

# MyPEAK-1 Interim Data Readout

June 3, 2026



# Forward-looking statements

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# Today's speakers and agenda



**Faraz Ali, MBA**  
Chief Executive Officer



**Kathy Ivey, Ph.D.,**  
Senior Vice President,  
Research



**Whit Tingley, M.D., PhD**  
Chief Medical Officer

## *Today's Agenda*

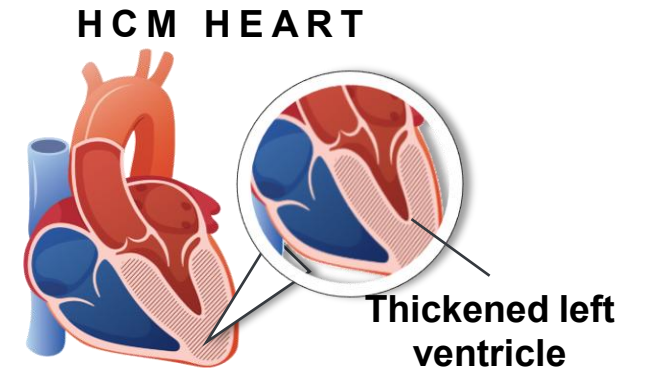
Introductory remarks	Faraz Ali
MyPEAK-1 objectives	Whit Tingley
Clinical findings	Whit Tingley
Biopsy results	Kathy Ivey
Safety findings	Whit Tingley
Closing remarks	Faraz Ali
Q&A	

# *MYBPC3*-associated HCM is estimated to affect 120,000 people in the U.S. alone<sup>1</sup>

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

~57% of identified genetic variants underlying familial HCM are *MYBPC3* mutations<sup>2</sup>

>30% of genetic variants underlying childhood-onset HCM are *MYBPC3* mutations<sup>3</sup>

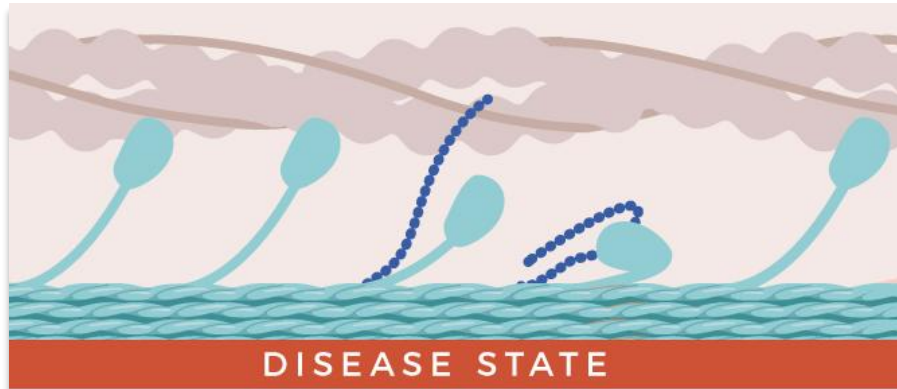


- Significant functional impairment
- Social and psychological impacts
- Symptoms include shortness of breath, fainting, chest pain, fatigue, palpitations, arrhythmias
- Elevated risk of sudden cardiac death and heart failure

GABE | AGE 10  
Living with *MYBPC3*+ HCM

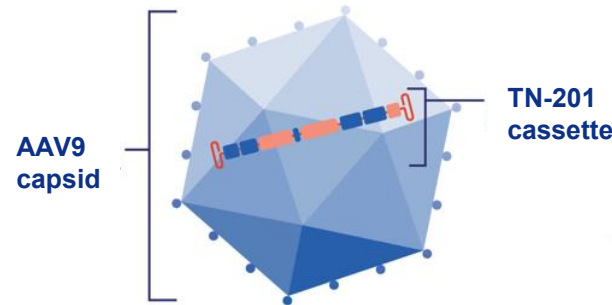
# TN-201 is the first gene therapy being developed for *MYBPC3*-associated HCM<sup>1</sup>

## *MYBPC3* Pathophysiology

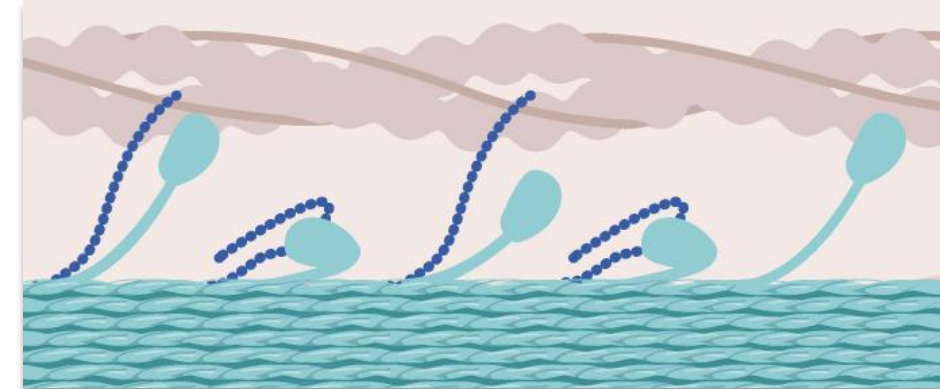


Heterozygous mutations in the *MYBPC3* gene lead to significantly **lower levels of MyBP-C protein** and dysregulated cardiac contractility<sup>1</sup>

