Corporate Presentation

Jefferies Global Healthcare Conference

June 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 and TN-401, preclinical efforts and timelines; clinical outcomes, which may materially change as patient enrollment continues or more patient data become available; availability and content of data from MyPEAKTM-1 and RIDGETM-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 10Q for the quarter ended March 31, 2026, 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

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

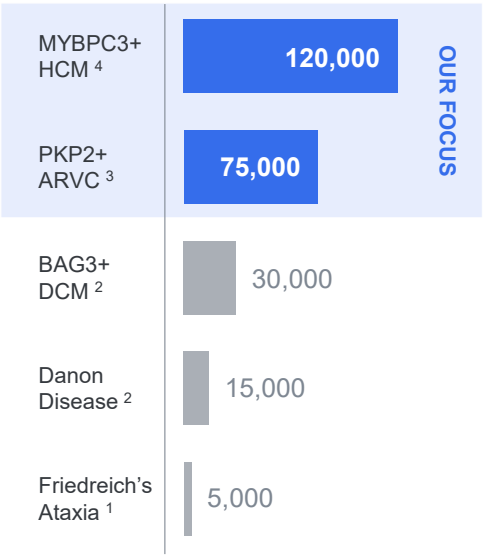
Track record of execution

IMMEDIATE OPPORTUNITY:

Advancing TN-201 and TN-401 towards pivotal studies

Large market potential in rare disease setting

Addressable populations in the U.S.



Early evidence of clinically meaningful benefit

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

TN-401 achieved meaningful reductions 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

TN-201

- Interim MyPEAK-1 data for Cohort 2 and updates from Cohort 1 (1H)
- **One-year Cohort 2 data and two-year Cohort 1 data (2H)**

TN-401

- **One-year data for Cohort 1 and initial Cohort 2 data (1H)**
- Interim Cohort 2 data (2H)

Seeking regulatory clarity on approvable endpoints and pivotal trial design

Updates expected in 2H'26

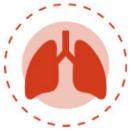
1. Lexeo presentation, Oct 2025
2. Rocket Pharma presentation, Sep 2025
3. Sedaghat-Hemedani, et al., *Clin Res Cardiol*. 2018
4. Groeneweg, et al, *Circ Cardiovasc Gen 2015* & McKenna, et al, *Nature Rev Cardio* 2021

NEXT OPPORTUNITY:

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

Broad utility demonstrated by Tenaya and others

• HFpEF
• (Genetic) DCM



• PH-HFpEF
• PAH

DMD / DMD-cardiomyopathy (+ other MDs)

MoA of HDAC6 inhibition well understood

DECREASES
- Inflammation
- Oxidative stress
- Fibrosis
- Metabolic dysregulation

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

Safety established as foundation for future investigation

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

MODALITY AGNOSTIC PIPELINE

Broad clinical stage programs supported by innovation engine

CLINICAL-STAGE PIPELINE

Program	Modality	Epidemiology	Research	Preclinical	Phase 1b/2
TN-201 *MYBPC3*+ HCM	AAV9 gene therapy	120K			
TN-401 *PKP2*+ ARVC	AAV9 gene therapy	75K			
TN-301 HFpEF/cardiac, muscular or metabolic disorders	Small Molecule	Prevalent & Rare			

EARLY-STAGE INNOVATION ENGINE

TN-101 Post-MI Heart Failure	Cellular regeneration	Prevalent			
TN-501 PLN$^{R14\ del}$ DCM	Gene editing	Rare			
DWORF DCM & HFrEF	AAV gene therapy	Rare & Prevalent			
Multiple undisclosed targets	Genetic medicines Other	Prevalent & Rare		*Partnered with* Alnylam PHARMACEUTICALS	

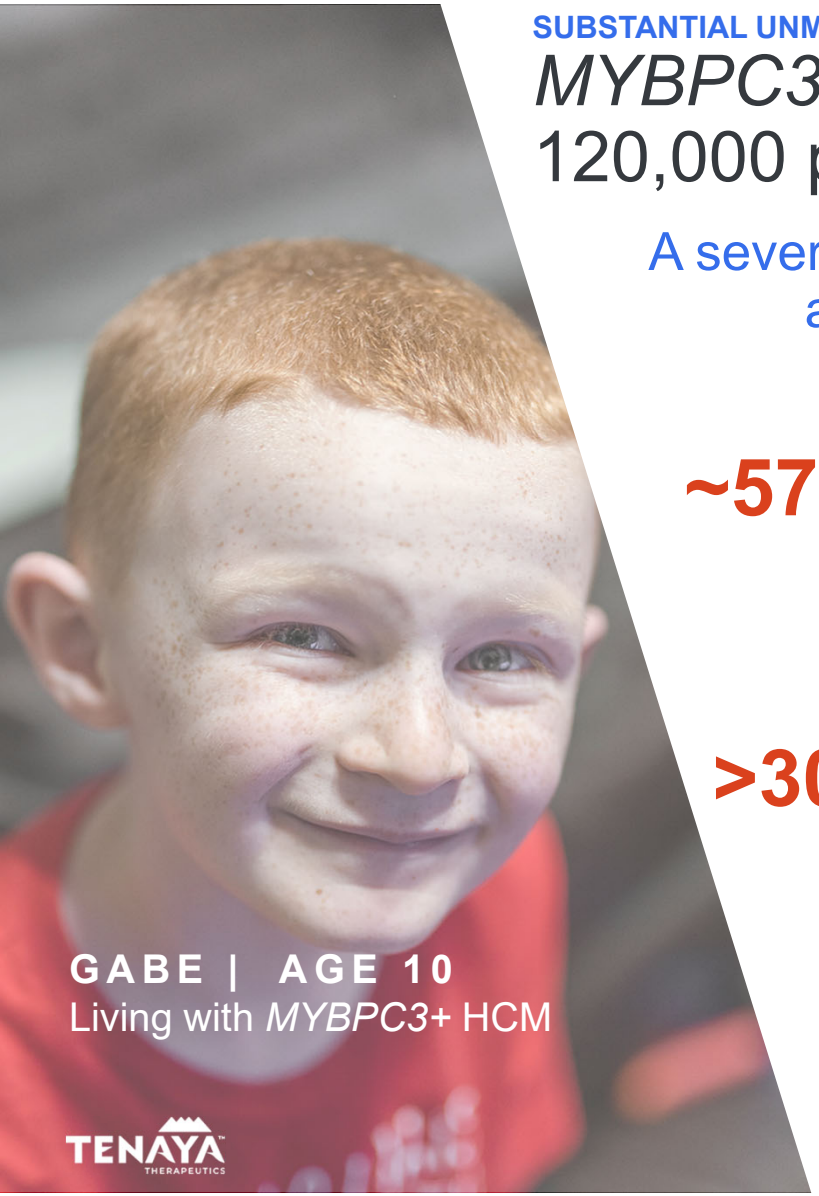
MYBPC3 = Myosin binding protein C3 (gene)
HCM = hypertrophic cardiomyopathy
AAV9 = adeno-associated virus, serotype 9

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

TENAYA™ THERAPEUTICS

TN-201 for *MYBPC3*-associated HCM



SUBSTANTIAL UNMET NEED

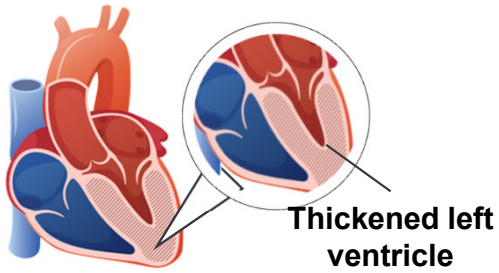
MYBPC3-associated HCM is estimated to affect 120,000 people in the U.S. alone(1)

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)

