



INTERIM DATA FROM RIDGE™-1:

A PHASE 1B/2 STUDY OF TN-401, AN AAV9 INVESTIGATIONAL GENE THERAPY, IN ADULTS WITH *PKP2*+ ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY (ARVC)

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PKP2+ ARVC: AN AUTOSOMAL DOMINANT DISEASE, RESULTING IN LIFE-THREATENING ARRHYTHMIAS

PKP2+ ARVC Pathophysiology...

- Plakophilin (PKP2) is a structural protein required for normal heart development and performance
- Mutations in *PKP2* reduce plakophilin levels, leading to unstable electrical and structural connectivity between cardiomyocytes
- Electrical instability leads to ventricular arrhythmias, including PVCs, NSVTs, and sudden cardiac arrest
- Progression results in heterogeneous, patchy fibrofatty infiltration across affected myocardial regions¹

Image of an ARVC Heart¹



ARVC: arrhythmogenic right ventricular cardiomyopathy
PVC: premature ventricular cardiomyopathy
NSVT: non-sustained ventricular tachycardia

...Results in Severe Arrhythmia Burden

90% have more than 500 PVCs per day, despite standard of care²

55% have a history of ventricular tachycardia²

16% present with cardiac arrest, most without prior symptoms³

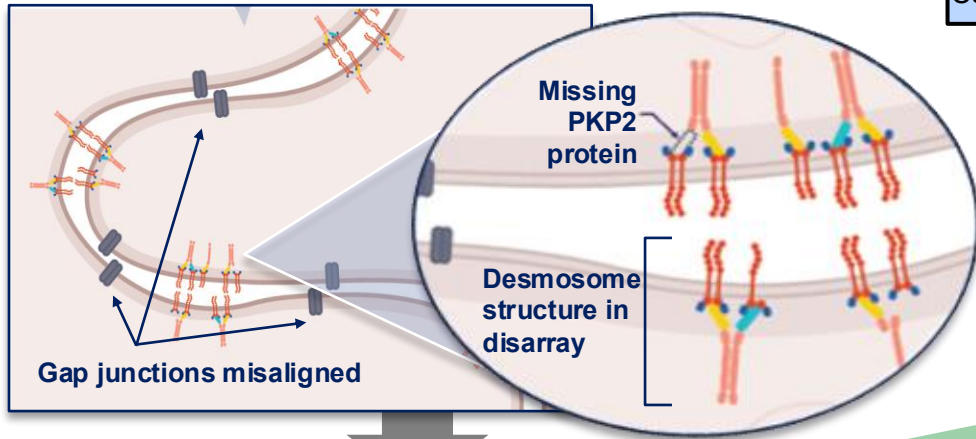
¹Basso, et al., *Circ* 2016

²Calkins, et al., *HRS* 2025

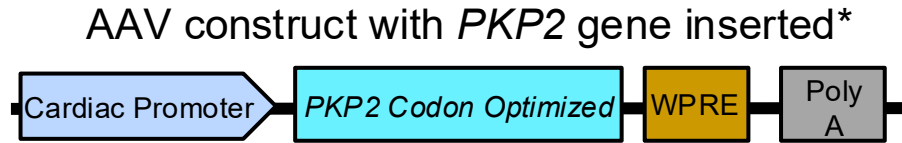
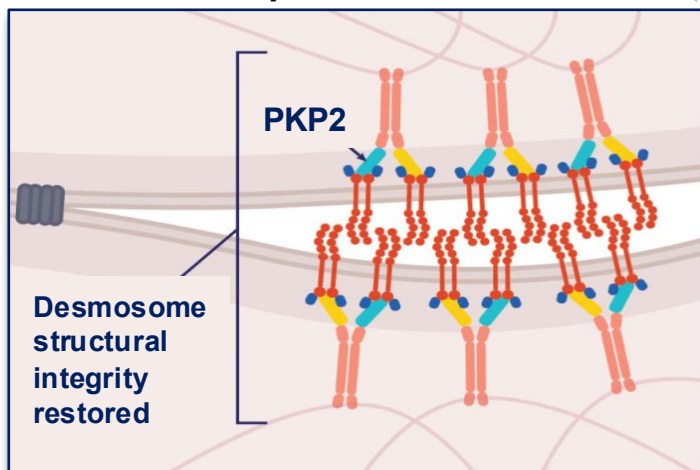
³Gupta, et al., *Am J Cardiol* 2017

