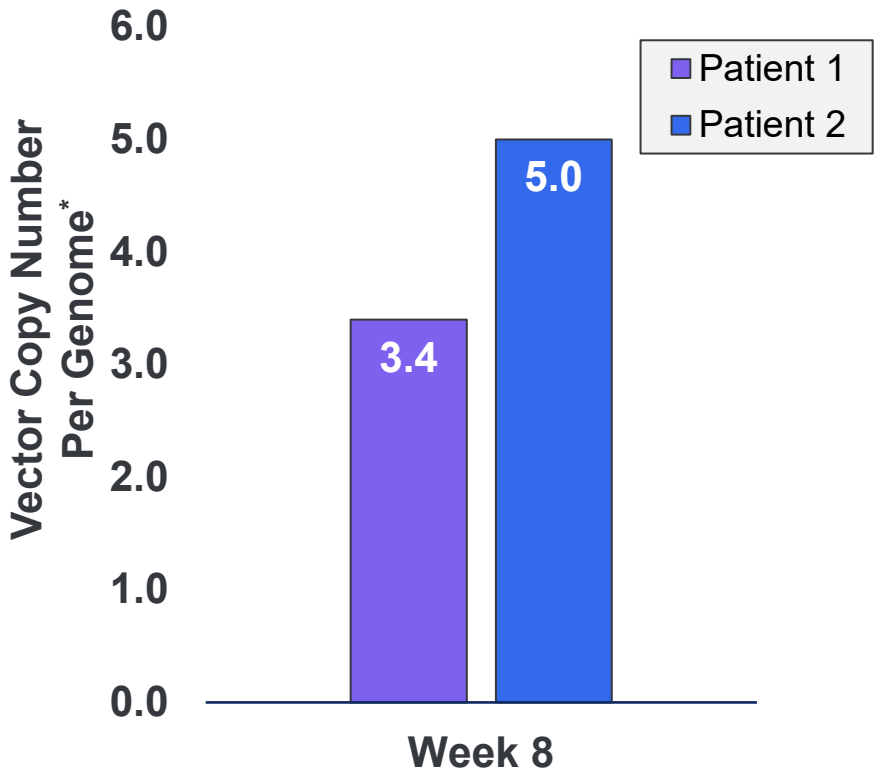
Cohort 2 (6E13 vg/kg) Preview

- ✓ Dosing complete
- ✓ No TN-401-related SAEs reported to date

Data cut as of October 2025
AE = adverse events
SAE = serious adverse event
TMA = thrombotic microangiopathy
MRI = magnetic resonance imaging

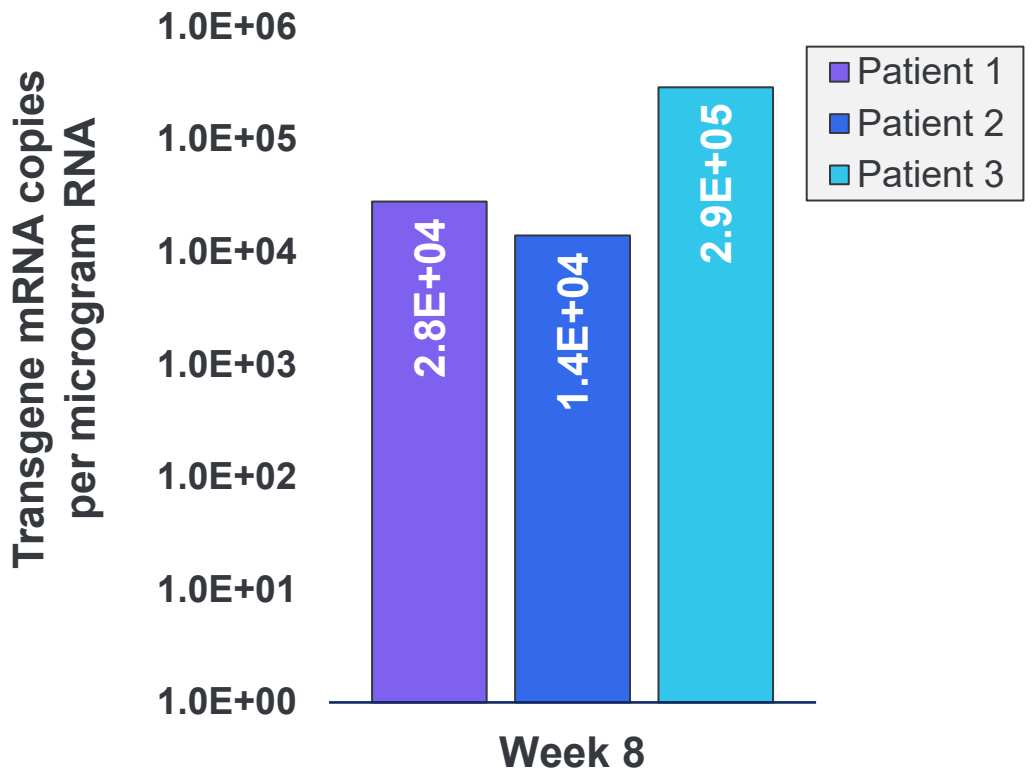
Robust transduction and consistent expression detected in all patients within first 8 weeks

