Scaling New Heights in the Fight Against Heart Disease

Corporate Presentation

September 2022

Forward-looking Statement

This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended 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 the sufficiency of projected cash flows, business strategy and plans, the clinical, therapeutic and market potential of and expectations regarding our product candidates, programs, GMP manufacturing facility and objectives of management for future operations, the expected timing for submission of regulatory filings, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "vision," "mission," "anticipate," "expect," "intend," "may," "objective," "ongoing," "plan," "potentially," "will" or the negative of these terms or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions described in our filings with the Securities and Exchange Commission, including, but not limited to the section titled "Risk Factors" in our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2022. Such risks include, among other things: the timing of the initiation, progress, completion and potential results of our preclinical studies and clinical trials; our ability to advance product candidates into, and successfully complete, preclinical studies and clinical trials; the timing or likelihood of regulatory filings and approvals; the negative impacts of the COVID-19 pandemic on our manufacturing and operations; 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; the potential for clinical trials of our product candidates to differ from preclinical, preliminary, interim or expected results; the commercializing of our product candidates, if approved; our ability to successfully manufacture and supply our product candidates for preclinical studies, clinical trials and for commercial use, if approved; future strategic arrangements and/or collaborations and the potential benefits of such arrangements; our estimates regarding expenses, capital requirements and needs for financing, and our ability to obtain capital; the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements; our ability to retain the continued service of our key personnel and to identify, hire and retain additional qualified professionals; the implementation of our business model and strategic plans for our business; our ability to obtain and maintain intellectual property protection for our platforms, programs and product candidates; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the pricing, coverage and reimbursement of our product candidates, if approved; and developments relating to our competitors and our industry, including competing product candidates and therapies; general economic and market conditions; and other risks. These risks are not exhaustive. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. The forward-looking statements made in this presentation relate only to events as of the date on which such statements are made. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Our vision is to **transform and extend** the lives of people and families fighting heart disease.

Our mission is to **discover, develop and deliver curative therapies** that address the underlying causes of heart disease.

Our therapies and capabilities are designed to provide new hope and new options for **millions of individuals and families** affected by heart disease, from **rare** genetic cardiomyopathies to the most **prevalent** forms of heart failure.

Tenaya Focus on Heart Disease

Why the Time is Now for Next Generation Precision Medicine Therapies

Heart Disease is Still the Leading Cause of Death in the World

- **>30MM** US adults diagnosed with heart disease
- **~40K** US children born each year with congenital heart disease
- Mortality rates are rising despite advances in standard of care

Increasing Genetic Insight and Diagnosis

- Guidelines recommend genetic testing for cardiomyopathies
- Accessible genetic testing for >150 genes for >35 conditions
  Genetic cardiomyopathies can run through families

Increasing Clinical Validation for Precision Medicine Approaches

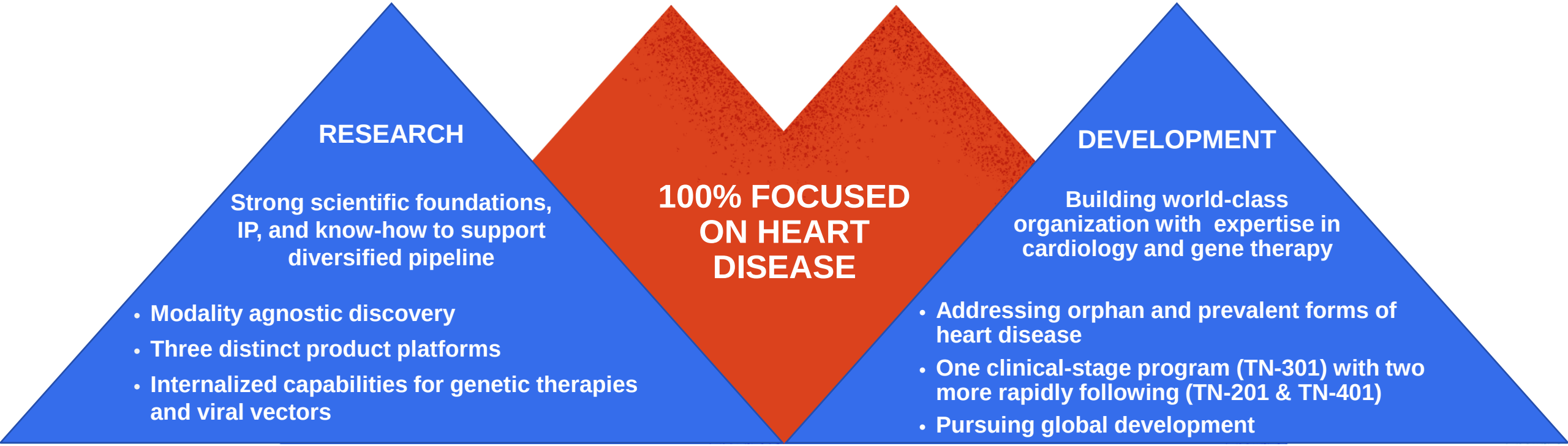
- Approvals for disease-specific therapies for cardiomyopathies
- Early but promising clinical data for cardiac gene therapies
- Potential for smaller studies with larger effect sizes

Stronger Drug Development Toolkit

- Better *in vitro* and *in vivo* disease models
- New modalities (gene therapy, gene editing, etc.)
- Methods to improve delivery and expression and specificity of genes in the heart (e.g., capsids, promoters, catheters)

Tenaya Overview

Combining Cardiovascular and Genetic Medicines Expertise to Target the Underlying Causes of Heart Disease