ADENO-ASSOCIATED VIRUS (AAV): *PKP2* GENE REPLACEMENT THERAPY

PKP2 haploinsufficiency
(reduced plakophilin 2 levels)



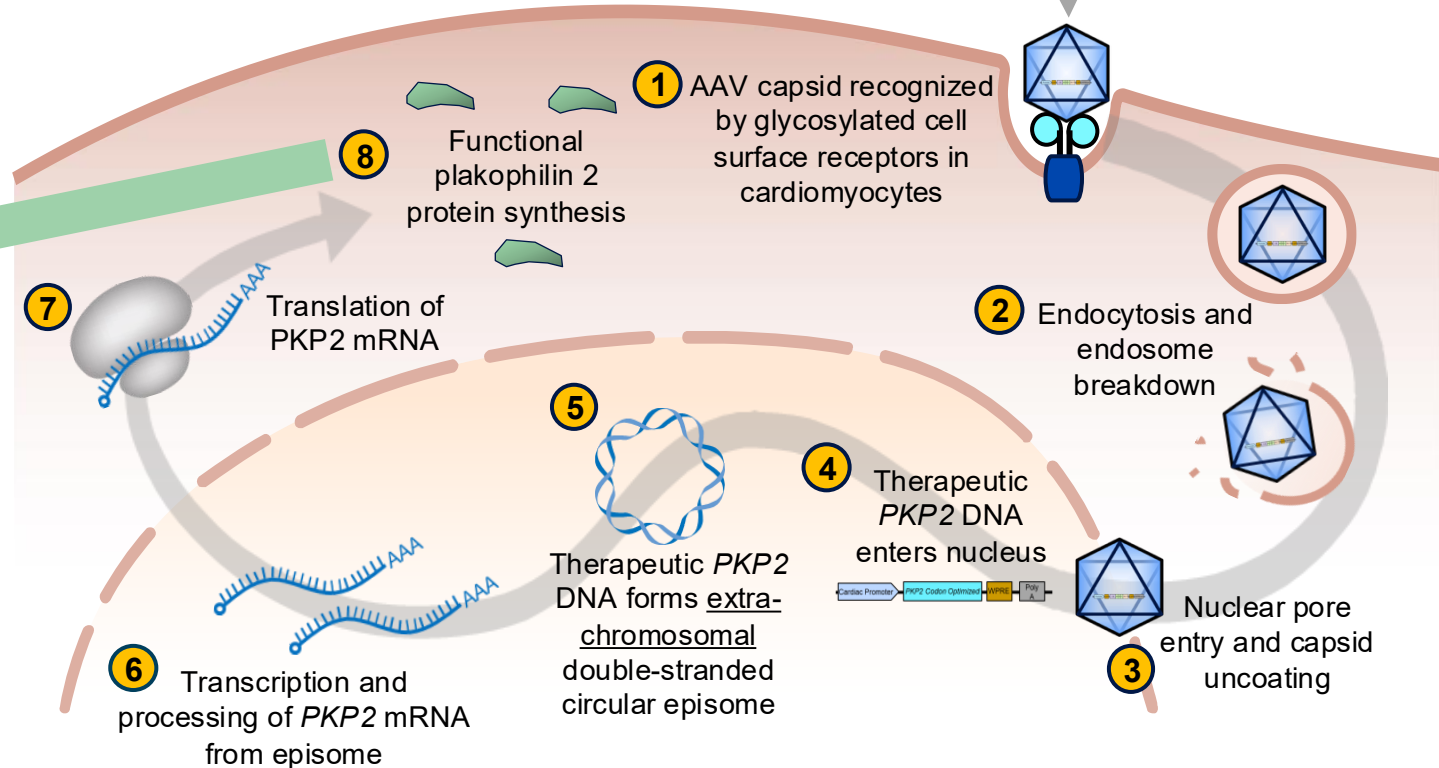
PKP2 expression restored



*AAVs are **naturally** occurring, non-integrating viruses that do not cause disease