Substantial Transduction at 3E13 vg/kg*



* Vector copy number from Patient 3 not yet available

Robust TN-401 mRNA Levels by 8 Weeks

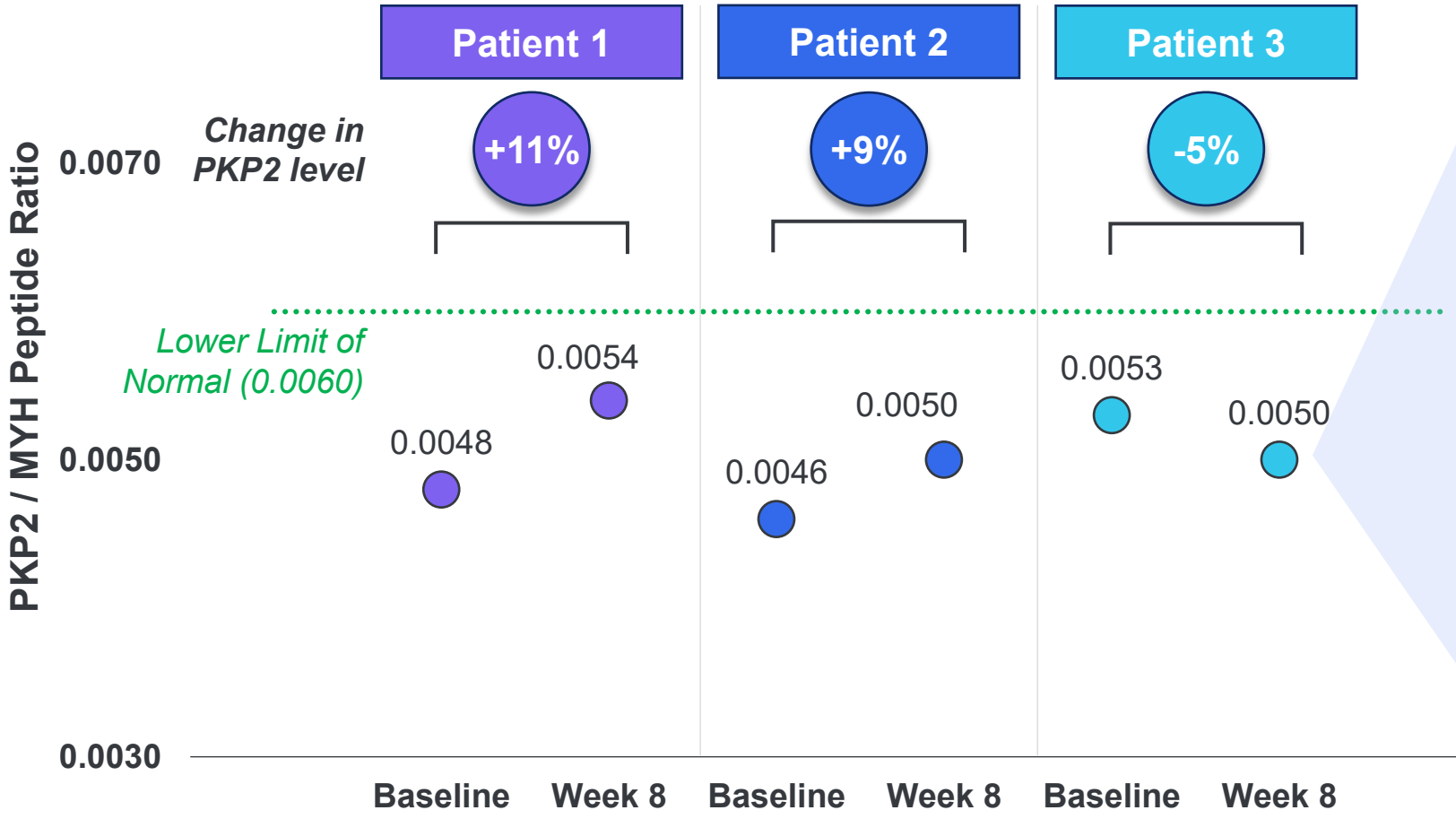


TN-401 DNA and mRNA were not detected in baseline biopsies before TN-401 administration, as expected

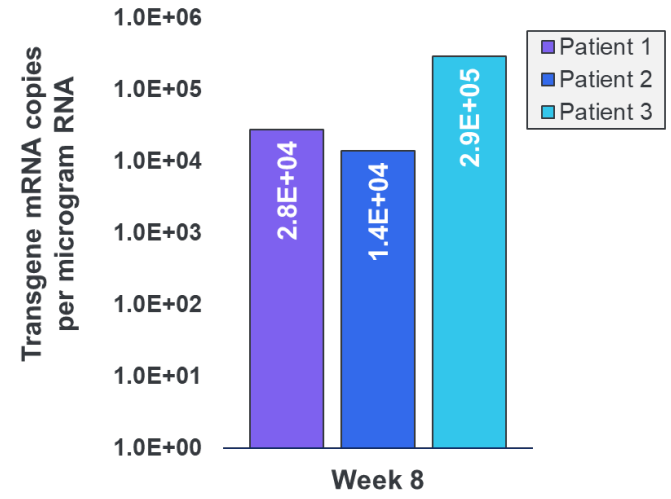
Data cut as of October 2025

Quantifiable increase in PKP2 protein expression in majority of Cohort 1 patients as early as Week 8

PKP2 Protein Levels Over Time in Cohort 1 (3E13 vg/kg)



In mRNA sample, Patient 3 has highest level of expression



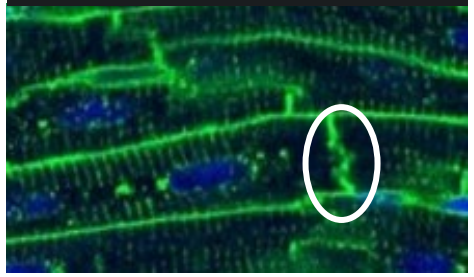
mRNA and protein analyses use tissue from separate biopsy samples

Data cut as of October 2025

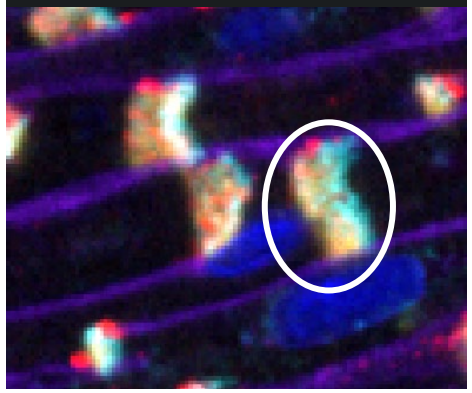
PKP2 localizes appropriately to intercalated discs after TN-401 administration