## 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<sup>2</sup>



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



MyBP-C protein present in sarcomere

## 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



# MyPEAK-1 Readout

## Trial objectives and clinical findings



# MyPEAK-1 Phase 1b/2 clinical trial design



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

## Study Objectives

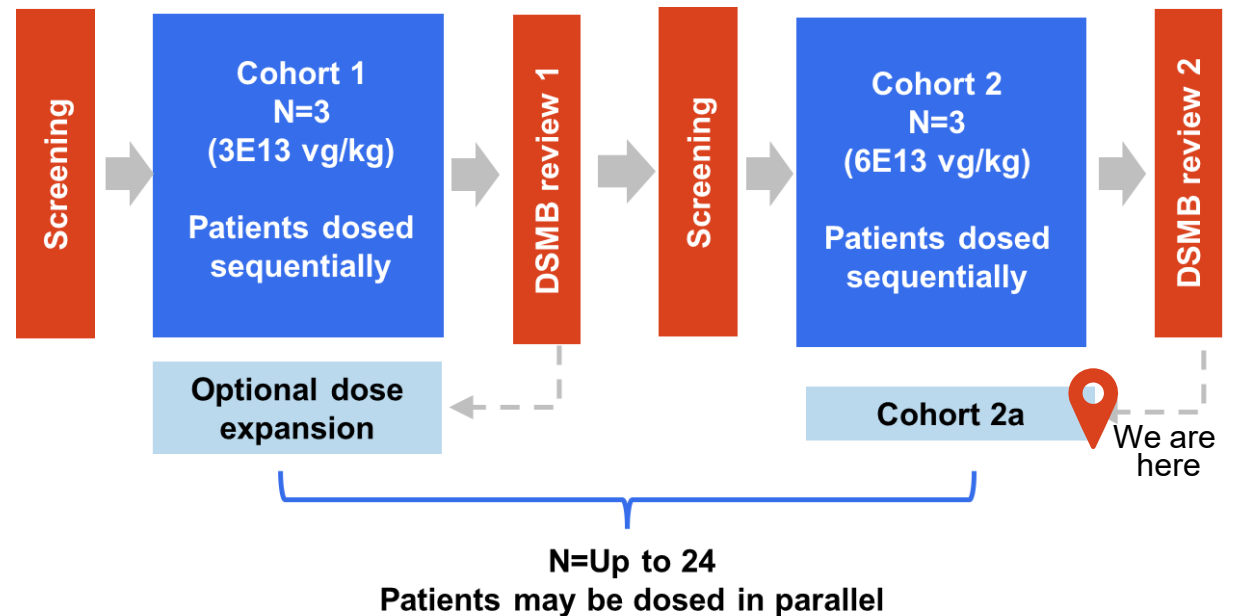
- Safety, tolerability
- Dose-finding
- Pharmacodynamics

## 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 patients

June 2026 readout includes 178-104 follow-up for Cohort 1 and 26-52 weeks follow-up for Cohort 2 patients

	Average / % of HCM	Cohort 1			Cohort 2			
		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5*	Patient 6	Patient 7
Gender	Male (63%) <sup>1</sup>	Female	Female	Male	Female	Female	Female	Female
Phenotype	nHCM (72%) <sup>1</sup>	nHCM	nHCM	nHCM	nHCM	nHCM	nHCM	nHCM
Age at Dosing	50y <sup>1</sup>	27	43	47	60	48	63	40
LVMI (g/m <sup>2</sup> )	F: 89   M: 104 <sup>2</sup>	174	105	178	121	181	139	117
Myectomy & Age	18% <sup>3</sup>   Mean = 54y <sup>4</sup>	24	30	39	-	35	-	-
ICD & Age	21% <sup>1</sup>   Mean = 38y <sup>5</sup>	27	37	36	58	38	49	36
NT proBNP	563 pg/ml <sup>6</sup>	1884	351	913	337	1013	465	158
Troponin I (ng/L)	27 <sup>7</sup>	46	34	53	10	27	8	108
NYHA Class	50% ≥ Class II <sup>8</sup>	II	III	II	II	II	II	II