HCM HEART



- 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

TRIAL DESIGN

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

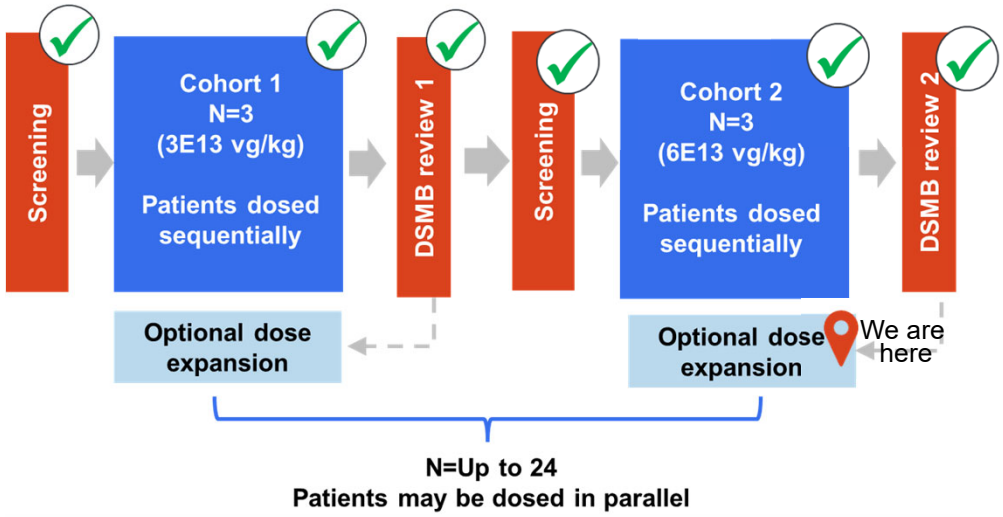
- Safety, tolerability
- Dose-finding
- Pharmacodynamics

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; no baseline for patients 1-2

HIGHLIGHTS

Interim MyPEAK-1 Cohort 1 & 2 Data

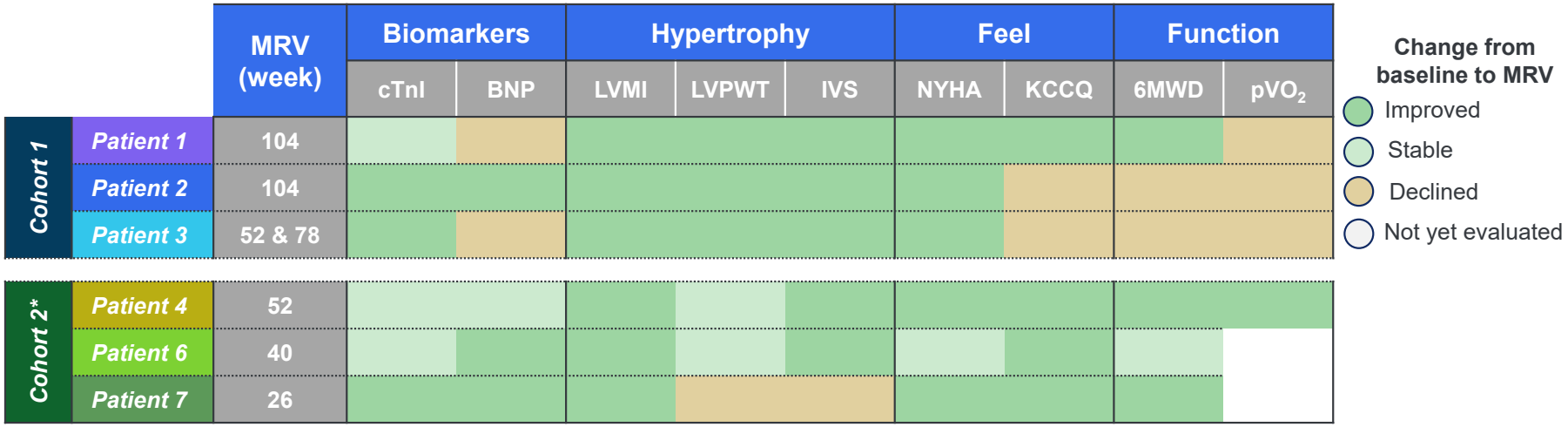
1. **CLINICAL: Multiple parameters of disease improving; All evaluable patients show signs of cardiac remodeling plus improvements in symptoms**

2. **BIOPSY: TN-201 is reaching heart cells and being expressed**

3. **SAFETY: TN-201 well tolerated at both doses**

CLINICAL RESULTS

Multiple parameters improving with durable responses in Cohort 1 and signals of deeper/faster responses in Cohort 2



- All patients show signs of cardiac remodeling and symptom improvement
  - Cohort 1 responses are durable out to 2 years
  - Cohort 2 responses suggest greater or equivalent responses within shorter post-dose timeframe
- Biopsy evidence of TN-201 transduction and expression in heart cells
- TN-201 was well tolerated at both doses

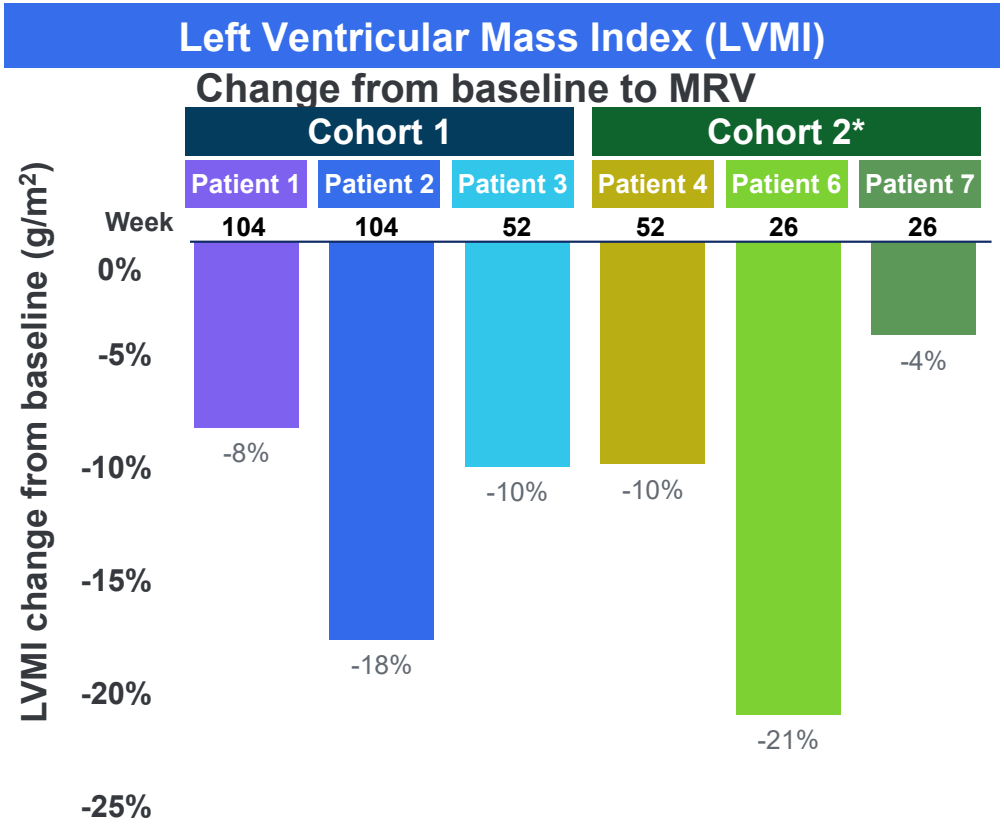
May 2026 data cut off

**Patient 5 lost to follow up after tapering from immunosuppressives*

cTnI = cardiac troponin
BNP = N-terminal pro B-type natriuretic peptide

CLINICAL RESULTS

Decreases in multiple measures of hypertrophy suggest cardiac remodeling occurring over time