Healthy Donor Heart

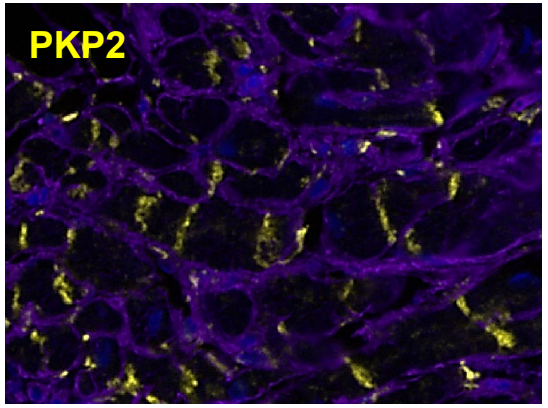
Intercalated disc

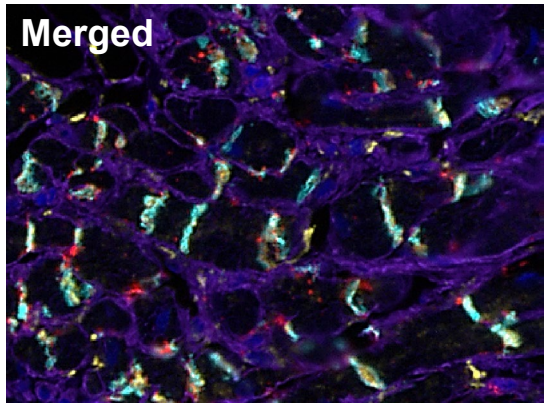


Merged image of PKP2, Cx43, & N-Cad

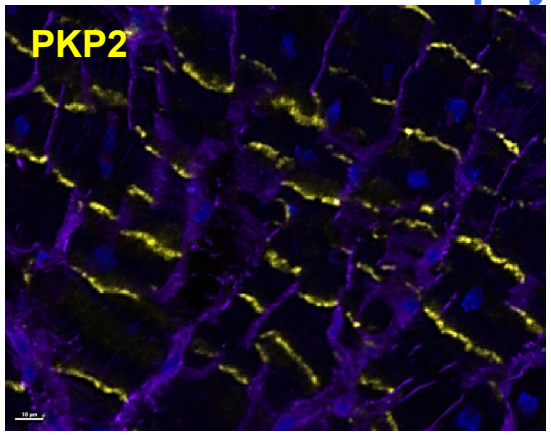


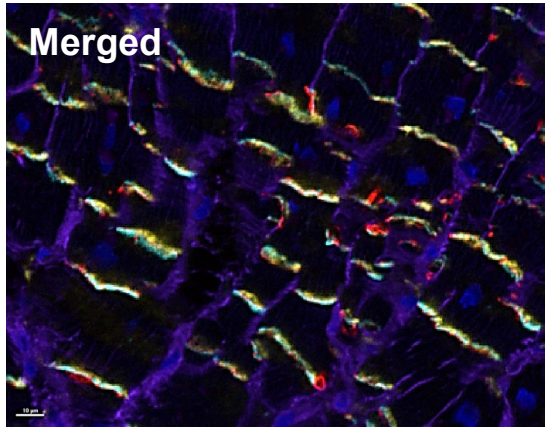
Patient 1: Baseline Biopsy





Patient 1 Week 8 Biopsy





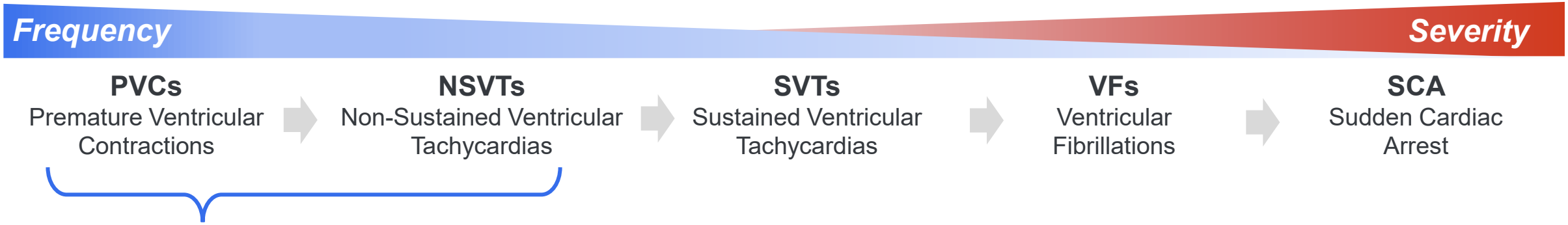
PKP2 protein colocalizes with gap junction (Connexin 43) and intercalated disc (N-Cadherin) proteins based on multiplexed immunofluorescence (mIF) imaging

PKP2
Connexin43
N-Cadherin
Membrane
Nucleus

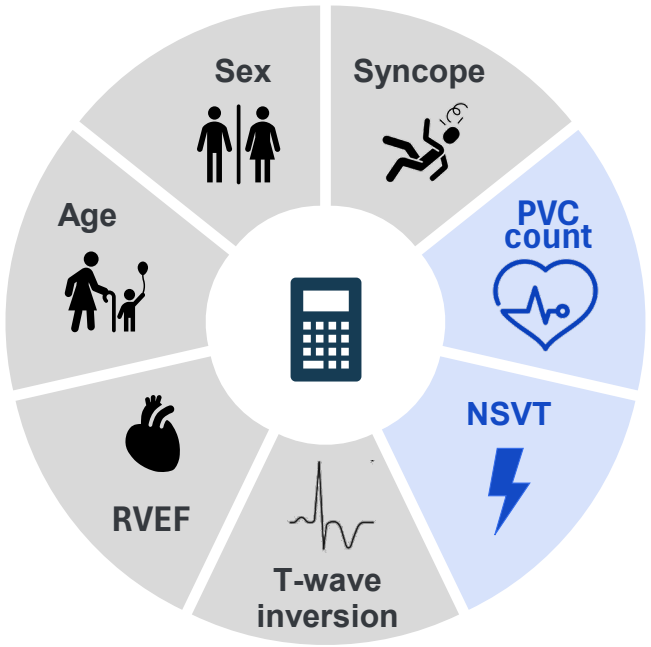
Data cut as of October 2025

Cx43 = Connexin 43
N-Cad = N-Cadherin

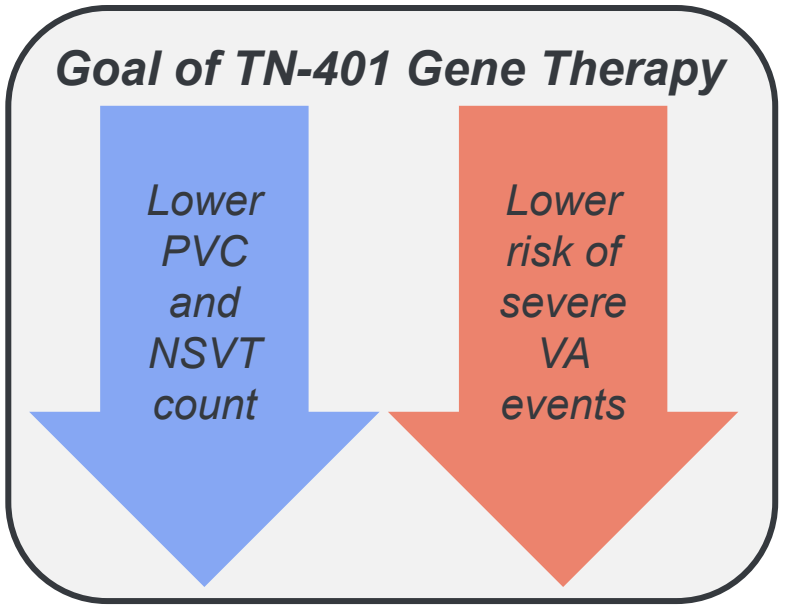
PVC and NSVT burden are key indicators of electrical instability and risk of life-threatening events