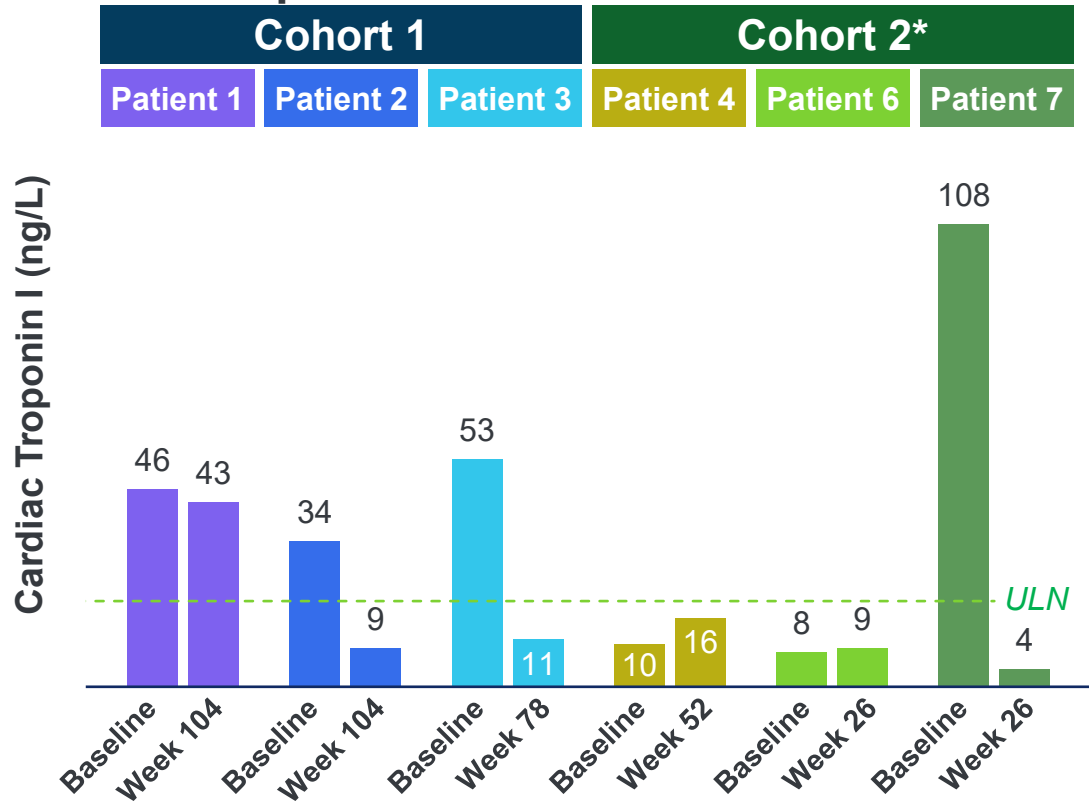
\*Patient 5 lost to follow up after tapering off immunosuppression

More severe vs. average

# Cardiac biomarkers improved or remained stable up to 104 weeks after dosing

## Cardiac Troponin I

### Comparison of baseline to MRV



May 2026 data cut off

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

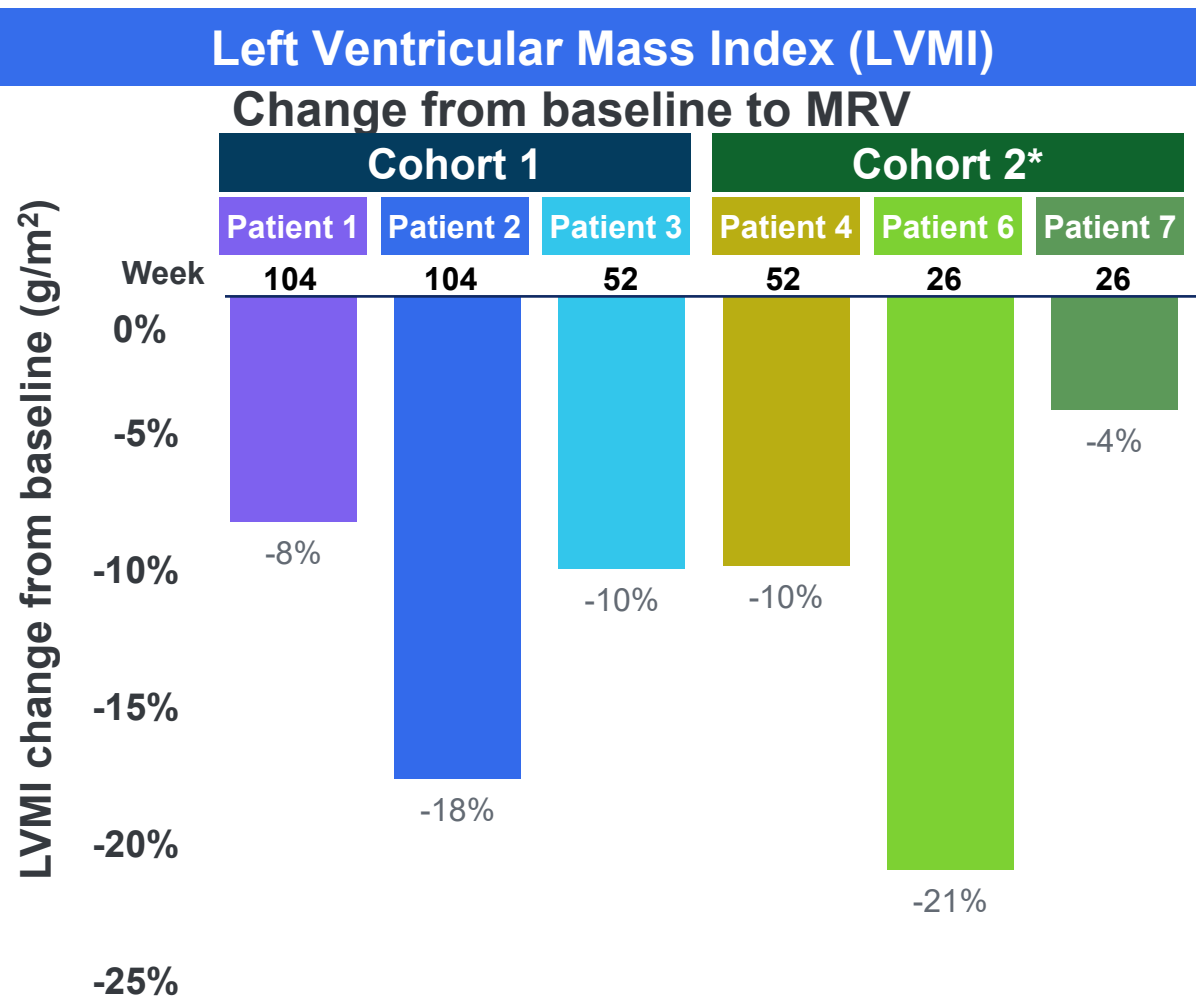
Cardiac troponin declined or remained stable within the normal/near normal range in five of six patients