All patients achieved reductions in LVMI

- MyPEAK-1 patients all severely hypertrophied with baseline LVMI of 139g/m2
- LVMI decreases sustained through year 2 for first two Cohort 1 patients
- Similar – or greater – reductions observed as early as Week 26 week in Cohort 2 vs. Cohort 1
- LVMI reduced by ≥10% in a majority of patients

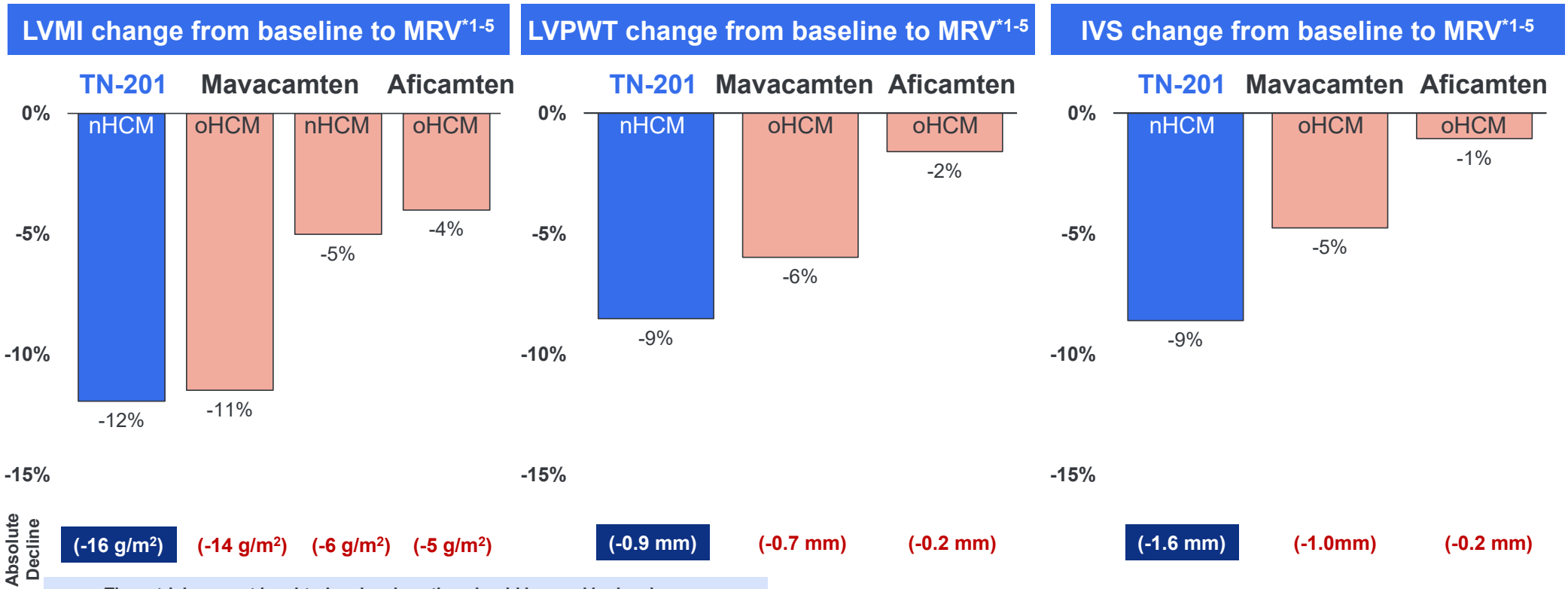
Consistent changes observed in other measures of wall thickness

- Interventricular septum thickness decreased for five of six patients
- Posterior wall thickness decreased for Cohort 1 patients and remained stable for the majority of Cohort 2

Other measures of cardiac structure and function remain largely stable

May 2026 data cut off
**Patient 5 lost to follow up after tapering from immunosuppressives*

TN-201 hypertrophy decreases compare favorably with results observed among peers



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.

LVPWT = left ventricular posterior wall thickness
IVS = interventricular septum

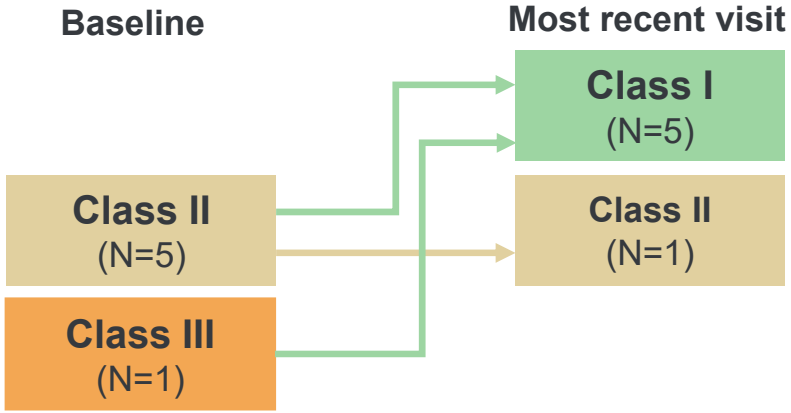
*Mavacamten oHCM & nHCM readouts at 128 and 48wk, respectively
*Aficamten oHCM readout at 24wk
Posterior and septal wall thickness not reported in nHCM

[1]Desai, et al., *Circ* 2025
[2]Hegde, et al., *JACC* 2021
[3]Desai, et al., *JACC* 2025
[4]Hegde, et al., *JACC* 2024
[5]Sun, et al., *JACC* 2022

CLINICAL RESULTS

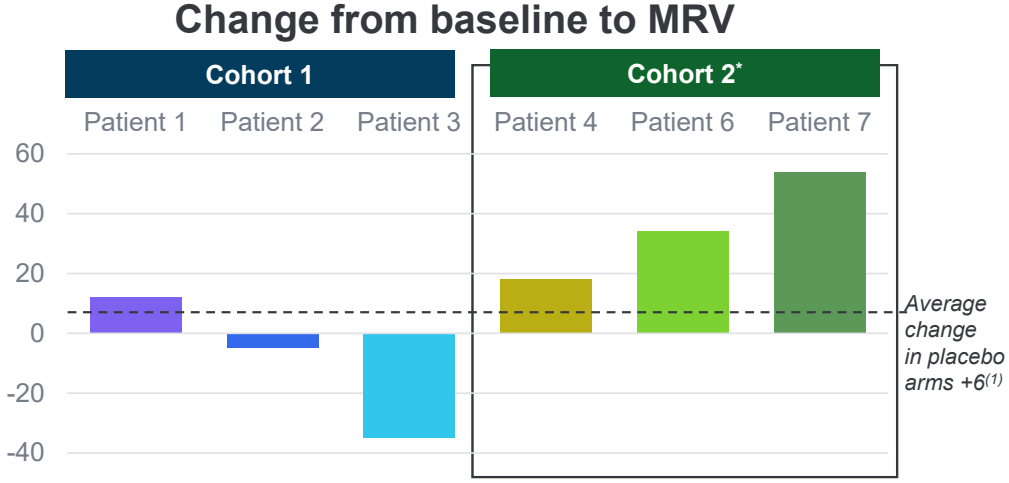
Symptom burden reduced in all patients by at least one measure following TN-201 treatment

New York Heart Assoc. Classification



- **83% achieved Class I (asymptomatic) status**
- Changes in NYHA class coincided with improvements in other parameters

Kansas City Cardiomyopathy Questionnaire



- **67% achieved meaningful improvements in KCCQ Clinical Summary Score(2)**
- Cohort 2 average change from baseline +36 points
- All Cohort 2 patients' scores are now in the "good to excellent" range (75-100 points)

May 2026 data cut off
**Patient 5 lost to follow up after tapering from immunosuppressives*

NYHA = New York Heart Association
KCCQ = Kansas City Cardiomyopathy Questionnaire

1. Averaged from mavacamten studies (MAVERICK, VALOR, EXPLORER, ODYSSEY) and aficamten studies (ACACIA, SEQUOIA published data)
2, Spertus, et al, JACC State-of-the-art review 2020