ARVC Risk Stratification Calculator



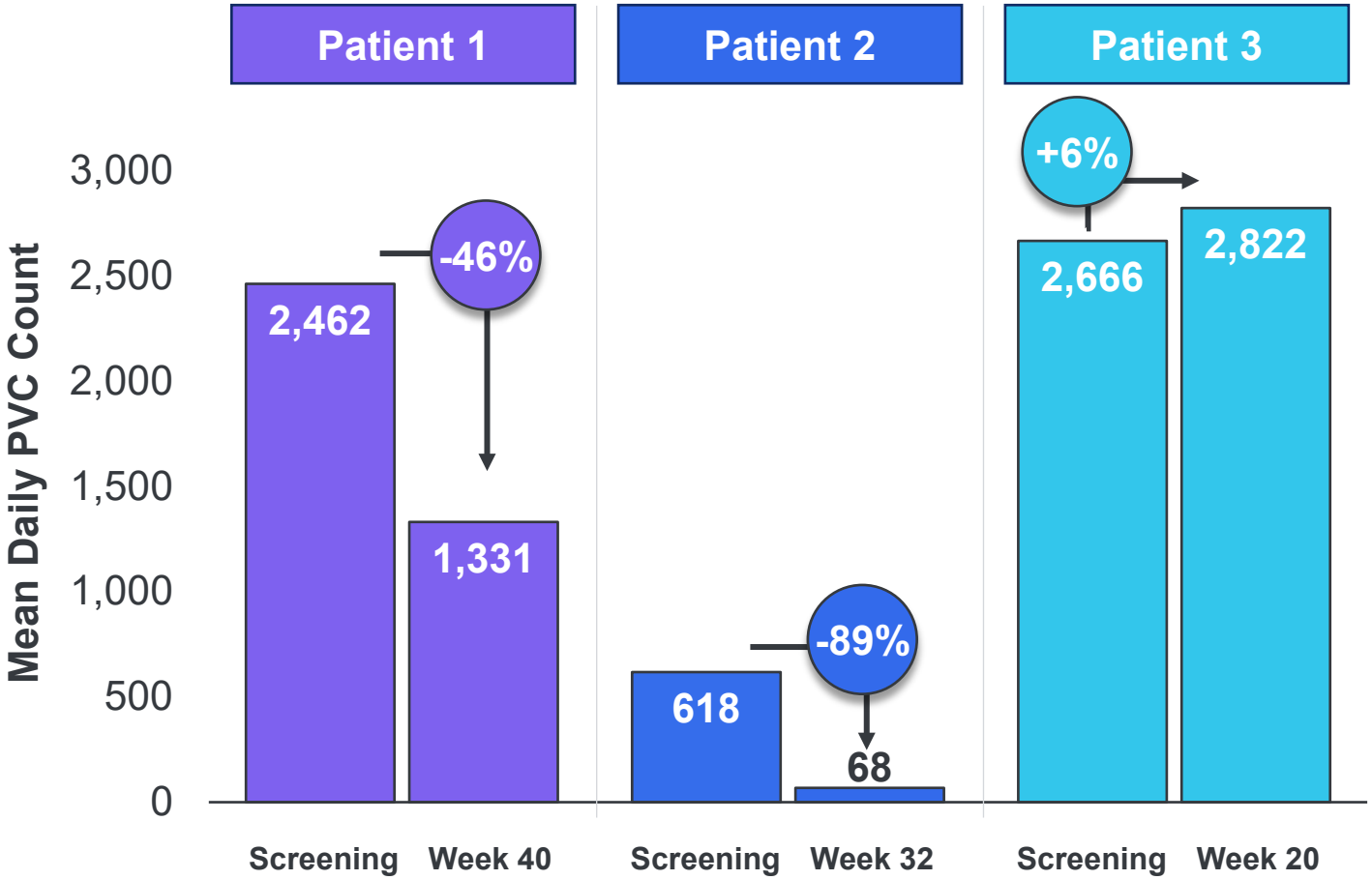
- PVCs are hallmark of PKP2+ ARVC and indicate electrical instability(1)
- Higher PVC counts are a recognized clinical predictor of higher 5-year risk of life-threatening VAs(2)
- PVC burden utilized as risk assessment tool for ICD placement(3)



1. Calkins, et al, HRS 2025
2. Carrick, et al, Circ Arrhythm and Electrophysiol 2022
3. https://arvcrisk.com/

Meaningful decline in PVC burden in first two patients with ≥6 months of follow-up after TN-401 treatment

Change in Mean Daily PVC Rate in Cohort 1 (3E13 vg/kg)



- Daily PVC counts are the average of 7-day ambulatory ECG monitors used for baseline and post-dose arrhythmia quantification
- Among the two patients with ≥6 months of follow-up post-dose, mean **reduction of 67% in PVC count**
- A 67% decrease in daily PVC count translates to **lower odds by 67%** of a sustained VA event over the next 12 months[1]

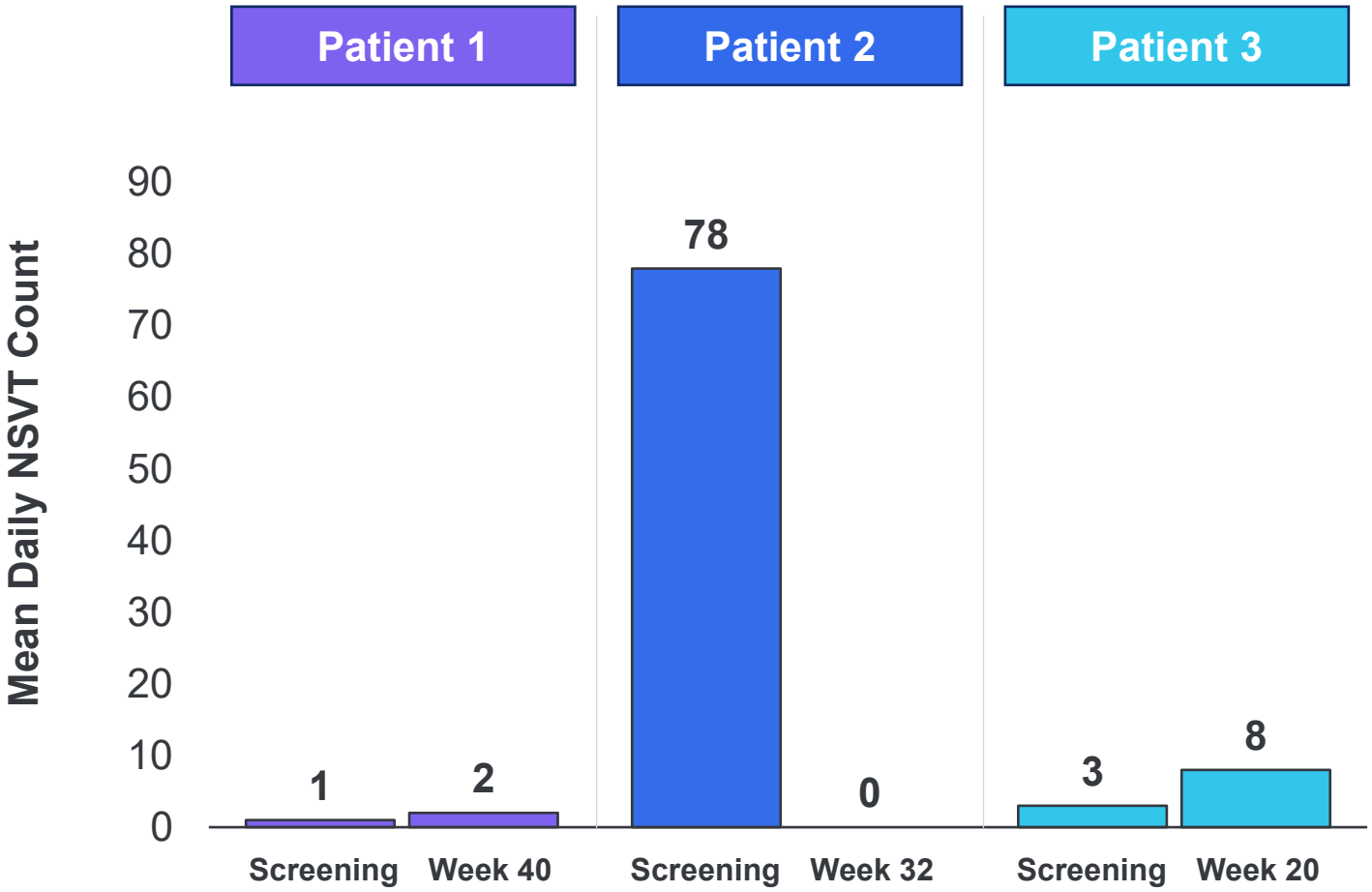
*PVC and NSVT rates calculated using counts over 7-day ambulatory monitoring period
Data cut as of October 2025