2022 MILESTONES

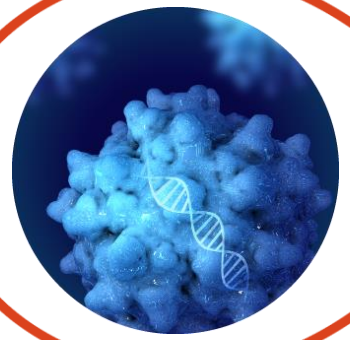
- ✓ Launched Genetic Medicines Manufacturing Center cGMP facility
- ✓ Presented preclinical data for TN-301, TN-401, and AAV capsid engineering at major conferences
- ✓ Initiated Phase 1 clinical study of TN-301 for HFpEF
- Expect to submit IND for TN-201 for MYBPC3+ HCM
- Expect to initiate natural history study for *PKP2*+ ARVC

HFpEF = Heart failure with preserved ejection fraction
HCM = Hypertrophic cardiomyopathy
ARVC = Arrhythmogenic right ventricular cardiomyopathy
MYBPC3 = Myosin Binding Protein C3
PKP2 = Plakophilin-2
AAV = Adeno-Associated Virus

Multi-Modality Drug Discovery Engine

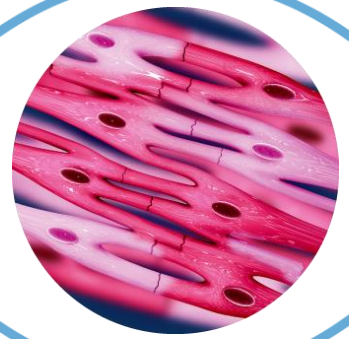
Three Product Platforms Powered by Proprietary Capabilities

GENE THERAPY



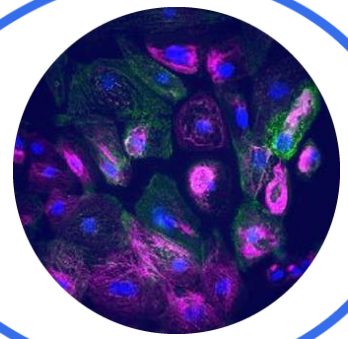
Restore cell function by using viral vectors to deliver healthy copies of genes or other therapeutic payloads

CELLULAR REGENERATION



Regenerate new heart cells *in vivo* by using viral vectors to deliver proprietary combinations of genes

PRECISION MEDICINE

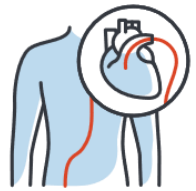


Expand pipeline by using human iPSC-CM disease models and analysis of human genetics to identify new targets and therapies

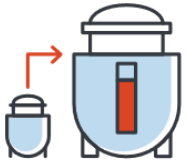
DISEASE MODELS

CAPSID ENGINEERING

PROMOTERS AND REGULATORY ELEMENTS



DRUG DELIVERY



MANUFACTURING

iPSC = induced pluripotent stem cells
CM = cardiomyocyte

Pipeline

Deep, Diverse, Wholly-Owned Pipeline Addressing Rare and Prevalent Indications

Program	Modality	Indication(s)	USA Prevalence	Discovery	Preclinical Development	Phase 1	Phase 2	Phase 3
Advanced Pipeline (INDs 2022-2023)								
TN-301	Small Molecule	Heart Failure w/ Preserved Ejection Fraction (HFpEF)	> 3MM			• **IND Cleared, Clinical Data in 2023** • **Preclinical data presented ESC-HF 2022**		
TN-201	AAV	MYBPC3+ Genetic Hypertrophic Cardiomyopathy (gHCM)	> 115K			• **Expected to file IND 2H 2022**		
TN-401	AAV	PKP2+ Genetic Arrhythmogenic RV Cardiomyopathy (gARVC)	> 70K			• **Expected to file IND in 2023** • **Preclinical data presented ASGCT 2022**		
Earlier Pipeline (INDs 2024+) and Platform								
DWORF	AAV	Dilated Cardiomyopathy (DCM)	> 1MM			• **Preclinical data presented ASGCT 2022**		
		Heart Failure w/ Reduced Ejection Fraction (HFrEF)	~ 4MM					
Reprogramming	AAV	Heart Failure Due to Prior Myocardial Infarction (MI)	> 4MM					
Undisclosed Targets	AAV	Multiple Genetic and Non-Genetic Indications	Rare and Prevalent					
Platform Enhancements	Genetic Therapies	AAV Capsid Engineering				• **Preclinical data presented ASGCT 2022**		

AAV = Adeno-associated virus
IND = Investigational New Drug application
MYBPC3 = Myosin Binding Protein C3
PKP2 = Plakophilin-2