FUNCTIONAL CAPACITY

Functional improvements observed in at least one measure for a majority of Cohort 2 patients

Six-minute Walk Test

Cohort 2* change in 6MWD from baseline to MRV

	Baseline	MRV	Difference
Patient 4	500	755	+255
Patient 6	420	390	-30
Patient 7	247	297	+50

Measured in meters

Cardiopulmonary Exercise Capacity

Cohort 2* change in pVO_2 from baseline to MRV

	Baseline	MRV	Difference
Patient 4	16.0	18.4	+2.4 (15%)
Patient 6	13.3	Not yet evaluated	
Patient 7	13.8		

Measured as mL/kg/min

- Majority of Cohort 2 demonstrated increased exercise capacity in 6MWD, peak VO_2 or both at an early timepoint
- All improvements exceeded the minimal clinically important difference for both assessments[1,2]
- Cohort 1 performance may be confounded by preexisting functional limitations and/or relatively longer duration and higher dose of immunosuppression

May 2026 data cut off

**Patient 5 lost to follow up after tapering from immunosuppressives*

6MWD = 6-minute walk distance
pVO_2 = Peak oxygen uptake

[1]MCID= >30m; Shoemaker, et al., *Cardiopulm Phys Ther J* 2013
[2] MCID=6% increase; Swank, et al., *Circ Heart Fail* 2014

SAFETY OBSERVATIONS

TN-201 has been well tolerated at both doses with no new treatment-related safety events to report

- Adverse events (AEs) associated with TN-201 treatment were **mild, transient and/or reversible**
  - Following (previously reported) Grade 3 liver enzyme elevation in Patient 1, immune monitoring and management changes were undertaken
- **No clinical TMA**
- **No need for complement inhibitors**
- **No signs of cardiotoxicity**

The most common AE related to TN-201 were reversible, asymptomatic liver enzyme elevations

TN-201-related AEs	Cohort 1* (3E13 vg/kg; n=3)				Cohort 2* (6E13 vg/kg; n=3)			
	Gr 1	Gr 2	Gr 3	**Total**	Gr 1	Gr 2	Gr 3	**Total**
Liver enzyme elevations	1	1	1	**3**	1	-	-	**1**
Platelet reduction/ thrombocytopenia	-	-	-	**0**	2	-	-	**2**
Complement elevation	-	-	-	**0**	2	-	-	**2**

Two events were classified as serious adverse events due to in-patient treatment and monitoring:

- Moderate (Grade 2) transaminase elevations, treated with IV steroids
- Mild (Grade 1) complement elevation monitored in hospital

*Previously disclosed, no new related AEs since November 2025 presentation

Data cut as of May 2026

LOOKING AHEAD

Opportunity to explore TN-201 in the full spectrum patients with *MYBPC3-associated HCM* 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

Recent engagements with regulators globally reflect potential future directions

Tenaya is engaging with regulators to pursue alignment on pivotal endpoints with an initial focus on the pediatric population where there is significant need

EMA
EUROPEAN MEDICINES AGENCY

PRIME designation received

- Recognizes potential of TN-201 to address significant unmet medical needs
- Enables the EMA support to optimize data generation and accelerate assessment of medicines applications

FDA U.S. FOOD & DRUG ADMINISTRATION

Rare Disease Evidence Principles acceptance for biallelic pediatric patients

- New FDA initiative to support development of therapies for ultra-rare genetic diseases (<1,000 patients)
- Enables early and ongoing collaboration to align on regulatory strategy, trial design, and innovative approaches to generating evidence needed to support potential approval

MyCLIMB FINDINGS

Children with *MYBPC3*+ disease are at heightened risk for heart failure, arrhythmias, hospitalizations and death[1]

The unmet need in pediatric patients

~3000 diagnosed patients currently under age 18 in the U.S.[2]

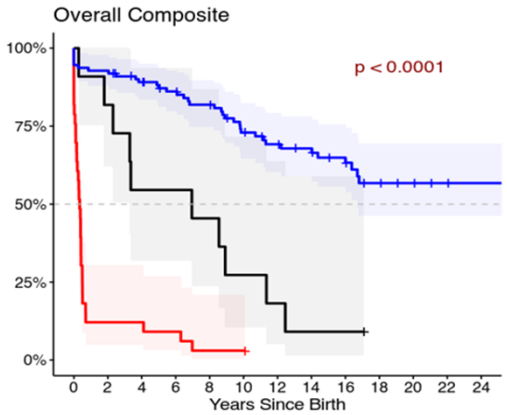
>90% of patients in MyClimb have non-obstructive HCM[1]

36% more likely to develop life-threatening ventricular arrhythmias[3]

0 treatment options targeting the underlying cause of disease or capable of slowing progression

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

Genotype status impacts outcomes[1]



MyClimb Natural History Study

HOMOZYGOUS: 85% die or require transplant before age 1

COMPOUND HETEROZYGOUS: 64% experienced heart-failure related hospitalizations before age 10; 27% required transplant or died

HETEROZYGOUS: Median age of diagnosis was 6.5 years. Significant burden of cardiomyopathy including potentially fatal arrhythmias and hospitalization

1. Brugada, et al, ESC 2025
2. SHaRe registry; Data on file
3. Marston, et al, *Eur Heart Journal* 2021

TENAYA™ THERAPEUTICS

TN-401 for *PKP2*-associated ARVC

SUBSTANTIAL UNMET NEED

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

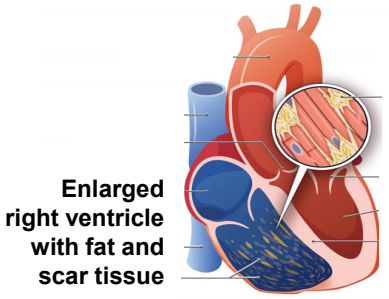
ARVC is a severe and progressive genetic heart disease lacking therapeutic treatment options

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

~40% Of those diagnosed with ARVC carry pathogenic *PKP2* mutations [2]

90% have >500 PVCs/day, despite standard of care[3]

ARVC HEART



- 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. Hermida, et al, Eur J Heart Failure, 2019
3. Calkins, HRS 2025

TRIAL DESIGN

RIDGE-1 Phase 1b/2 clinical trial

Treatment goal: demonstrate reduction in arrhythmic events

Study Objectives

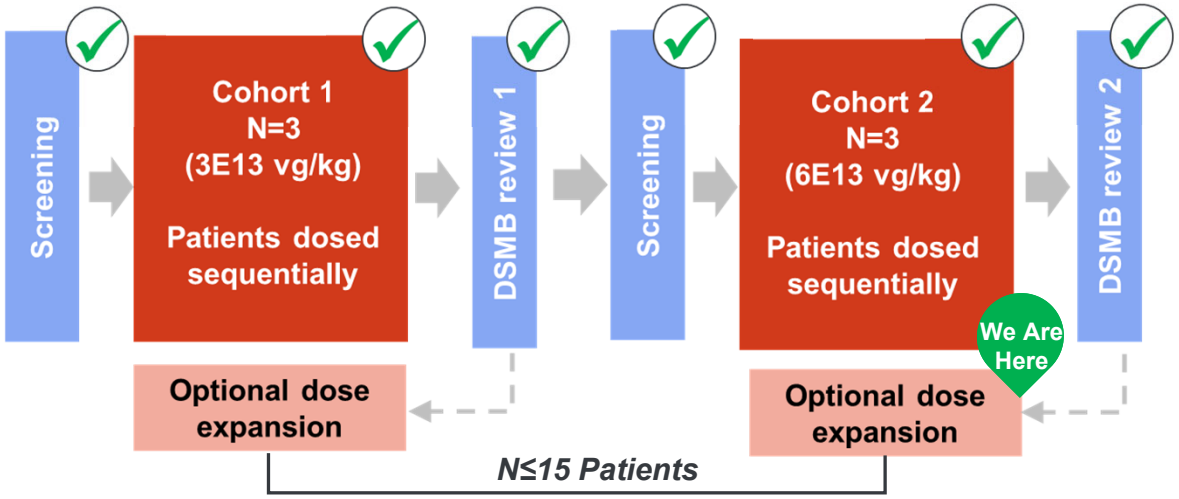
- Safety and tolerability
- Dose-finding
- Pharmacodynamics