ECG = electrocardiogram

1. Gasperetti, *JAMA Cardiol* 2022

NSVT burden was eliminated or stable in first two patients ≥6 months post-dose with TN-401

Change in Mean Daily NSVT Count in Cohort 1 (3E13 vg/kg)



- Patient 1 had low NSVT count at baseline and **remains low**
- Patient 2 had **no NSVTs detected** at most recent visit vs. significant NSVT burden prior to treatment
- Patient 3 had slight increase in NSVTs at <6 months follow up
- Other measures of clinical response, including QRS duration, T-wave inversions, heart function, and NYHA class, were in the normal range or remained stable

*PVC and NSVT rates calculated using counts over 7-day ambulatory monitoring period
Data cut as of October 2025

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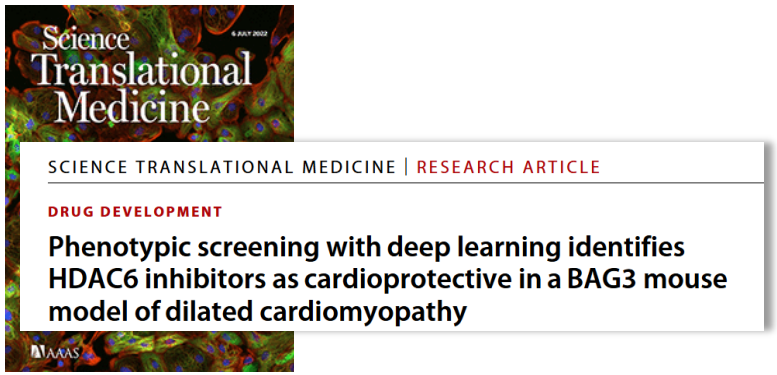
TN-301 HDAC6 Inhibitor

Growing conviction in TN-301 opportunity supported by external preclinical and clinical data

Tenaya has extensively studied HDAC6 inhibition in multiple disease models

Preclinical validation for TN-301 in HFpEF, genetic DCM, PAH, and DMD



HDAC6 inhibition multi-modal MOA externally validated

- >1200 articles
- HDAC6 inhiition efficacy in multiple disease models – including cardiac & cardiac adjacencies – confirm Tenaya insights

Clinical results with pan-HDAC inhibition de-risks TN-301 opportunities

Duvyzat™ (givinostat)

- Givinostat significantly slowed disease progression in ambulatory DMD patients (4SC, NSAA)
- MOA attributed to anti-inflammatory effects of HDAC inhibition
- Approved in US & EU for patients age > 6 yo
- Robust commercial uptake, including use on top of μ–dystrophin therapies

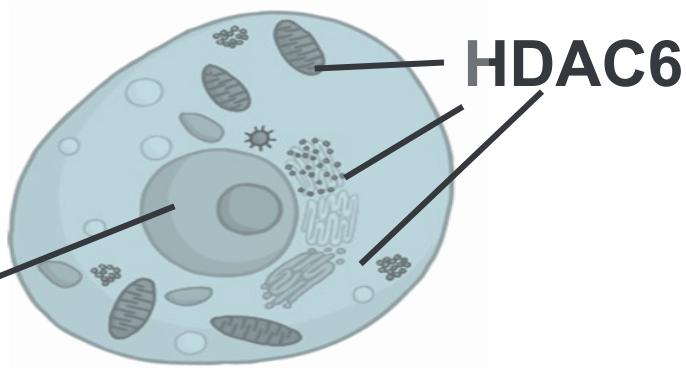
DCM = dilated cardiomyopathy
PAH = pulmonary hypertension
MOA = Mechanism of action

4SC = 4 Stair Climb
NSAAI = North Star Ambulatory Assessment

Tenaya's HDAC6 inhibitors offer distinct advantages

HDACs vs. HDAC6

Histone deacetylases are enzymes that regulate cellular processes and gene expression

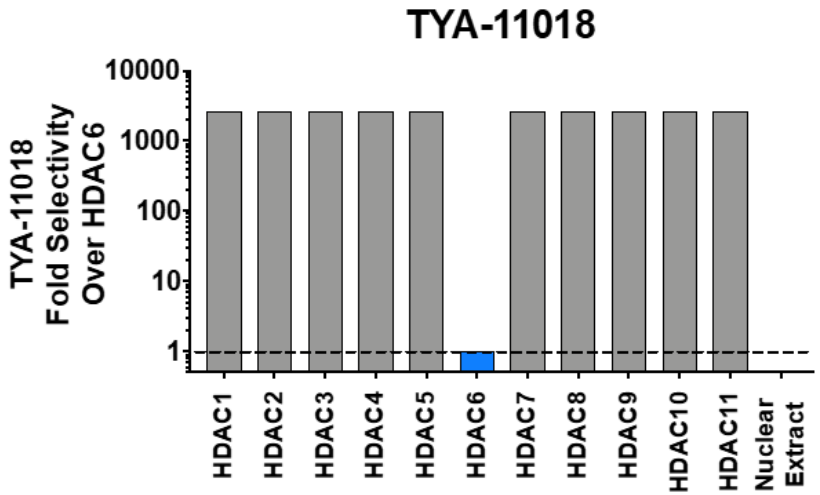


HDACs 1-3, 5, 8 and 11 primarily work inside the cell nucleus. HDACs 4, 7 and 9 shuttle between nucleus and cytoplasm.

HDAC6 is a cytoplasmic enzyme that acts on proteins (e.g., Hsp90, tubulin, SMAD 2/3, cortactin) to modulate cytoskeleton structure, protein quality control and cellular stress responses.