TENAYA™ THERAPEUTICS

TN-301

Small Molecule HDAC6 Inhibitor for HFpEF

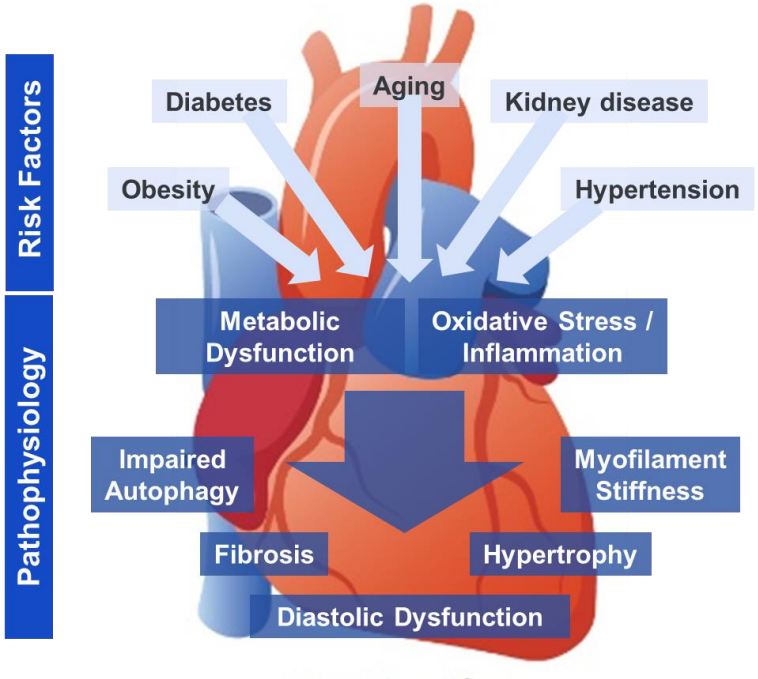
TN-301: Small Molecule HDAC6 Inhibitor for HFpEF

Potential to Address the Greatest Medical Need in Heart Disease

Disease Overview

What is HFpEF?

- Complex syndrome characterized by poor relaxation and filling of the left ventricle (diastolic dysfunction)
- Defined as heart failure with LVEF ≥50%
- High overlap with diabetes and obesity



Disease Symptoms and Severity

- **~24%** of HFpEF population has NYHA Class III or IV disease
  - Fatigue, shortness of breath, tissue swelling, edema
  - Diminished quality of life and reduced capacity for physical activity
- **75%** mortality rate over 5-year period following first hospitalization

Epidemiology

- **50%+** of all heart failure
- **3MM** patients in the U.S.; **13MM** worldwide
- Incidence is on the rise

Standard of Care

- Standard heart failure medications (beta blockers, calcium channel blockers, ACEs, ARBs) to alleviate symptoms
- SGLT2 inhibitors (e.g., empagliflozin) originally approved for diabetes have recently demonstrated positive impact on HFpEF

HFpEF = Heart Failure with Preserved Ejection Fraction
LVEF = Left Ventricular Ejection Fraction
NYHA = New York Heart Association
ACEs, ARBs = Angiotensin-Converting Enzyme and Angiotensin Receptor Blockers
SGLT2 = Sodium-glucose cotransporter-2

TN-301: Small Molecule HDAC6 Inhibitor for HFpEF

HDAC6 Inhibition Represents a Promising Novel Target for HFpEF

Tenaya Product Candidate	
TN-301: HDAC6 Inhibitor Program	
Target	**Histone deacetylase 6 (HDAC6) enzyme**
Modality	**Highly selective small molecule HDAC6 inhibitor**
MOA	**HDAC6 inhibition has a multi-modal MOA leads to alternations in cellular processes impacting metabolism, inflammation and cardiac function**

- HDAC6 part of a class of enzymes localized to cytoplasm
- Does *not* modify histones and does *not* directly regulate gene expression

- TN-301 2000x selective inhibition of HDAC6 vs other HDACs
- TN-301 selectivity for HDAC6 is higher vs other partially selective HDAC6 inhibitors already in clinical development

Multi-Modal MOA

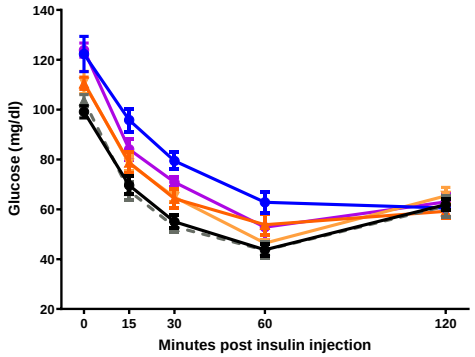
	Inflammation	Metabolic Dysfunction	Fibrosis	Hypertrophy	Impaired Autophagy	Diastolic Dysfunction
Cardiac fibroblasts (in vitro)			✓	✓		
hiPSC-cardiomyocytes (in vitro)		✓				
BAG3 DCM mouse model (in vivo)	✓	✓			✓	
Diet induced obesity mouse model (in vivo)	✓	✓				
HFpEF mouse model (ex vivo analysis of heart & adipose tissue)	✓	✓	✓			
HFpEF mouse model (in vivo)		✓	✓	✓	✓	✓

TN-301: Small Molecule HDAC6 Inhibitor for HFpEF

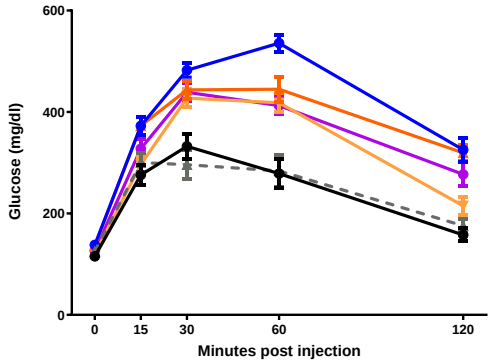
HDAC6 Inhibition Improves Hallmarks of Disease Preclinically