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



PVC = Premature ventricular contractions
NSVT = Non-sustained ventricular tachycardia
ICD = impantable cardio defibrillator
VT = ventricular tachycardia
DSMB = Data safety and monitoring board

HIGHLIGHTS

Interim RIDGE-1 Cohort 1 & 2 Data

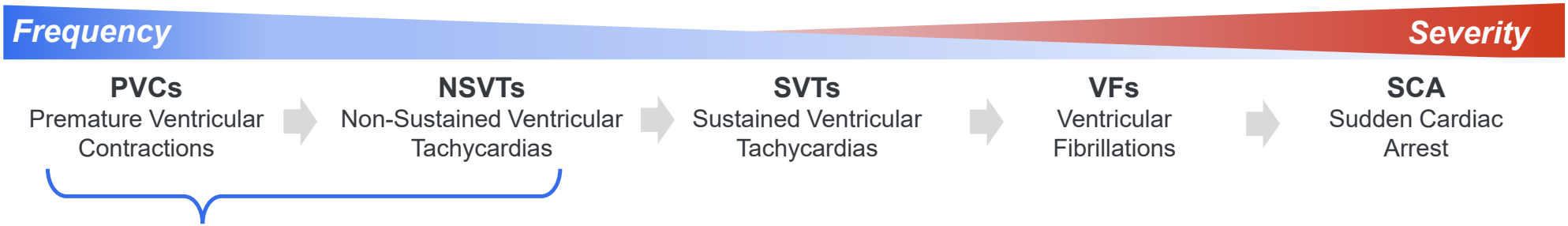
1. **CLINICAL: All patients on study achieved consistent and meaningful reductions in arrhythmia burden that were sustained up to 1 year for Cohort 1**

2. **BIOPSY: TN-401 is reaching cardiomyocytes and achieving expression**

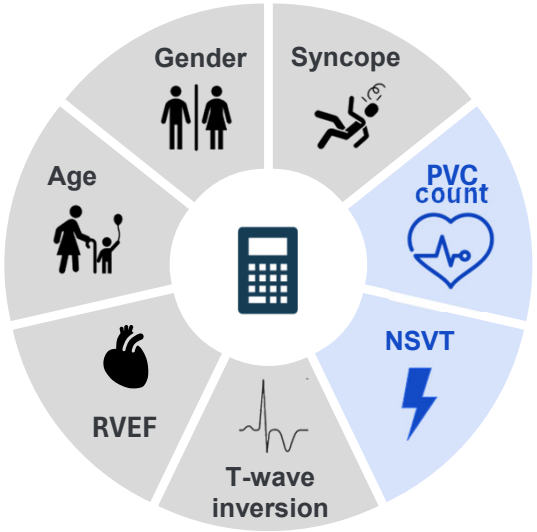
3. **SAFETY: TN-401 was well tolerated at both doses**

VENTRICULAR ARRHYTHMIA RISK FACTORS

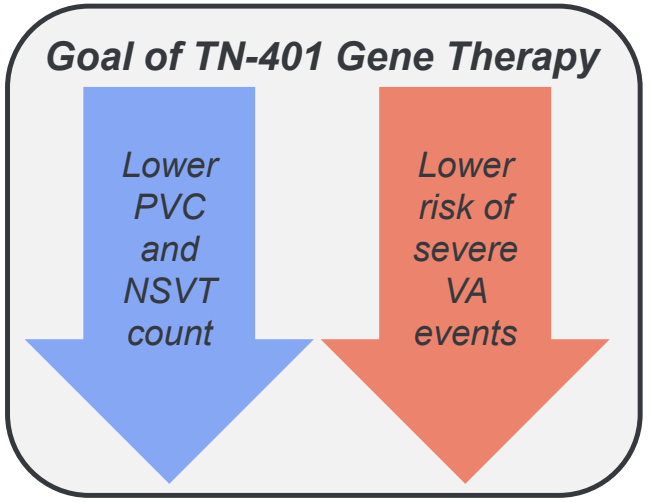
PVC and NSVT burden are key indicators of electrical instability and risk of life-threatening events



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]

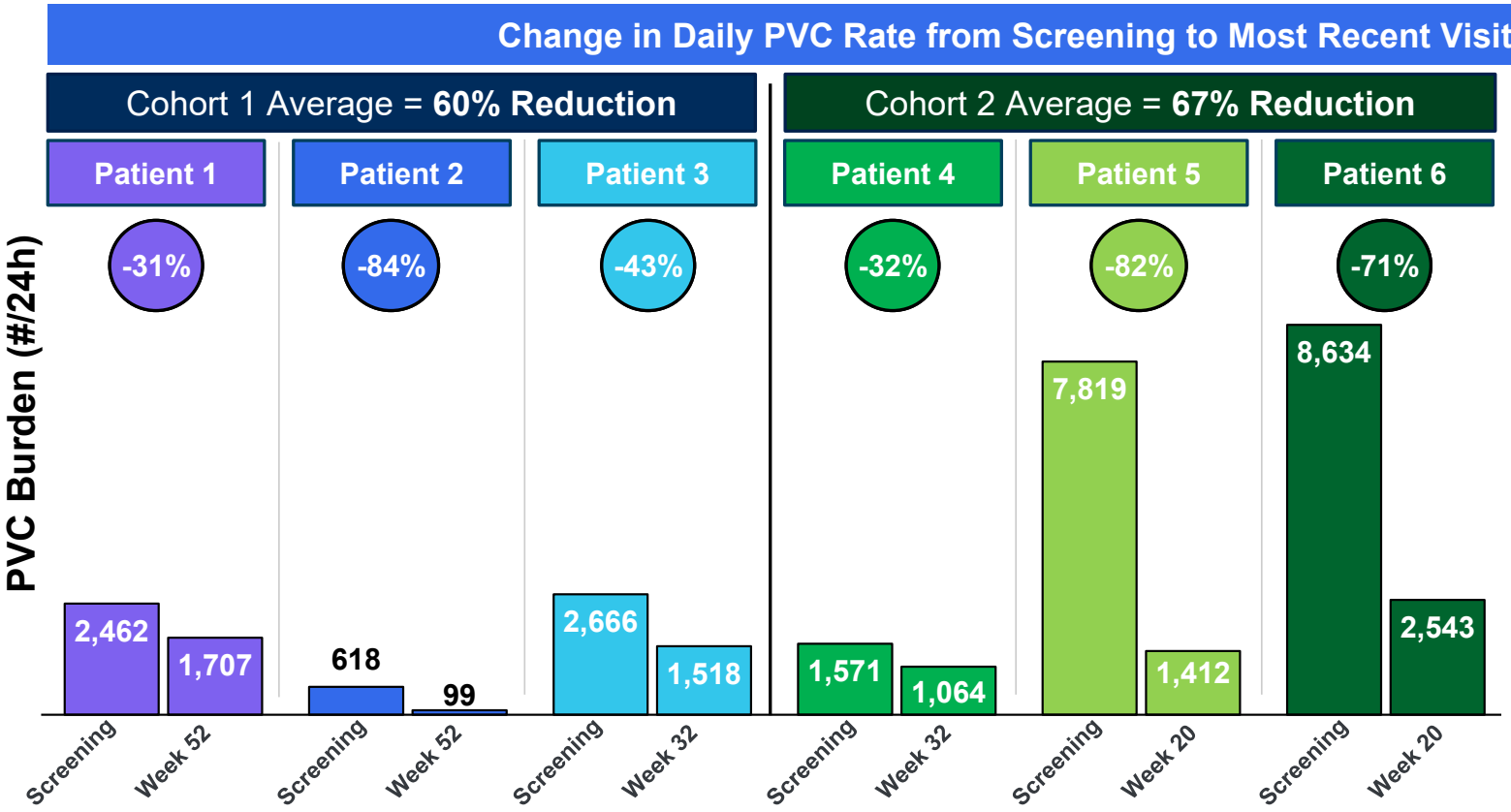


SVT = sustained ventricular tachycardia
RVEF = Right ventricular ejection fraction