Tenaya's HDAC6 Inhibitors

- Highly specific: ≥3500x selectivity for HDAC6 vs. other HDAC
- Selectivity provides potential safety advantages vs pan-HDAC inhibitors and allows for higher dosing to maximize efficacy



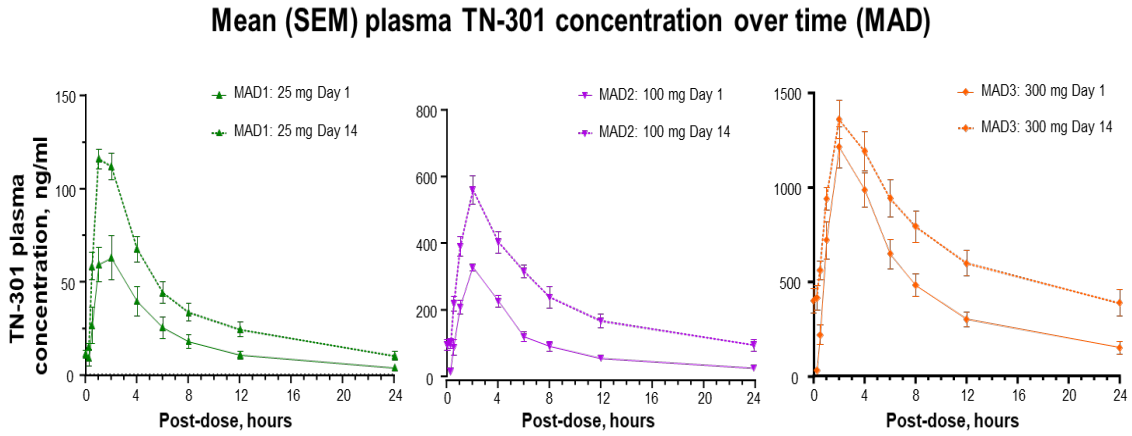
Hsp90 = heat shock protein 90
SMAD 2/3 = Suppressor of Mothers Against Decapentaplegic
BAG3 = Bcl2-associated athanogene 3

Phase 1 trial of TN-301 of healthy participants

TN-301 was generally well tolerated across broad dose ranges

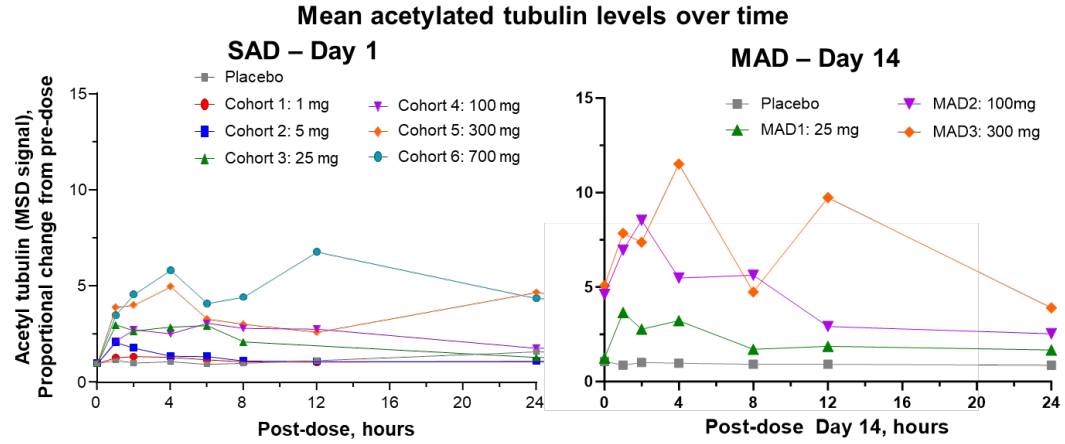
- Single-ascending doses (SAD) of 1mg – 700mg
- Multiple ascending doses (MAD) of 25mg, 100 mg and 300 mg for 14 days
- AEs (primarily GI related) occurred with similar frequency to placebo; no AE increase with dose
- No thrombocytopenia, no QT prolongation risk, and no histone modification seen

PK and half-life support once-daily dosing



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

Selective HDAC6 inhibition and target engagement at low doses



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

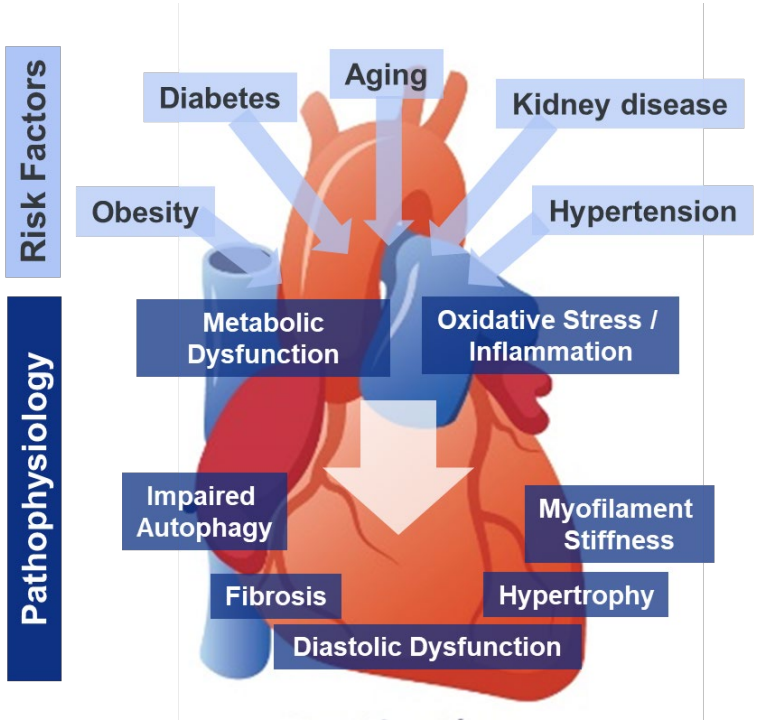
Increasing TN-301 exposure correlated with PD effect

AEs = Adverse events
GI = gastrointestinal
PK = pharmacokinetics

HDAC6 inhibition normalizes several biological hallmarks of HFpEF pathophysiology

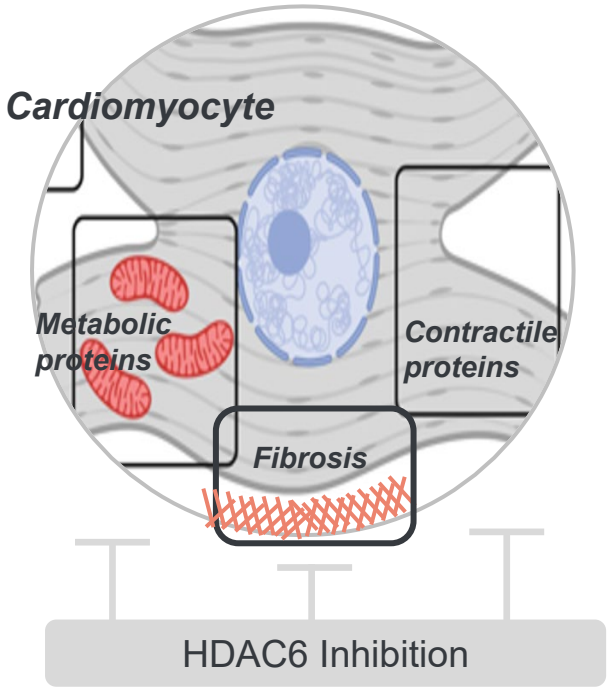
HFpEF is a complex syndrome

Multiple contributing risk factors resulting in shared pathophysiology



HDAC6 inhibition shows evidence of direct and systemic effects on the heart in models of HFpEF*

HDAC6 is localized to the cell cytoplasm where it interacts with multiple proteins to coordinate cellular processes



Direct

- Decreased hypertrophy
- Improved diastolic function
- Reduced fibroblast activation
- Enhanced energetics

Systemic

- Metabolic dysfunction
- Improved glucose tolerance
- Reduction of inflammation
- Improved autophagy