Improvement in Overall Metabolism

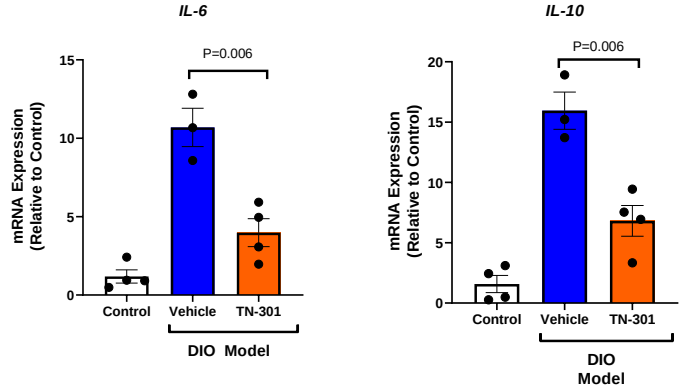
Glucose Tolerance



Insulin Sensitivity

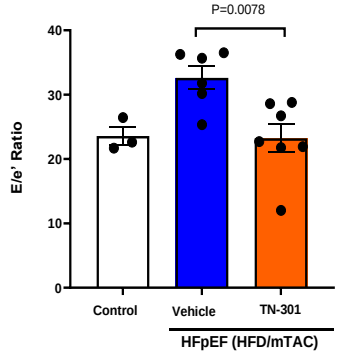


Reduced Inflammatory Markers

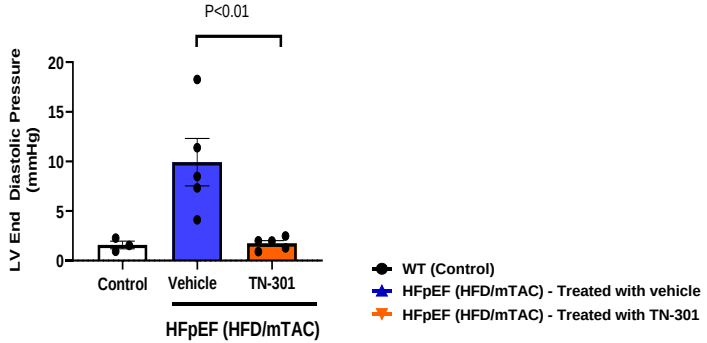


Improvement in Diastolic Function

E/e'

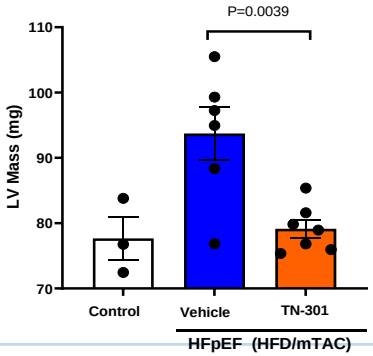


LVEDP

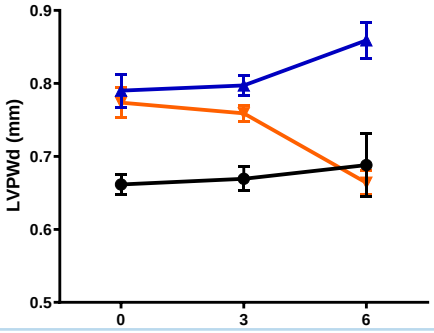


Reduced Hypertrophy

LV Mass



LV Wall Thickness



HFpEF - heart failure with preserved ejection fraction
LVEDP – Left Ventricular End Diastolic Pressure
E/e' – Measure of Left Ventricular Filling pressure

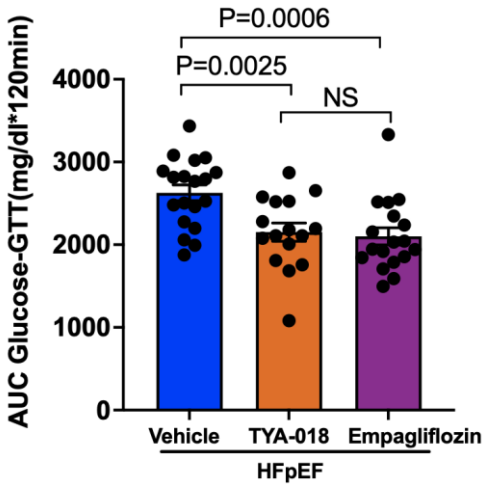
TN-301: Small Molecule HDAC6 Inhibitor for HFpEF

Comparable Efficacy to SGLT2 Inhibition Observed in Mouse Model

Head-to-head comparison of HDAC6i with empagliflozin validates preclinical HFpEF model and illustrates potential translation of preclinical results to clinical utility with differentiated mechanism