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

CLINICAL RESULTS

All patients had meaningful reductions in PVC burden post-TN-401



- PVCs assessed by 7-day continuous ECG
- **Consistent reductions** in all patients dosed
  - Reductions for Patients 1 and 2 **remain durable** up to 1 year
  - Cohort 2 reductions more **dramatic and rapid, potentially a dose effect**
- PVC reduction **associated with 55% lower VA odds**[1]

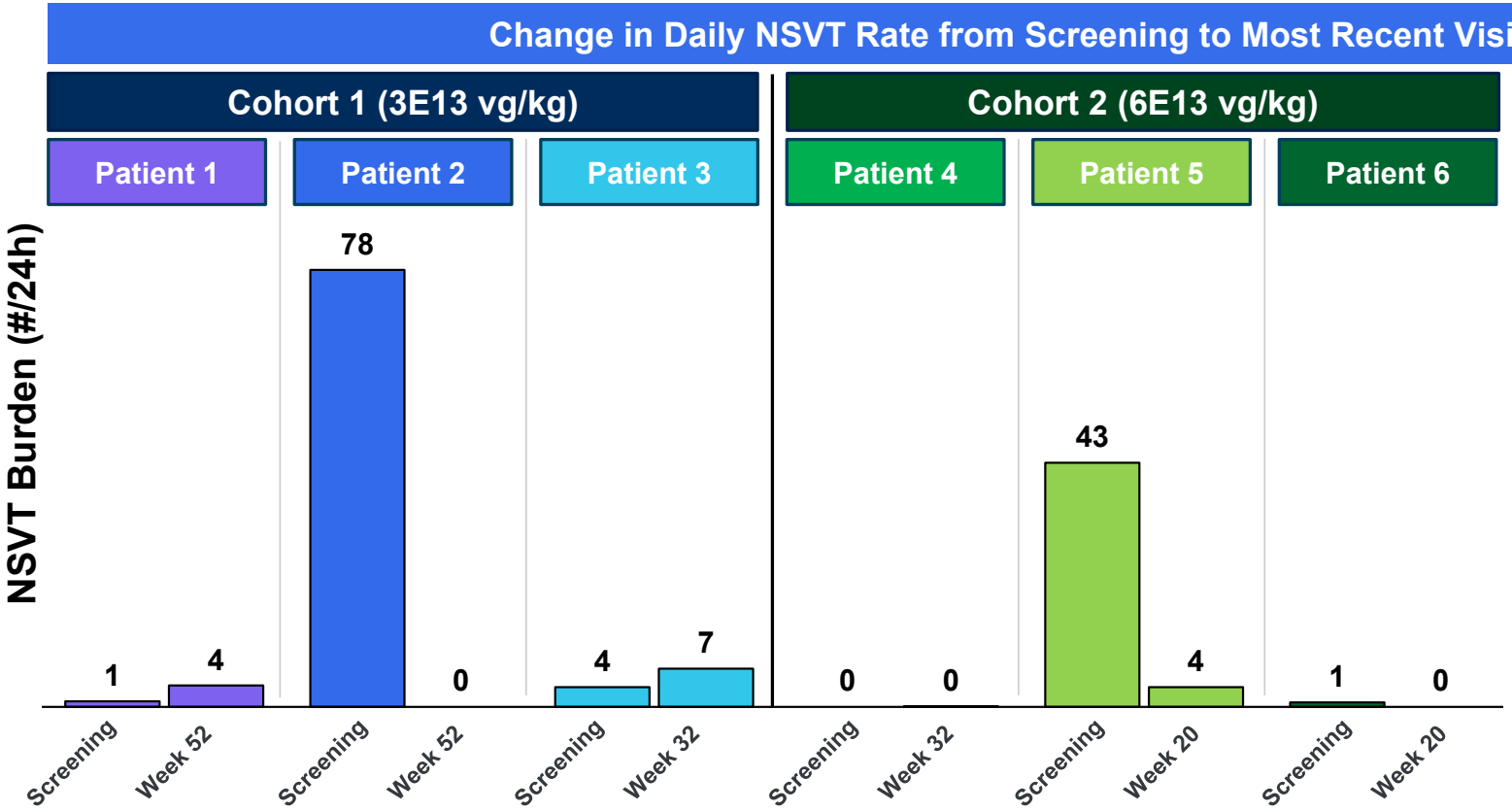
Data as of April 2026 data cut
Average change: geometric mean percent change from screening

ECG = electrocardiogram

[1]Gasperetti, et al., *JAMA Cardiol* 2022

CLINICAL RESULTS

Patients with high NSVT burden had dramatic reductions over time



- NSVT burden assessed by 7-day continuous ECG
- Patients 2 & 5 saw **major declines in NSVT rates**, consistent with PVCs
- Patients 1, 3, 4, and 6 with **low & stable NSVT** rates at most recent visit
- All patients **are stable across ECG measures**, including T-wave inversions & QRS durations
- **Echo parameters remain stable** over time

Data as of April 2026 data cut

SAFETY OBSERVATIONS

Both TN-401 doses equally well tolerated

Majority of TN-401-related AEs mild, asymptomatic and manageable

Relevant Adverse Event	Cohort 1* (3E13 vg/kg; n=3)				Cohort 2 (6E13 vg/kg; n=3)			
	Gr 1	Gr 2	Gr 3	**Total**	Gr 1	Gr 2	Gr 3	**Total**
Liver enzyme elevation	3	-	-	**3**	1	-	1**	**2****
Troponin elevation	2	-	-	**2**	1	-	-	**1**
Thrombocytopenia†	-	-	-	**0**	-	-	1**	**1****

*Previously disclosed, no new AEs since December 2025 release
**Event attributed to or associated with immunosuppression medication error
†Unrelated to TN-401

- Cohort 1 AEs **previously disclosed**
- Cohort 2 AEs include two grade 3 AEs in the same patient due to a **medication error**:
  - 1 Grade 3 AE of liver enzyme elevation associated with medication error resulting in steroid interruption
  - 1 Grade 3 SAE of thrombocytopenia due to medication error with sirolimus overdose (serum level 40.4 ng/mL [target level 4-8 ng/mL])
- **No** clinical thrombotic microangiopathy
- **No** sustained VT, VF, or ICD therapy related to TN-401. No other cardiotoxicities observed
- **DSMB endorsed expansion** for both cohorts

TENAYA THERAPEUTICS

VT: ventricular tachycardia
VF: ventricular fibrillation
ICD: Implantable cardioverter device

DSMB: Data Safety Monitoring Board
IS: immunosuppression

COMMITTED TO THE *PKP2* COMMUNITY

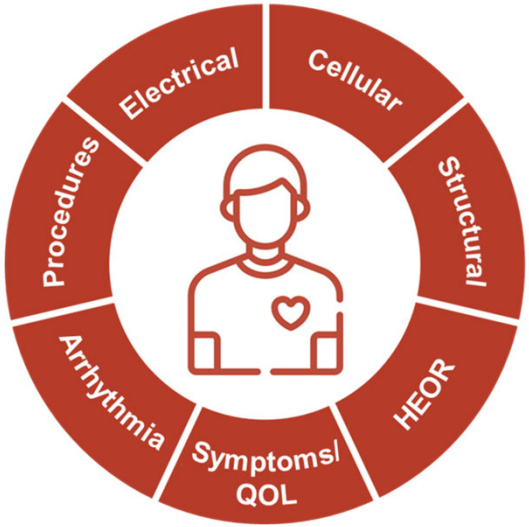
RIDGE™ the largest natural history study of *PKP2*+ ARVC in the world