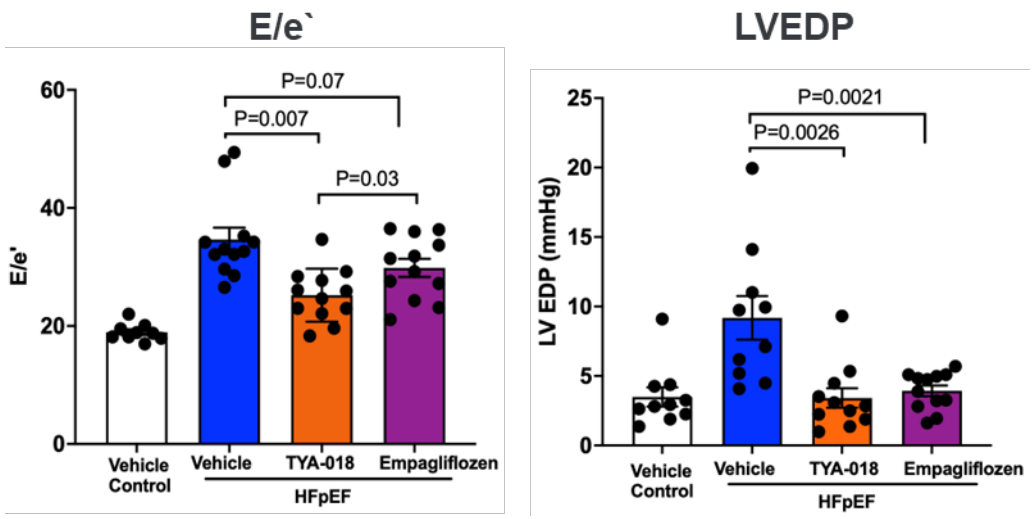
HDAC6 = Histone deacetylase 6 | HFpEF = heart failure with preserved ejection fraction

** Tenaya preclinical experiments*

HDAC6 inhibition demonstrates potential for use as single-agent or in combination with SGLT2 inhibitor in HFpEF models

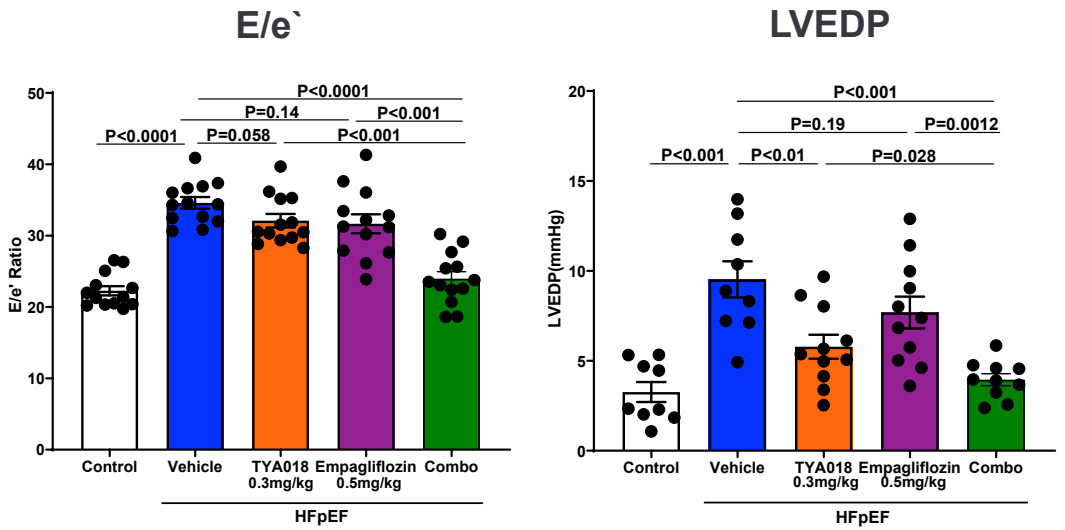
HDAC6 inhibition shows comparable efficacy to SGLT2 inhibitor

Preclinical single-agent HFpEF mouse model



HDAC6 inhibition combined with SGLT2 inhibitor shows additive benefit

Preclinical results in combination with SGLT2 inhibitors HFpEF mouse model



HDAC6 inhibition demonstrates greater impact on improving metabolism, oxidative stress and inflammation using gene set enrichment analysis of pathway and functional level HFpEF changes

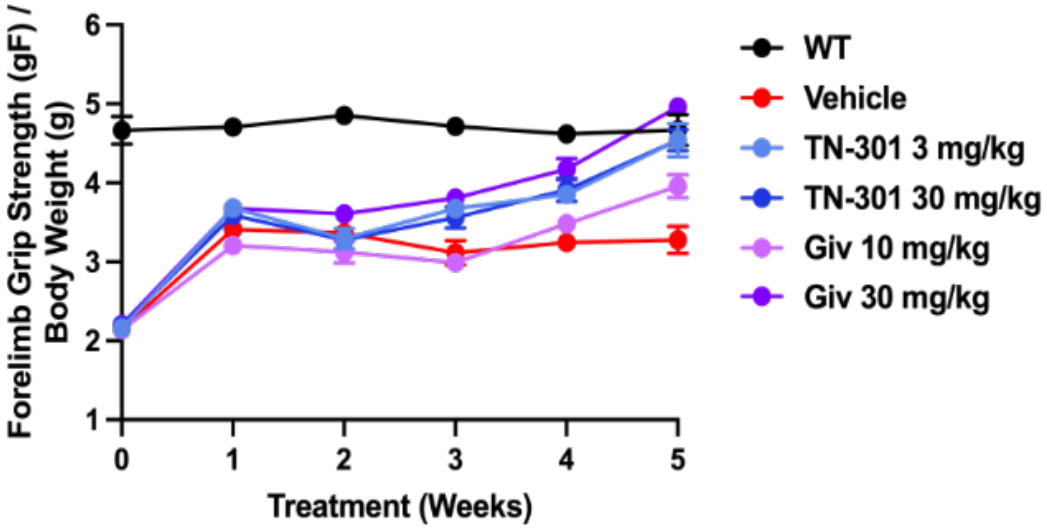
SGLT2 =sodium glucose cotransporter-2

TN-301 demonstrates potential to improve skeletal and cardiac muscle deficits in DMD model with fewer liabilities

Preclinical data suggest HDAC6 inhibition may be substantially driving the benefits observed to date with pan-HDAC inhibitors in DMD clinical studies

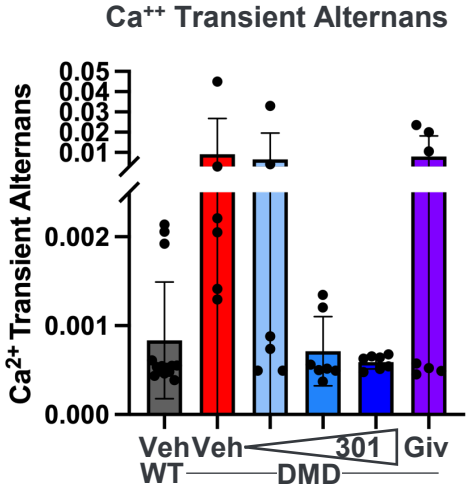
Low-dose TN-301 improved grip strength to WT levels and outperformed givinostat clinical dose