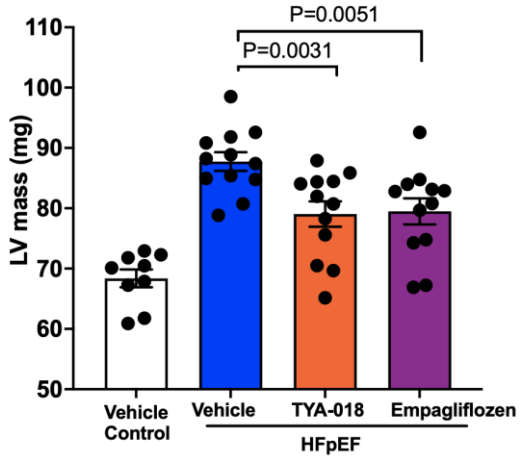
Improvement in Glucose Tolerance

Single dose

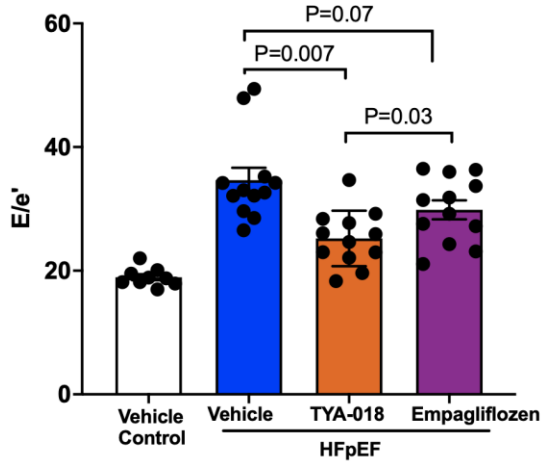


Improvement in LV Mass

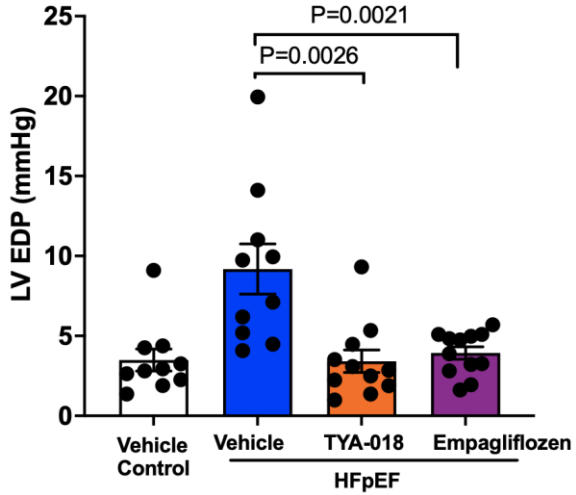
Chronic dosing



Improvement in Diastolic Function



Improvement in LV End Diastolic Pressure



[1] TYA-11018 is an HDAC6i analog of TN-301 demonstrating equivalent activity and efficacy in various *in vitro* and *in vivo* models.
[2] Empagliflozin = SGLT2 inhibitor (Jardiance® Boehringer Ingelheim/Eli Lilly, FDA approved for HFpEF as of February 2022)

SGLT2 = Sodium-Glucose Cotransporter-2
HFpEF = Heart Failure with Preserved Ejection Fraction
LV = Left Ventricle

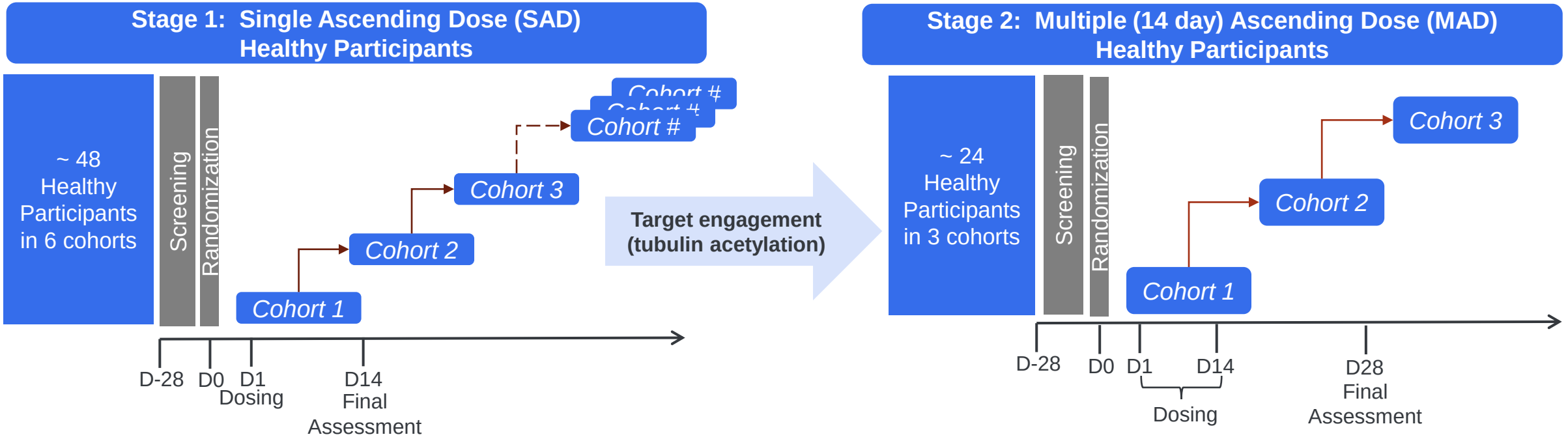
TN-301 HDAC6i Small Molecule Program for HFpEF

First-in-Human Phase 1 Study to Assess Safety and Tolerability

Phase 1 Data Anticipated in 2023

- **Study Objective:** Establish safety profile, confirm target engagement and identify dose ranges for later studies
- **Design:** Two-stage, single and multiple ascending dose, blinded, randomized (3:1), placebo-controlled

- **Primary Endpoint:** Safety and tolerability
- **Secondary endpoint:** Pharmacokinetics and pharmacodynamics (including target engagement)



TN-201

MYBPC3 Gene Therapy Program for Genetic Hypertrophic Cardiomyopathy (gHCM)

TN-201: MYBPC3 Gene Therapy Program for gHCM

Addressing the Leading Genetic Cause of Hypertrophic Cardiomyopathy

Disease Overview

Pathophysiology

- Mutation in *MYBPC3* disrupts contractile apparatus (sarcomere)
- Cardiomyocyte hypertrophy, disarray and fibrosis
- Stiff heart muscle contributes to poor heart filling (diastolic dysfunction)
- Abnormal heart rhythms

Disease Symptoms and Severity

- Heterogeneous presentation
- Heart failure, sudden cardiac death can occur in adults and children
- Premature infant death in the most severe cases