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

NT-proBNP (not shown) declined or remained stable from baseline after completion of IS in three of six patients

- NT-proBNP is a biomarker that indicates strain of the heart muscle

# 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/m<sup>2</sup>
- 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

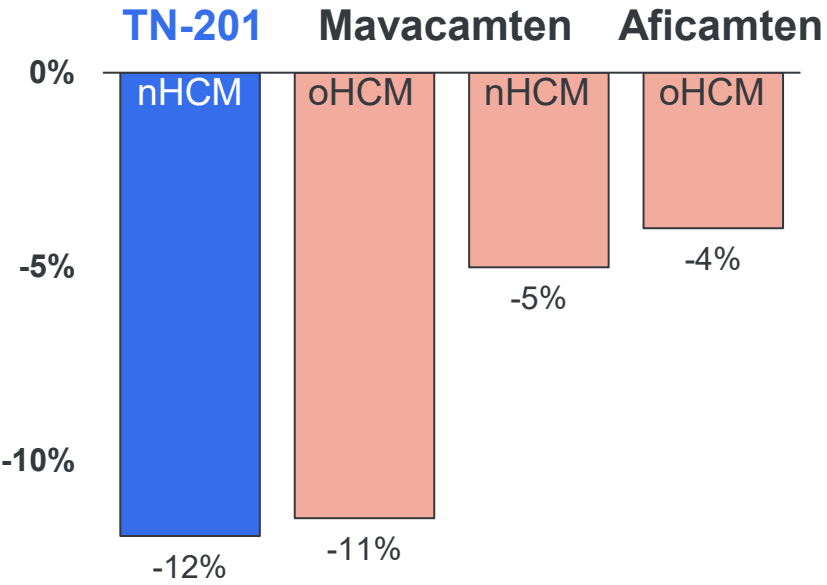
Consistent changes observed in other measures of wall thickness

- 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

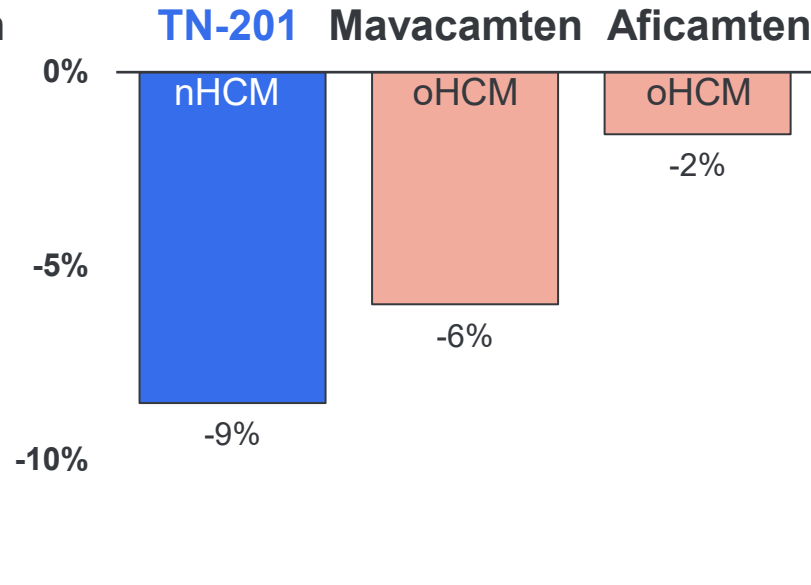
Other measures of cardiac structure and function remain largely stable