***Mdx* mouse model of DMD**



TN-301 corrected key drivers of DMD cardiomyopathy and outperforms givinostat

Engineered heart tissue from human DMD hiPSC-CMs



- TN-301 corrected Ca+ handling abnormalities and mitochondrial respiration
- Givinostat did not improve these clinically relevant drivers of DMD-CM

EHT = Engineered Heart Tissue
hiPSC-CM = Human Induced Pluripotent Stem Cell Derived Cardiomyocytes

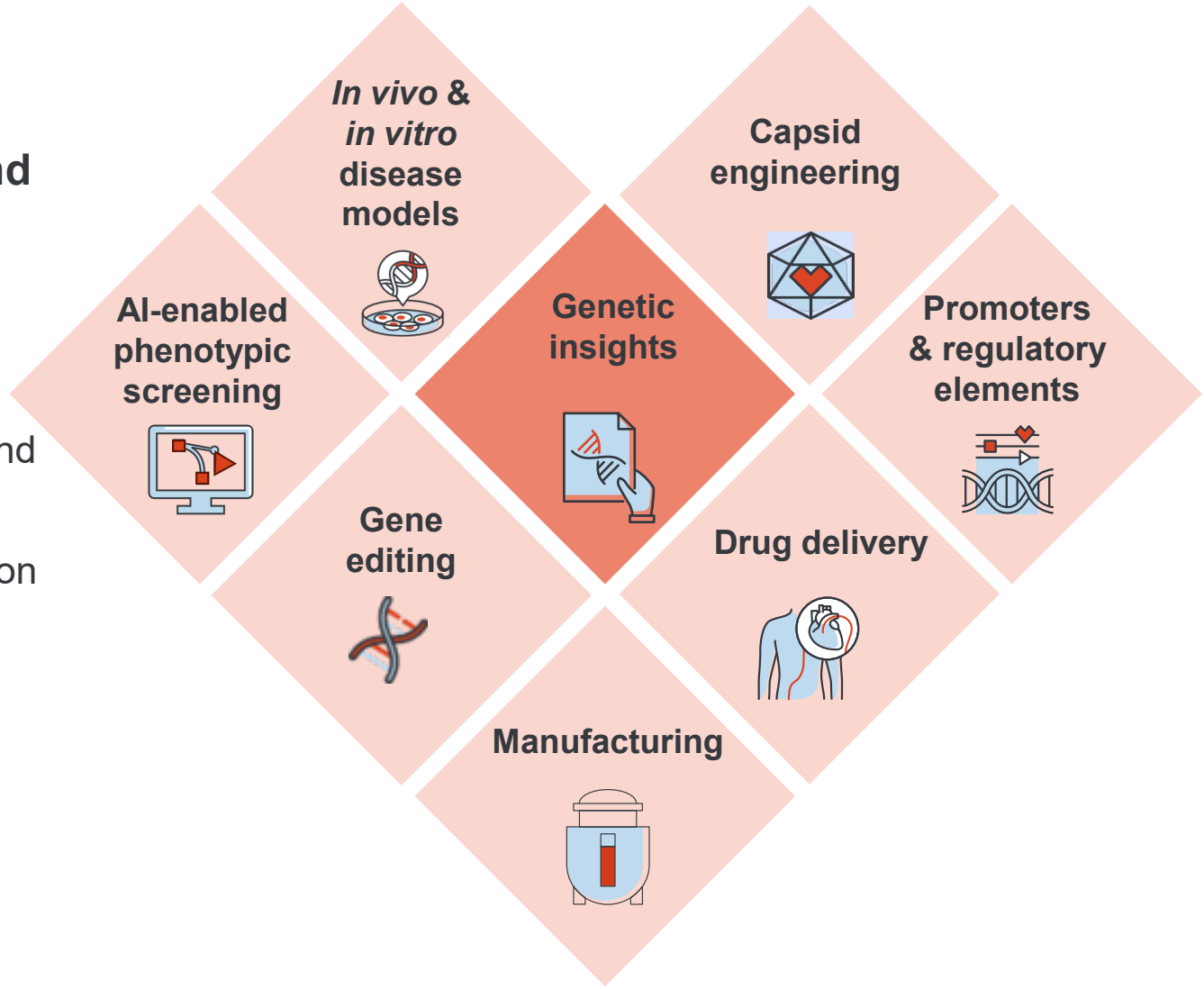
TENAYA™ THERAPEUTICS

Enabling Capabilities

Integrated internal capabilities power modality-agnostic drug discovery engine

Target Discovery and Validation

- ✓ Deep insight
- ✓ Rapid design iterations
- ✓ Encouraging efficacy and safety signals
- ✓ Human genetic validation



Design, production, and delivery of genetic medicines

- ✓ Targeted delivery
- ✓ Robust expression
- ✓ Better product profiles
- ✓ Growing IP portfolio

TENAYA THERAPEUTICS

Research collaboration with Alnylam

Goal

- Multi-target research collaboration
- Identify and validate novel genetic targets for cardiovascular indications

Responsibilities

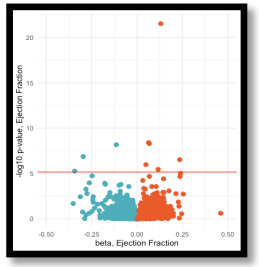
- Tenaya consucts target validation
- Alnylam obtains WW license to any selected leads and is responsible for all clinical development and commercial activities

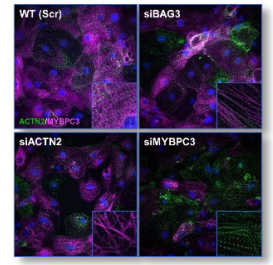
Financial Terms

- Up to $10M upfront
- Research reimbursement
- Up to $1.1B in future milestone payments

TARGET IDENTIFICATION

Human Genetics + *AI-powered Phenotypic Screening*





IN VITRO & IN VIVO VALIDATION

Proprietary disease models


Human iPSC-CMs


Engineered human heart tissue


In vivo disease models

TENAYA™ THERAPEUTICS

Upcoming Milestones

2026 anticipated program milestones

TN-201 for *MYBPC3*-associated HCM

1H

- Enroll 6E13 vg/kg expansion cohort
- MyPEAK-1 interim Cohort 2 data

2H

- MyPEAK-1 ~2-year Cohort 1 and ~52-week Cohort 2 data
- Continue MyPEAK-1 enrollment
- Pursue regulatory alignment on pivotal plans

TN-401 for *PKP2*-associated ARVC

1H

- Conduct Cohort 2 DSMB
- Enroll RIDGE-1 expansion cohort
- RIDGE-1 ~52-week Cohort 1 and initial Cohort 2 data

2H

- RIDGE-1 interim Cohort 2 data
- Continue RIDGE-1 enrollment
- Pursue regulatory alignment on pivotal plans

Thank you