AAV9 containing *PKP2* gene

Single IV Infusion



RIDGE-1: PHASE 1B/2 TRIAL OF TN-401 IN ADULTS WITH *PKP2*+ ARVC

Treatment goal: Demonstrate Reduction in Arrhythmic Events

Study Objectives

- Safety and tolerability
- Dose-finding
- Pharmacodynamics

Endpoints

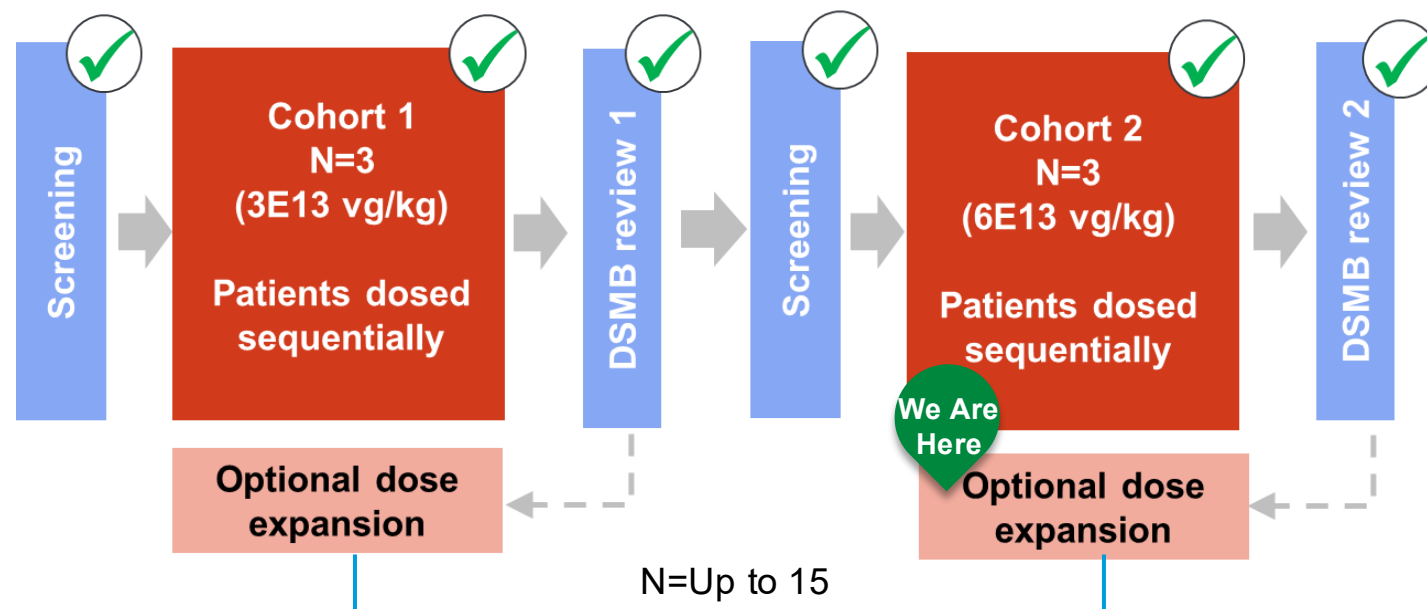
- Safety and tolerability
- Transgene uptake and expression
- Changes in PVC and NSVT counts
- ICD shock and VT frequency
- Structural/hemodynamic changes
- Plasma biomarkers
- Patient-reported outcomes

PVC: premature ventricular contraction
NSVT: non-sustained ventricular tachycardia
ICD: implantable cardiac defibrillator
VT: ventricular tachycardia