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

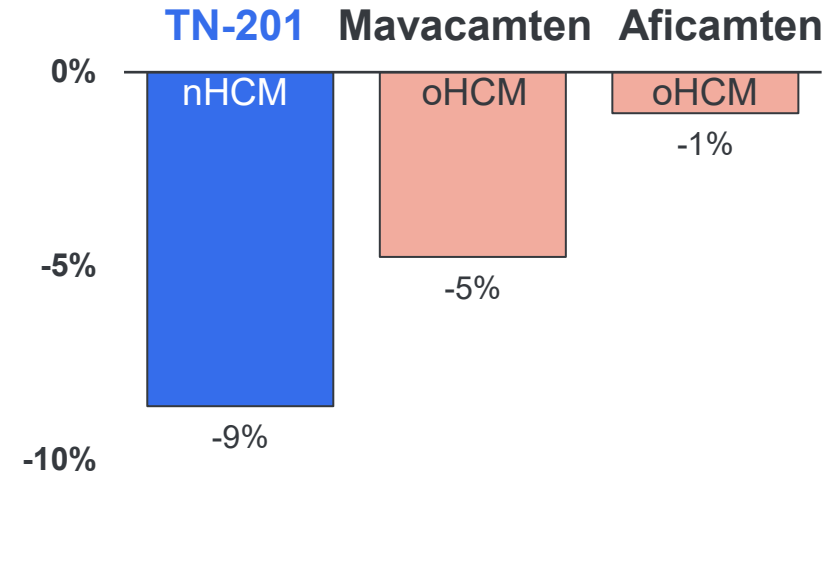
**LVMI change from baseline to MRV<sup>\*1-5</sup>**



**LVPWT change from baseline to MRV<sup>\*1-5</sup>**



**IVS change from baseline to MRV<sup>\*1-5</sup>**



**Absolute Decline**

<b>(-16 g/m<sup>2</sup>)</b>	<b>(-14 g/m<sup>2</sup>)</b>	<b>(-6 g/m<sup>2</sup>)</b>	<b>(-5 g/m<sup>2</sup>)</b>	<b>(-0.9 mm)</b>	<b>(-0.7 mm)</b>	<b>(-0.2 mm)</b>	<b>(-1.6 mm)</b>	<b>(-1.0mm)</b>	<b>(-0.2 mm)</b>
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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.



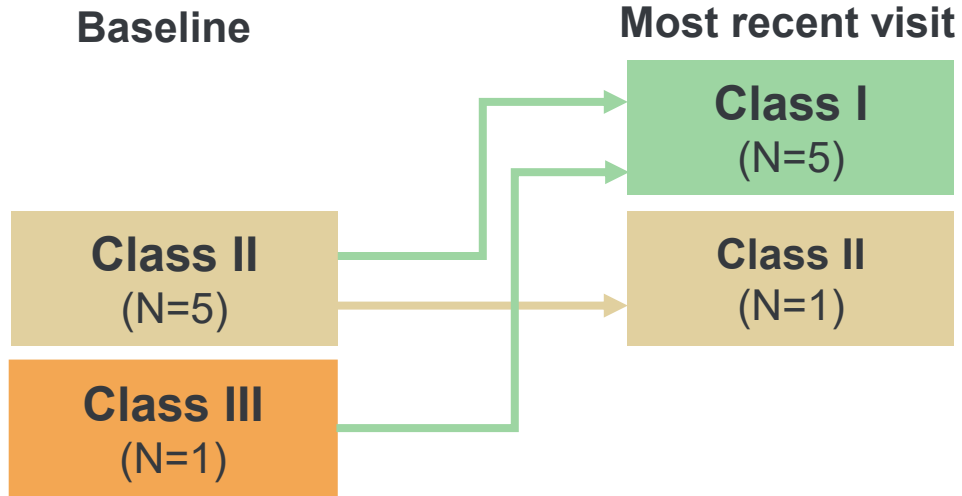
LVPWT = left ventricular posterior wall thickness  
IVS = intraventricular septum

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

<sup>1</sup>Desai, et al., *Circ* 2025  
<sup>2</sup>Hegde, et al., *JACC* 2021  
<sup>3</sup>Desai, et al., *JACC* 2025  
<sup>4</sup>Hegde, et al., *JACC* 2024  
<sup>5</sup>Sun, et al., *JACC* 2022

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

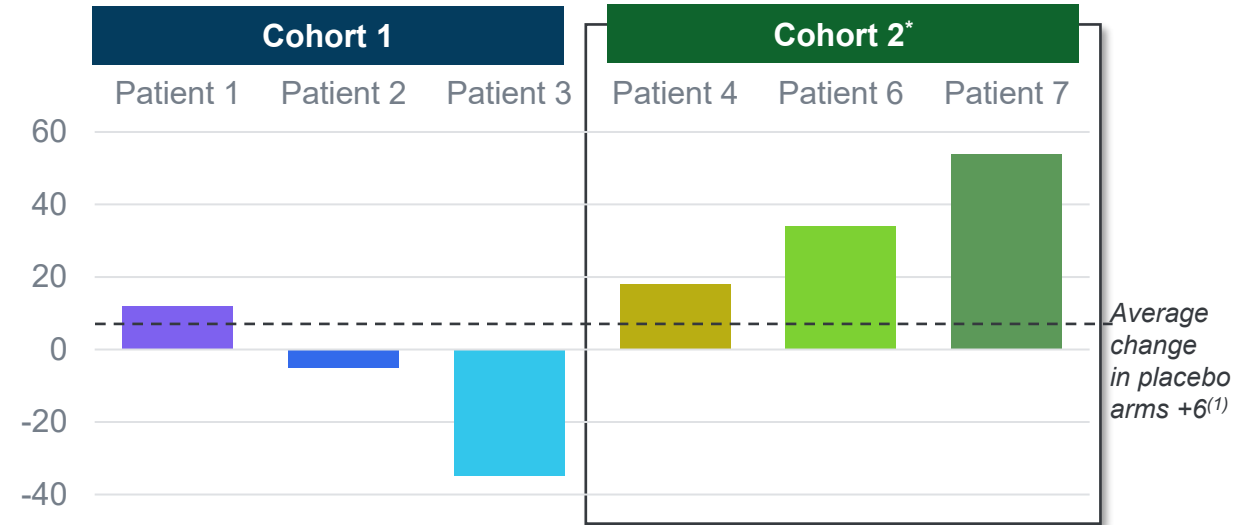
## New York Heart Assoc. Classification



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

## Kansas City Cardiomyopathy Questionnaire

### Change from baseline to MRV



- **67% achieved meaningful improvements in KCCQ Clinical Summary Score<sup>(2)</sup>**
- 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