Epidemiology

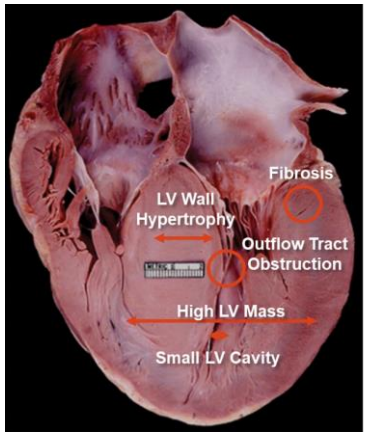
- *MYBPC3* mutations accounts for ~19% of all HCM
- Estimated >115K patients in U.S. alone

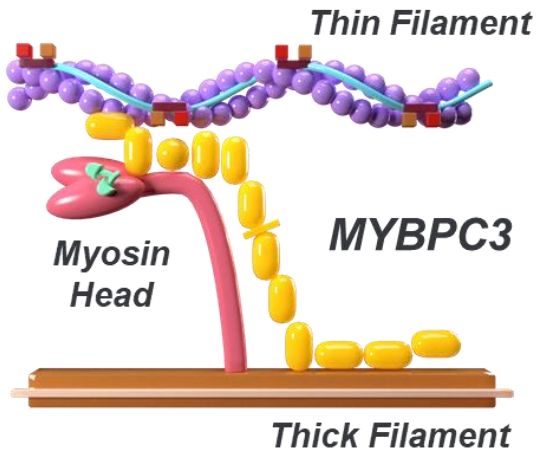
Standard of Care

- No treatments address the underlying genetic cause
- Myosin inhibitor (mavacamten) approved for use in oHCM patients

Tenaya Product Candidate

TN-201: MYBPC3 Program	
Target Cell	Cardiomyocyte
Modality	AAV9
Gene	*MYBPC3*
MOA	"Lock and key", replace a healthy copy of *MYBPC3* in patients with loss-of-function mutations
Stage	IND enabling





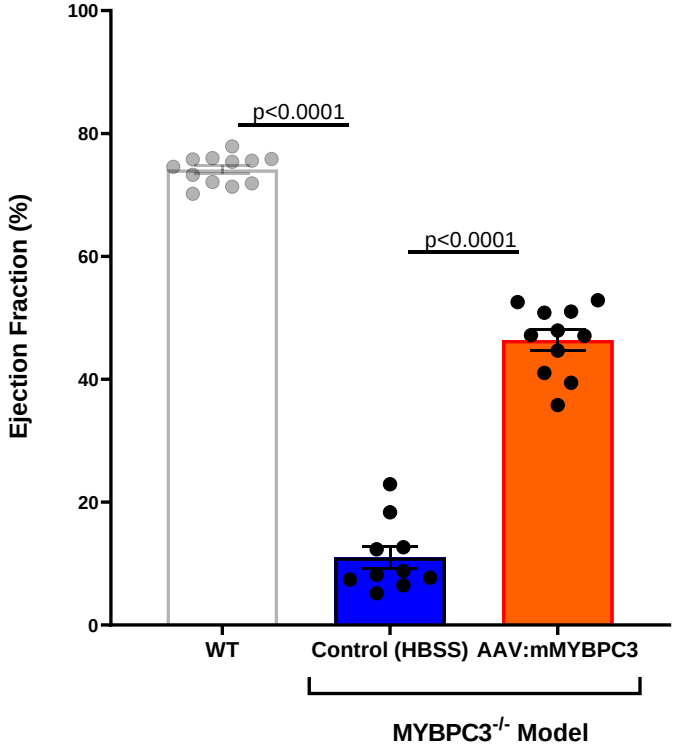
MYBPC3 = Myosin Binding Protein C3
HCM = Hypertrophic Cardiomyopathy
AAV9 = Adeno-Associated Virus Serotype 9
MOA = Mechanism of Action
IND = Investigational New Drug

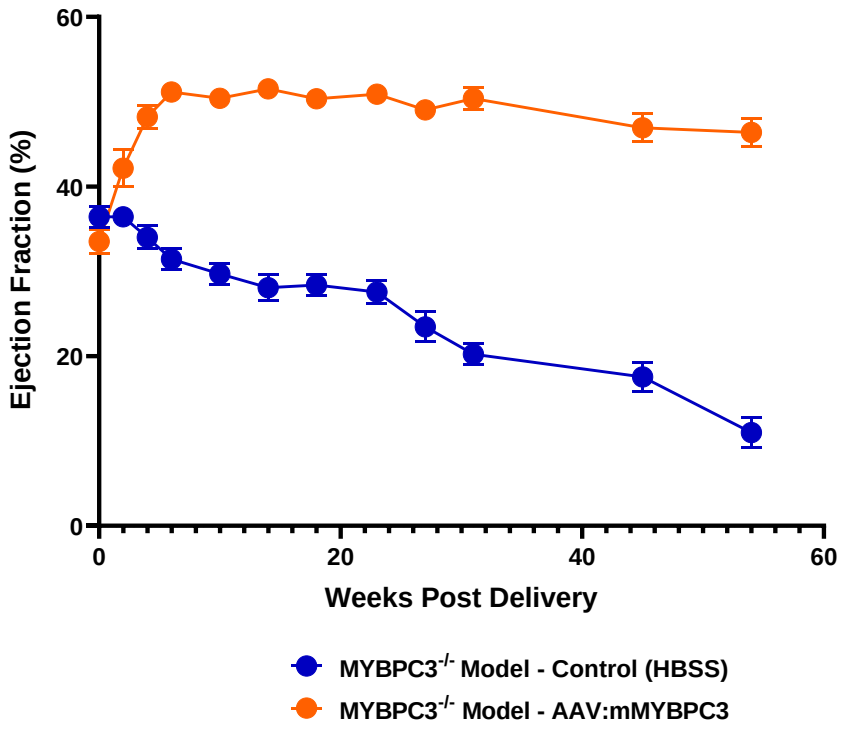
TN-201: MYBPC3 Gene Therapy Program for gHCM