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

Enrolling at
9 sites in
US and UK



RIDGE-1 PATIENTS' ARRHYTHMIA BURDEN MORE SEVERE THAN BROADER *PKP2+* ARVC POPULATION

Screening Characteristics of RIDGE-1 Participants

More severe vs. average	Avg. NHx <i>PKP2+</i> Pt ¹	Cohort 1 (3E13 vg/kg)			Cohort 2 (6E13 vg/kg)		
		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Follow-Up	-	52 weeks	52 weeks	40 weeks	32 weeks	26 weeks	20 weeks
Gender	Male (62%)	Male	Male	Male	Male	Male	Male
Age at Dosing (y)	-	41	37	56	40	31	27
Age at ARVC Dx (y)	34	26	16	53	20	16	17
PVC Count (#/24h)	2,480	2,462	618	2,666	1,571	7,819	8,634
NYHA Class	Class I (74%)	Class I	Class I	Class I	Class I	Class I	Class I
% ICD & Age (y)*	100%, 35	26	16	53	20	16	17
Severe VA**	No (61%)	Yes; 7x	Yes; 5x	No	No	Yes; 11x	Yes; 3x
VT Ablation	No (54%)	Yes; 2x	Yes	No	Yes	No	Yes; 2x
RV Dysfunction	Yes (54%)	Yes	Yes	Yes	Yes	Yes	Yes
Background meds	Yes (88%)	Yes	Yes	Yes	Yes	Yes	Yes

*RIDGE Natural History Study of *PKP2+* ARVC patients required ICD. Published estimates suggest 35-80% have ICD²

**Severe VAs include sustained VT, VF, and appropriate ICD therapy

NHx: RIDGE Natural History Study
PVC: premature ventricular contraction
NYHA: New York Heart Association

ICD: implantable cardioverter defibrillator
VA: ventricular arrhythmia
VT: ventricular tachycardia
VF: ventricular fibrillation
RV: right ventricular

¹Calkins, et al., HRS 2025

²Gasperetti, et al., *EP Europace* 2023

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BOTH TN-401 DOSES EQUALLY WELL TOLERATED

Summary of Safety, Tolerability, and Immunosuppression Across Cohorts 1 and 2

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

**Event attributed to or associated with immunosuppression medication error

†Unrelated to TN-401

- Majority of TN-401-related AEs have been **mild, asymptomatic, and manageable**
- Cohort 1 AEs have been **previously disclosed**
- Cohort 2 AEs include 2 AEs in the same patient due to a **medication error**:
 - 1 Grade 3 liver enzyme elevation associated with medication error resulting in steroid interruption
 - 1 Grade 3 SAE of thrombocytopenia due to medication error with sirolimus (trough 40.4 ng/mL)
- **No** clinical thrombotic microangiopathy (TMA)
- **No** sustained VT, VF, or ICD therapy related to TN-401. No other cardiotoxicities observed
- All patients have **completed IS**; duration and dose equivalent across cohorts
- **DSMB endorsed expansion** for both cohorts