# 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
<b>Patient 4</b>	<b>500</b>	<b>755</b>	<b>+255</b>
<b>Patient 6</b>	<b>420</b>	<b>390</b>	<b>-30</b>
<b>Patient 7</b>	<b>247</b>	<b>297</b>	<b>+50</b>

Measured in meters

## Cardiopulmonary Exercise Capacity

### Cohort 2\* change in pVO<sub>2</sub> from baseline to MRV

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

Measured as mL/kg/min

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

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

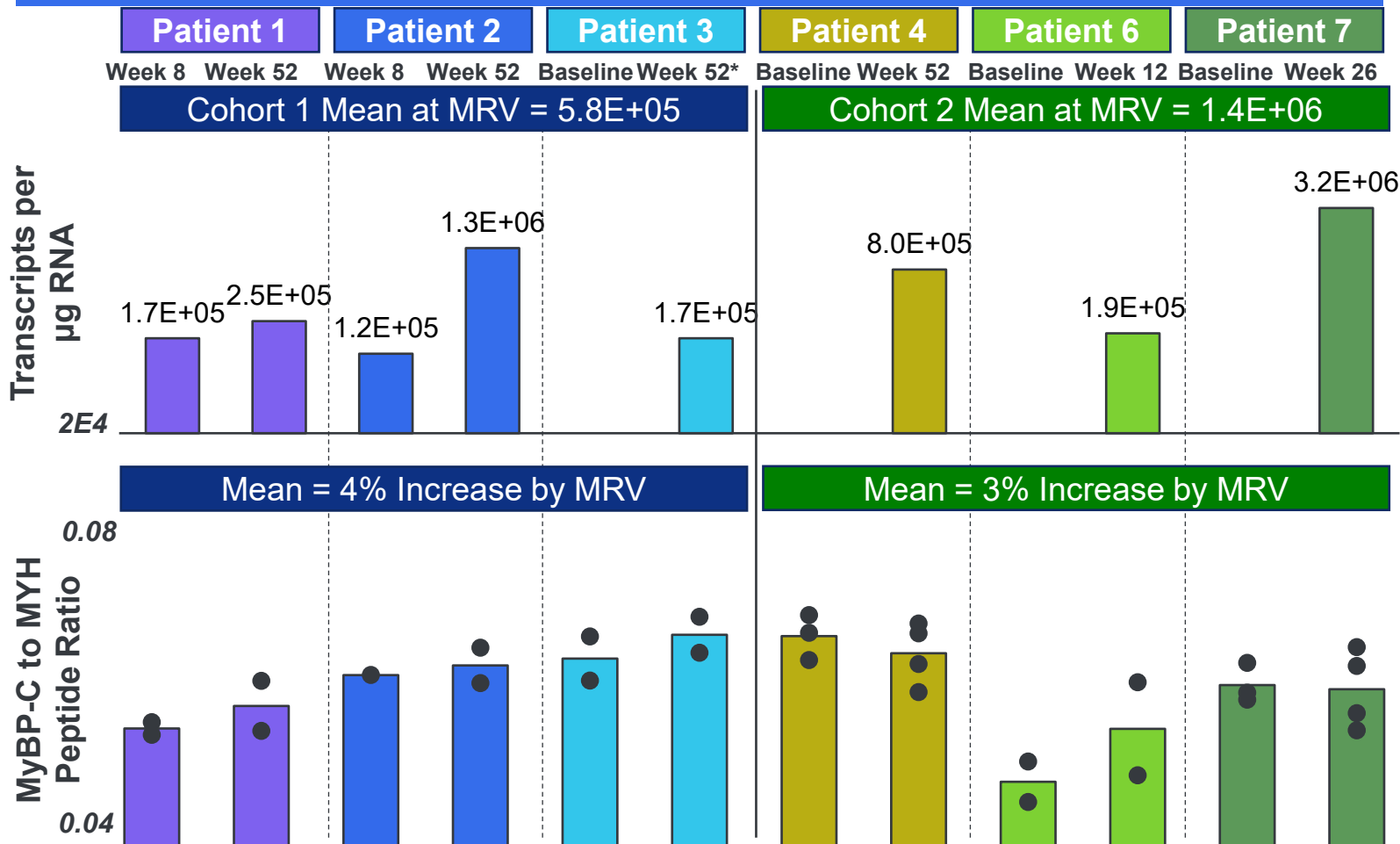


# MyPeak-1 Readout TN-201 heart biopsy findings



# RNA and protein levels across cohorts suggest TN-201 expression increases with dose and over time

## Change in TN-201 Expression Over Time



### TN-201 mRNA

- RNA measures are specific for TN-201
- Cohort 2 mRNA levels ~2X higher compared to Cohort 1, even at earlier timepoints; consistent with DNA transduction levels (not shown)