Durable Disease Reversal and Survival Benefit Observed with a Single Dose

Significant and Durable Improvement in Heart Function (13 Months Post-Treatment)

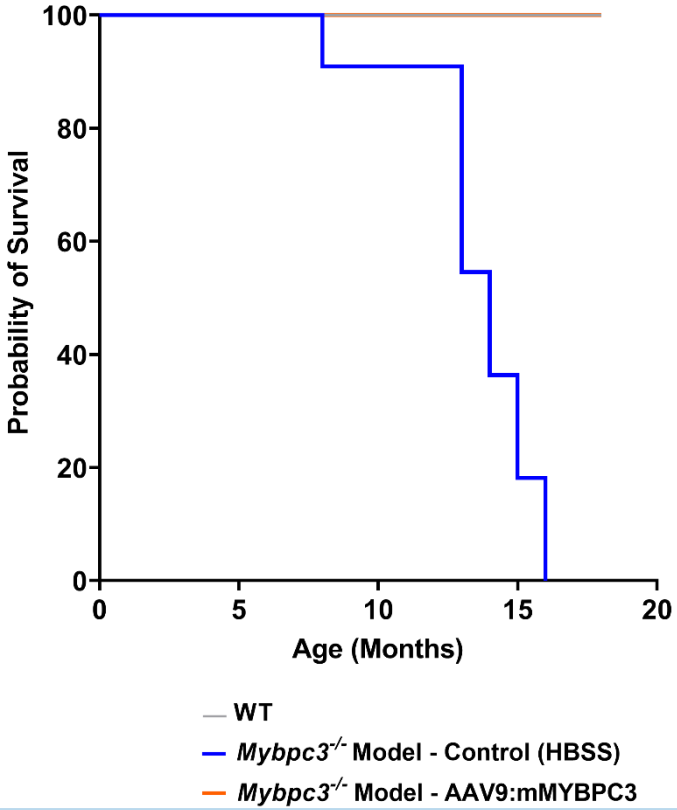
- Animals treated at 2 weeks of age, impact on heart function seen within 6 weeks
- Initial EF improvement of > 20% eventually grows to > 30%





Survival Benefit (18 Months Post-Treatment)

- 100% survival in AAV:MYBPC3 arm
- 100% mortality in control arm

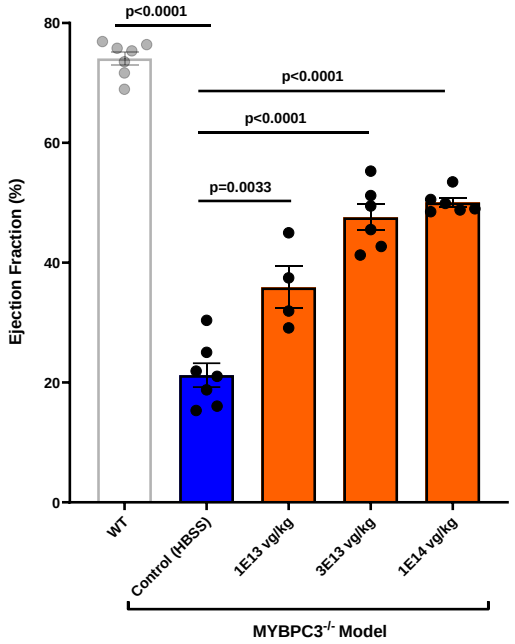


AAV9 = Adeno-Associated Virus Serotype 9
EF = Ejection Fraction

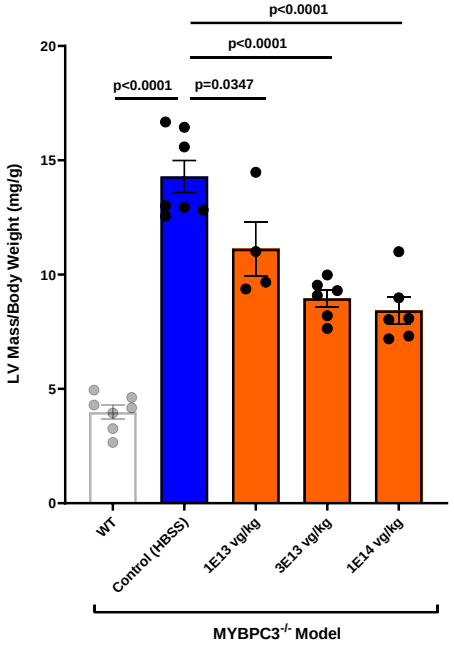
TN-201: MYBPC3 Gene Therapy Program for gHCM

Dose-Dependent Disease Reversal at Clinically Relevant Doses

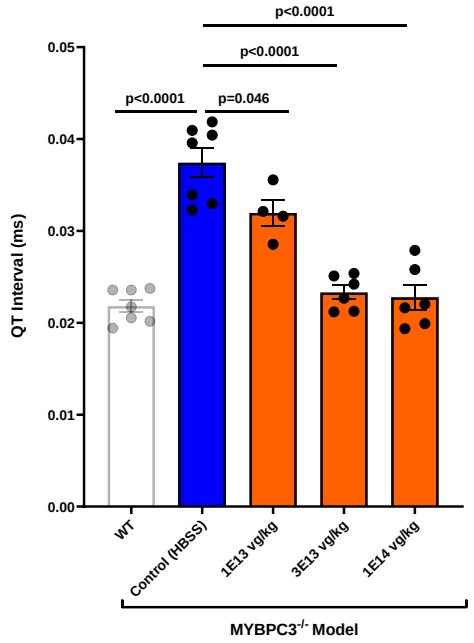
Improvement in Measures of Heart Contraction (8 Months Post Treatment)