Largest Ever *PKP2*+ ARVC Natural History Study…

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 discussions with health authorities about potential approvable endpoints, pivotal trial design

~70% of RIDGE patients eligible for RIDGE-1

TENAYA™ THERAPEUTICS

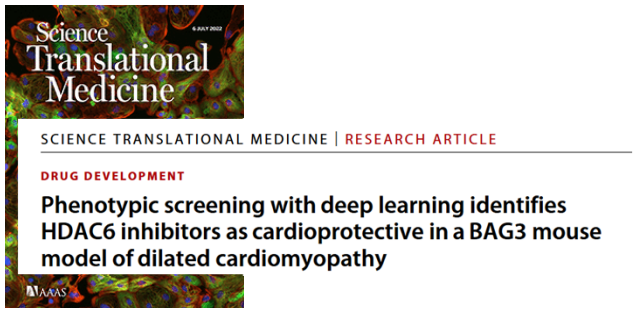
TN-301 HDAC6 Inhibitor

SMALL MOLECULE HDAC6 INHIBITOR

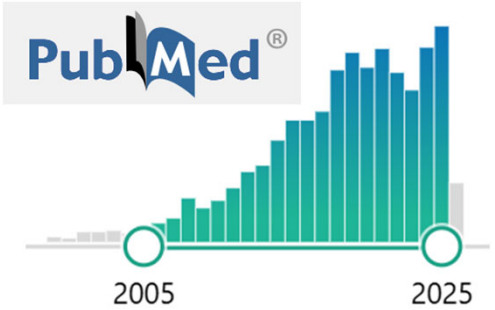
Growing conviction in TN-301 opportunity supported by external preclinical and clinical data

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

TENAYA THERAPEUTICS

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

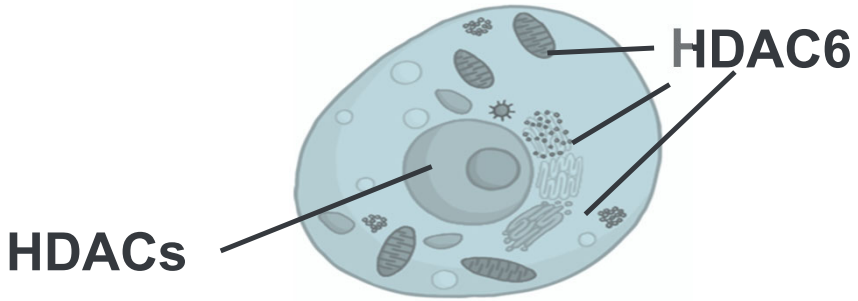
4SC = 4 Stair Climb
NSAAI = North Star Ambulatory Assessment

DIFFERENTIATION

Tenaya's HDAC6 inhibitors offer distinct advantages

HDACs vs. HDAC6

Histone deacetylases are enzymes that regulate cellular processes and gene expression

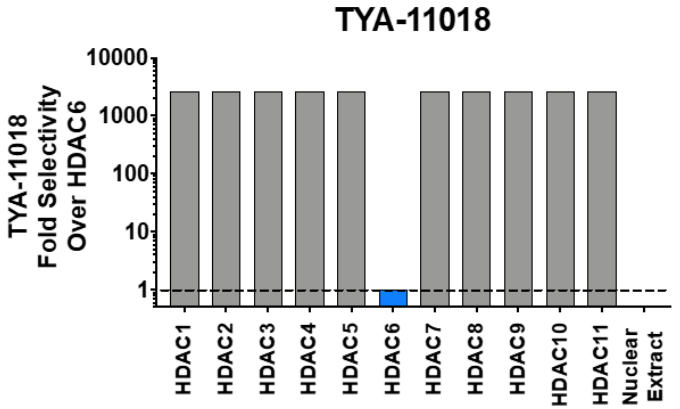


HDACs 1-3, 5, 8 and 11 primarily work inside the cell nucleus. HDACs 4, 7 and 9 shuttle between nucleus and cytoplasm.

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



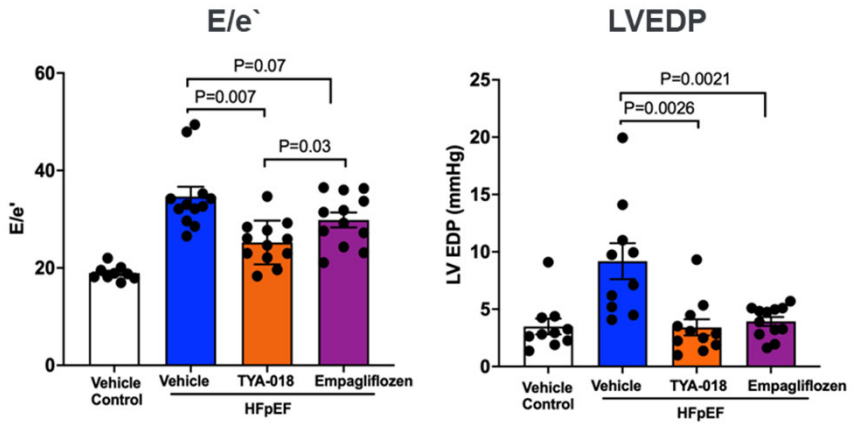
Hsp90 = heat shock protein 90
SMAD 2/3 = Suppressor of Mothers Against Decapentaplegic
BAG3 = Bcl2-associated athanogene 3

PRECLINICAL RESULTS

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

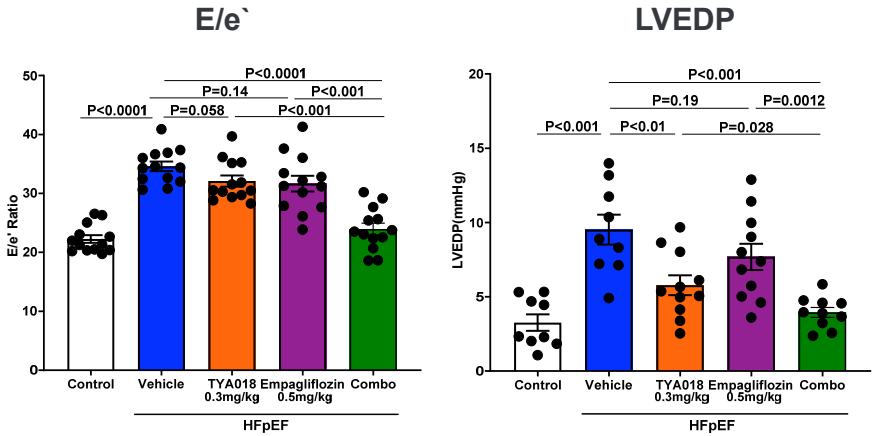
HDAC6 inhibition shows comparable efficacy to SGLT2 inhibitor