### MyBP-C Protein

- Endogenous & TN-201 protein indistinguishable
- Increase in Cohort 2 comparable to Cohort 1 even at earlier timepoint
- Variance among samples complicates interpretation

**Totality of molecular & clinical data signal TN-201 effect**



# MyPEAK-1 Readout

## Safety and immunosuppression



# 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

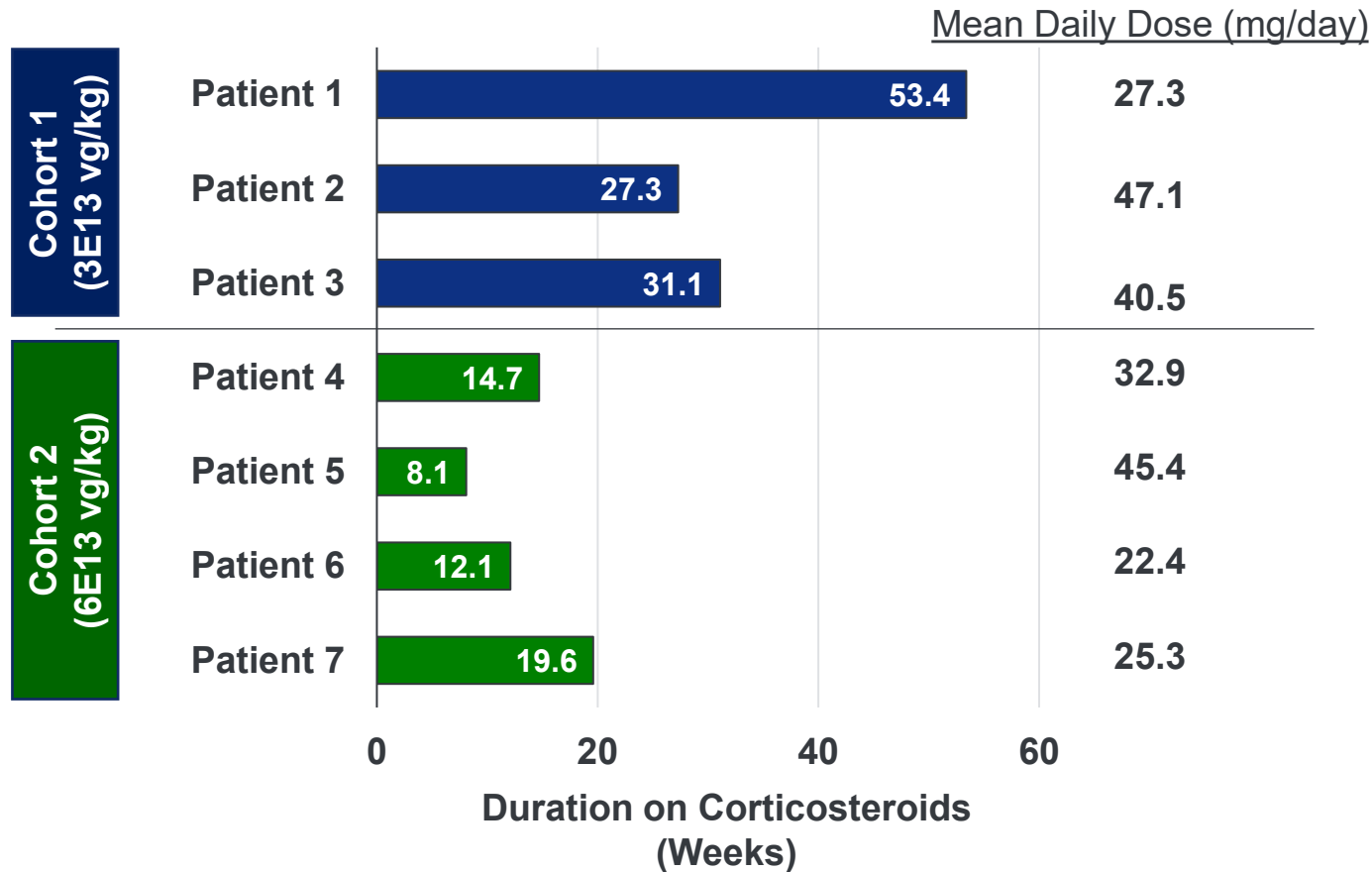
TN-201-related AEs	Cohort 1* (3E13 vg/kg; n=3)				Cohort 2* (6E13 vg/kg; n=3)			
	Gr 1	Gr 2	Gr 3	Total	Gr 1	Gr 2	Gr 3	Total
Liver enzyme elevations	1	1	1	3	1	-	-	1
Platelet reduction/ thrombocytopenia	-	-	-	0	2	-	-	2
Complement elevation	-	-	-	0	2	-	-	2