Improvement in Measures of Heart Mass (8 Months Post Treatment)



Improvement in Measures of Electrophysiology (8 Months Post Treatment)

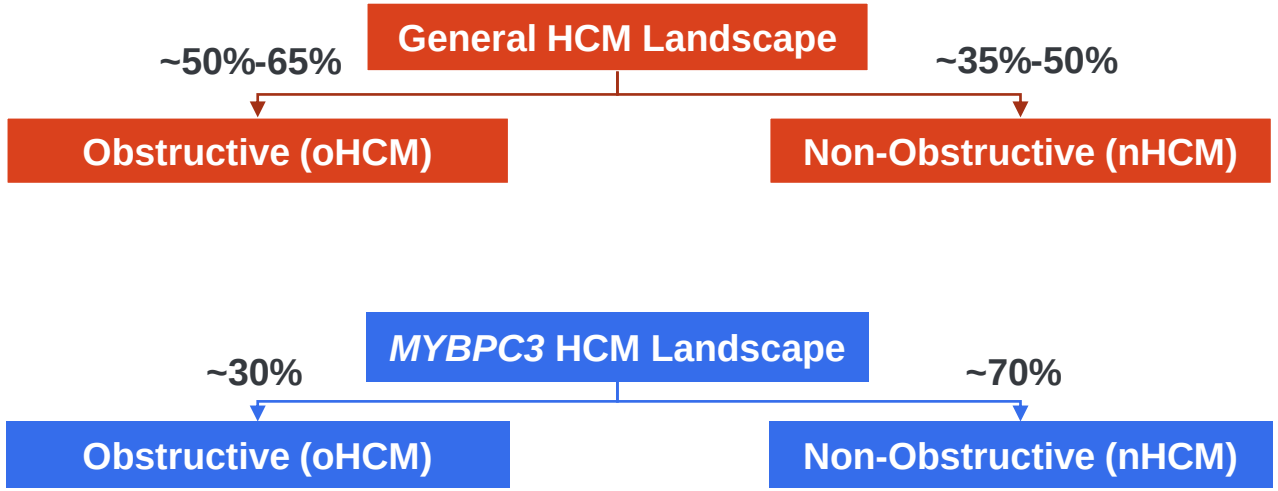


- TN-201 effect appears to plateau around 3×10^{13} vg/kg
- Based on these data, it may be feasible to consider doses for TN-201 in the 3×10^{13} vg/kg to 1×10^{14} vg/kg range during clinical development.
- Additional data from IND enabling studies, as well as feedback from the FDA, will inform the specific doses we use for early clinical development of TN-201.

AAV9 = Adeno-Associated Virus Serotype 9
IND = Investigational New Drug

TN-201: MYBPC3 Gene Therapy Program for gHCM

Initial Studies will Focus on Symptomatic nHCM Adults Potentially Broadly Relevant for Most Patients with *MYBPC3* Mutations



- Disease severity higher w/ pathogenic mutations in sarcomeric genes
- Majority of patients with *MYBPC3* mutations have nHCM
- *MYBPC3* mutations are enriched (~60%) in children with severe HCM
- Small molecule options have not demonstrated robust efficacy in preclinical models of *MYBPC3* HCM
- Endpoints for clinical studies in oHCM patients also relevant for nHCM

TN-201 Target Profile

- Targeting underlying cause of disease (*MYBPC3* mutations)
- Disease modifying therapy with durable response after a single dose
- MOA relevant for both oHCM and nHCM patients
- MOA relevant for both severe, rapidly progressing homozygous infants and heterozygous children and adults

TN-201 Clinical Development

- Safety and efficacy of TN-201 will initially be explored in symptomatic adult nHCM patients
- Phase 1 assessments will include clinically relevant PD markers and echo parameters that have been shown to have meaningful changes within a few weeks to months in prior HCM trials

HCM = hypertrophic cardiomyopathy
MOA = mechanism of action
PD = pharmacodynamic

Catalysts

	1H 2022	2H 2022	2023+
TN-301 Small molecule HDAC6 inhibitor for HFpEF	✓ Presented new preclinical data at ESC-HF	✓ IND submitted and cleared ✓ Initiated Phase 1 SAD/MAD clinical study	• Begin MAD portion of Phase 1 • Report Phase 1 SAD/MAD data
TN-201 AAV gene therapy for MYPBC3+ HCM		• Submit IND to U.S. FDA	• Initiate clinical studies
TN-401 AAV gene therapy for PKP2+ ARVC	✓ Presented preclinical data at HRS & ASGCT	• Support establishment of global natural history study/registry	• Submit IND to U.S. FDA • Initiate clinical studies
Research pipeline	✓ Presented preclinical data on AAV capsid engineering efforts		• Advance earlier-stage programs to IND-enabling stage
Manufacturing	✓ Launched operations of cGMP for Genetic Medicines Manufacturing Center at 1000L		• Scale up manufacturing of TN-401 in anticipation of clinical studies

Cash Balance of $180.9 MM*: Sufficient to Fund Operations At Least Into 2H 2023

TENAYA THERAPEUTICS

cGMP = current Good Manufacturing Practice
IND = investigational new drug application
AAV = adeno-associated virus

* Cash, cash equivalents and investments in marketable securities (current and noncurrent) as of June 30, 2022