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

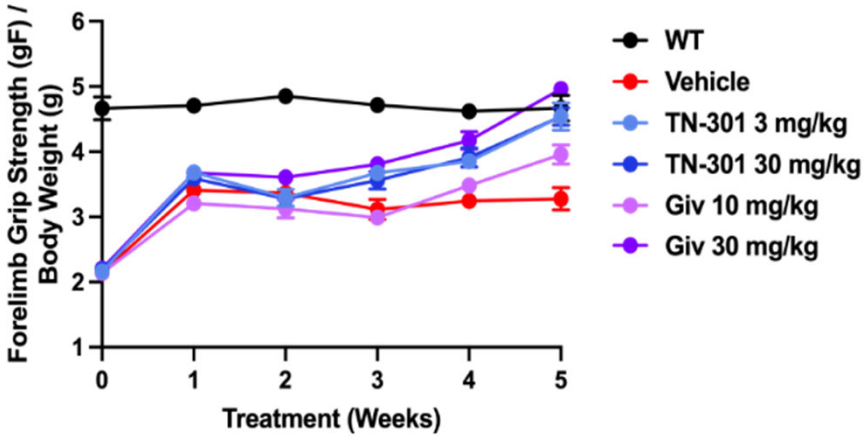
PRECLINICAL RESULTS

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

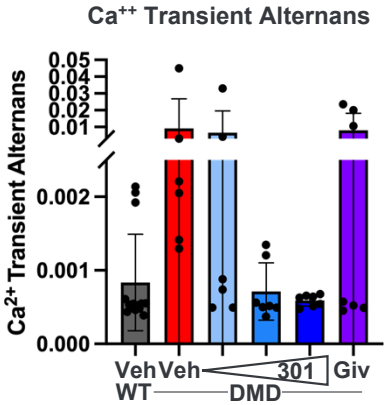
Low-dose TN-301 improved grip strength to WT levels and outperformed givinostat clinical dose

***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

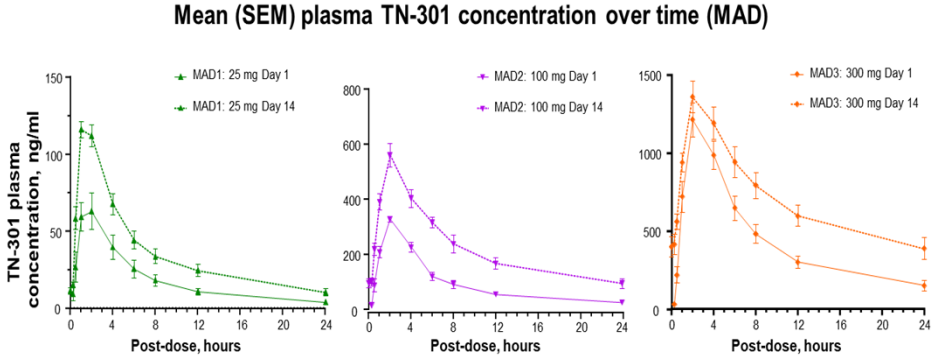
PRECLINICAL RESULTS

Phase 1 trial of TN-301 of healthy participants

TN-301 was generally well tolerated across broad dose ranges

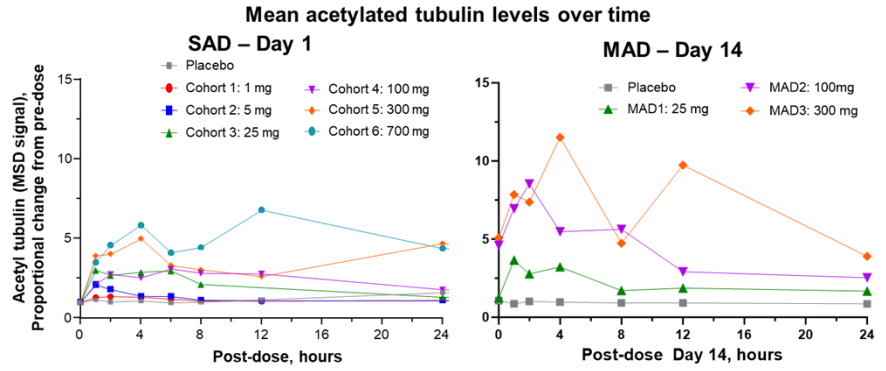
- Single-ascending doses (SAD) of 1mg – 700mg
- Multiple ascending doses (MAD) of 25mg, 100 mg and 300 mg for 14 days
- AEs (primarily GI related) occurred with similar frequency to placebo; no AE increase with dose
- No thrombocytopenia, no QT prolongation risk, and no histone modification seen

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

TENAYA™ THERAPEUTICS

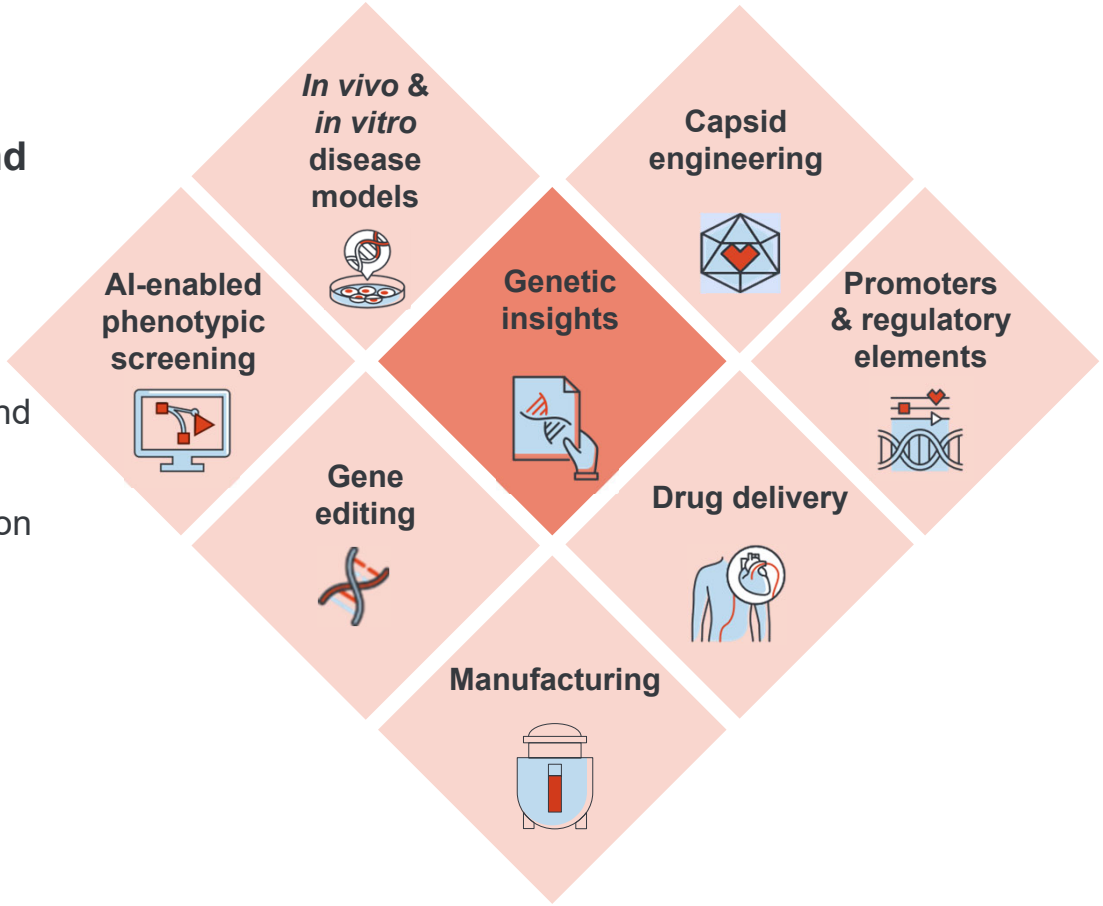
Enabling Capabilities

PLATFORM

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

PLATFORM

Research collaboration with Alnylam

Goal

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

Responsibilities

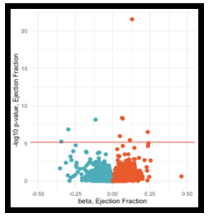
- Tenaya consucts target validation
- Alnylam obtains WW license to any selected leads and is responsible for all clinical development and commercial activities

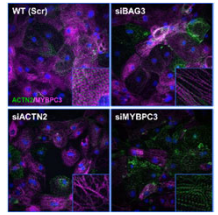
Financial Terms

- 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

AF1

MOMENTUM

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