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

# Immunosuppression regimen successfully managed immune response at both doses

## Duration & Mean Daily Corticosteroid Dose



### 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
- Mean corticosteroid taper was shorter and daily dose lower by patient for Cohort 2 (14 weeks at 32 mg/d) vs. Cohort 1 (37 weeks at 38 mg/d)



# Conclusions and future directions



## CONCLUSIONS

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

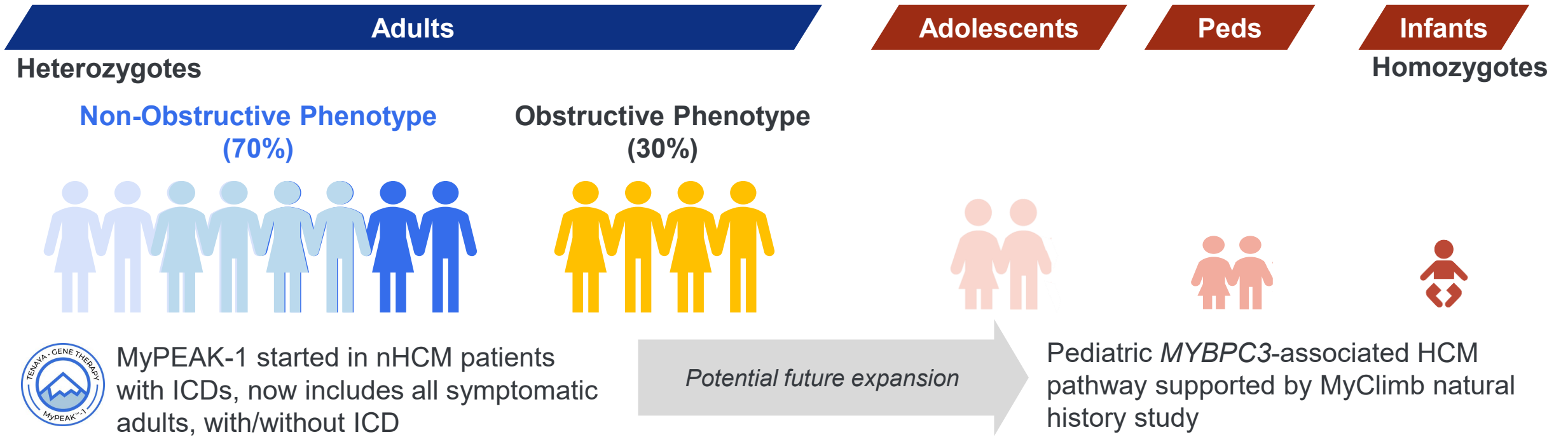
		MRV (week)	Biomarkers		Hypertrophy			Feel		Function		Change from baseline to MRV
			cTnl	BNP	LVMI	LVPWT	IVS	NYHA	KCCQ	6MWD	pVO <sub>2</sub>	
Cohort 1	Patient 1	104	Improved	Declined	Improved	Improved	Improved	Improved	Improved	Improved	Declined	Improved
	Patient 2	104	Improved	Improved	Improved	Improved	Improved	Declined	Declined	Declined	Declined	Improved
	Patient 3	52 & 78	Improved	Declined	Improved	Improved	Improved	Improved	Declined	Declined	Declined	Declined
Cohort 2*	Patient 4	52	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
	Patient 6	40	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
	Patient 7	26	Improved	Improved	Improved	Declined	Declined	Improved	Improved	Improved	Improved	Improved

- 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

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



- > 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



## **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



## **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

# Children with *MYBPC3*+ disease are at heightened risk for heart failure, arrhythmias, hospitalizations and death<sup>(1)</sup>

## The unmet need in pediatric patients

**~3000** diagnosed patients currently under age 18 in the U.S.<sup>(2)</sup>

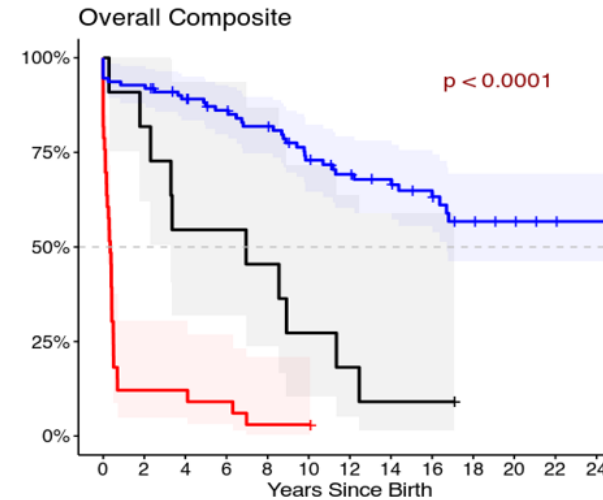
**>90%** of patients in MyClimb have non-obstructive HCM<sup>(1)</sup>

**36%** more likely to develop life-threatening ventricular arrhythmias<sup>(3)</sup>

**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<sup>(1)</sup>



**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

# 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

## ACKNOWLEDGEMENTS

We extend our deepest gratitude to the dedicated clinical and research staff at all participating institutions and to the participants who volunteered their time, health information, and trust in support of advancing this research.



# Thank you



  
**TENAYA**<sup>TM</sup>  
THERAPEUTICS