VT: ventricular tachycardia

VF: ventricular fibrillation

ICD: implantable cardioverter device

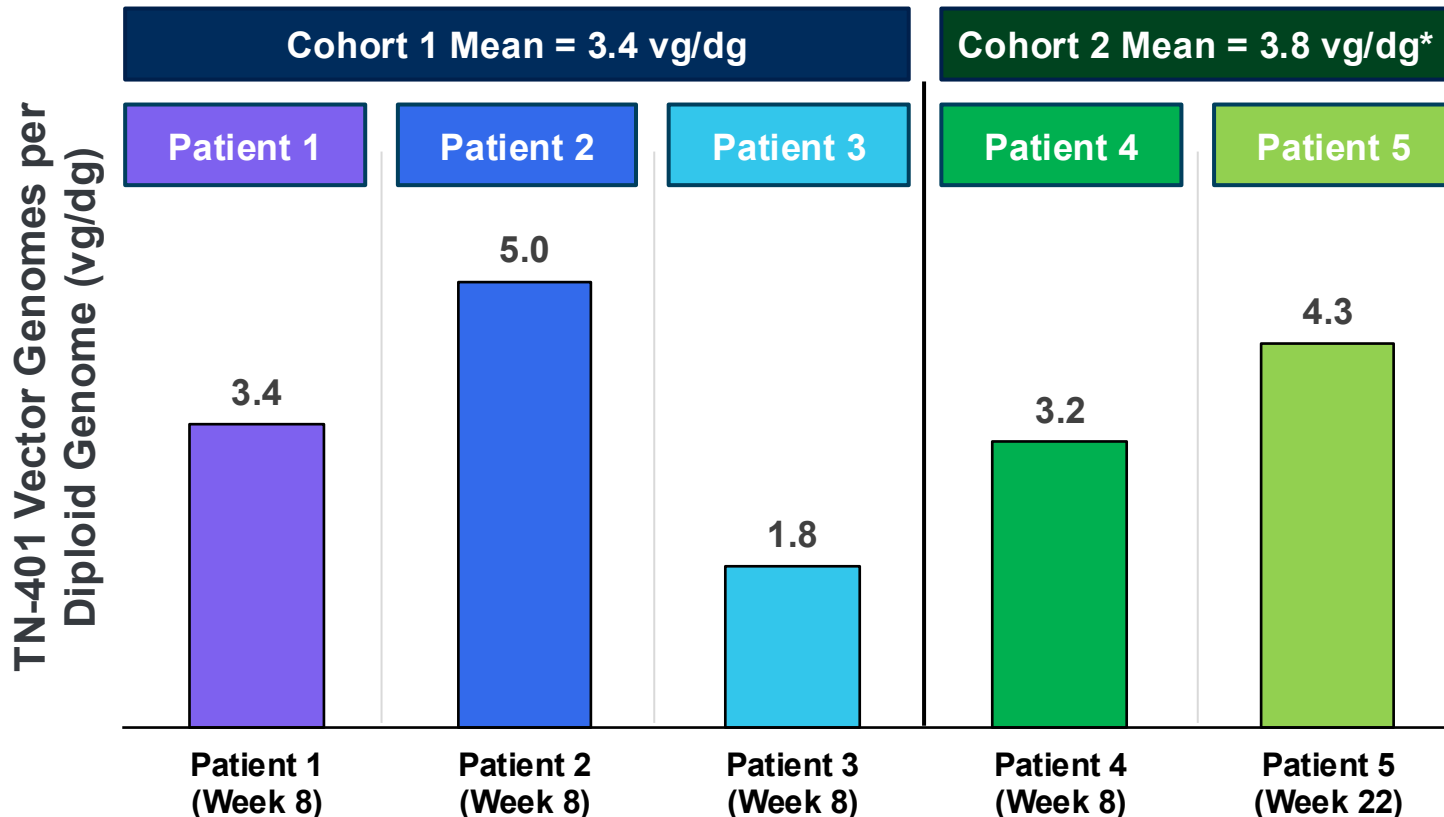
DSMB: Data Safety Monitoring Board

IS: immunosuppression

Data as of April 2026 data cut

TN-401 DNA LEVELS SHOW ROBUST CARDIAC TRANSDUCTION ACROSS BOTH DOSES

TN-401 DNA Levels at 1st Post-Dose Biopsy by Patient in Cohorts 1 and 2

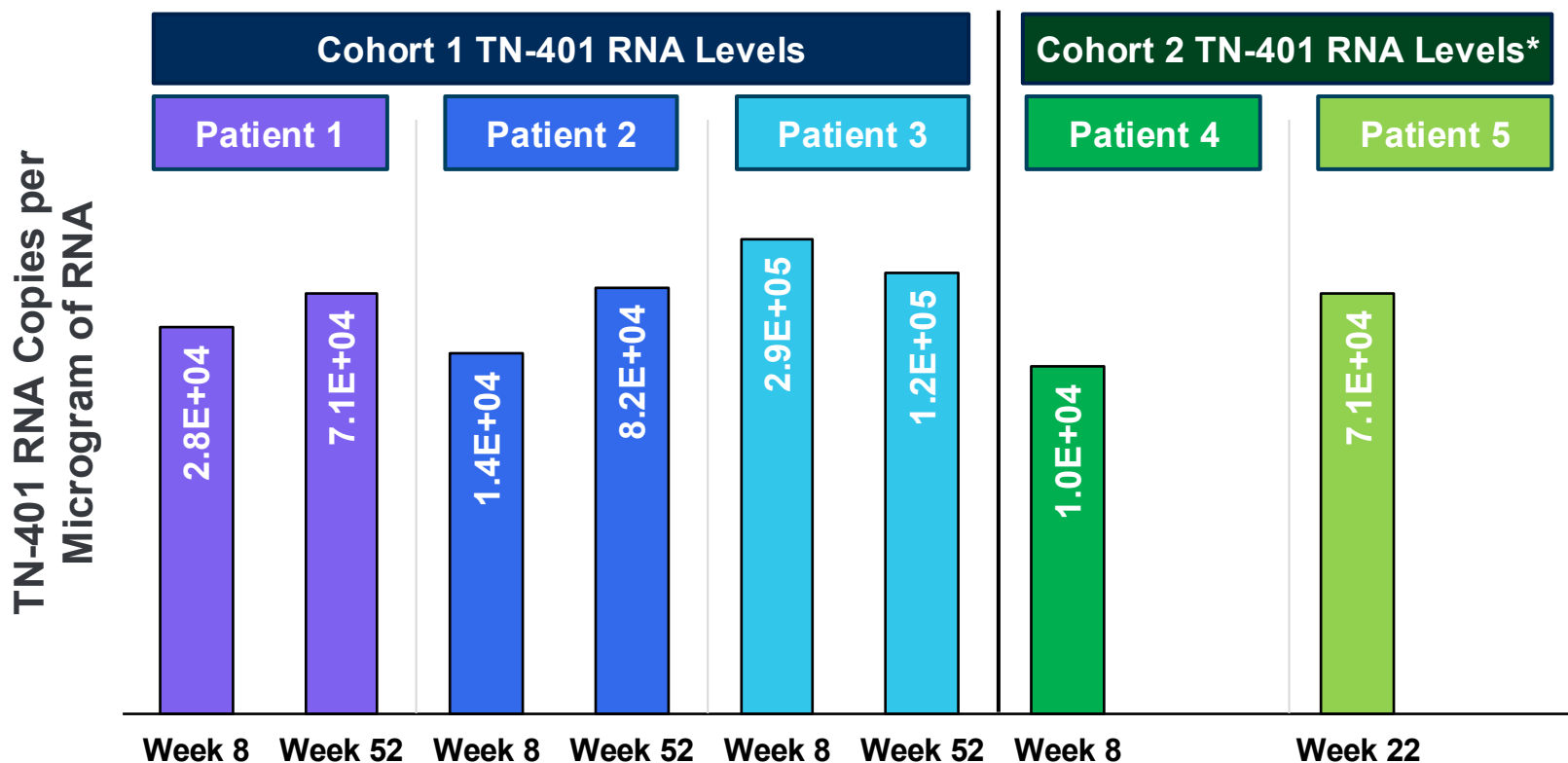


- Assay for assessing DNA levels specific to TN-401 vector genome
- TN-401 DNA is **undetectable at baseline as expected**
- Patients 1 through 4 had 1st post-dose biopsy performed at Week 8. Patient 5 1st post-dose biopsy taken at Week 22 to further assess TN-401 kinetics
- TN-401 DNA levels are **detectable after dosing and throughout follow-up**
- **Expect durable presence of TN-401 DNA in cardiomyocytes**, consistent with data from other cardiac gene therapies

*Patient 6 DNA analysis not completed by April 2026 data cut

TN-401 RNA LEVELS SHOW CARDIAC *PKP2* EXPRESSION IN ALL PATIENTS

Post-Dose TN-401 RNA Levels by Patient in Cohorts 1 and 2

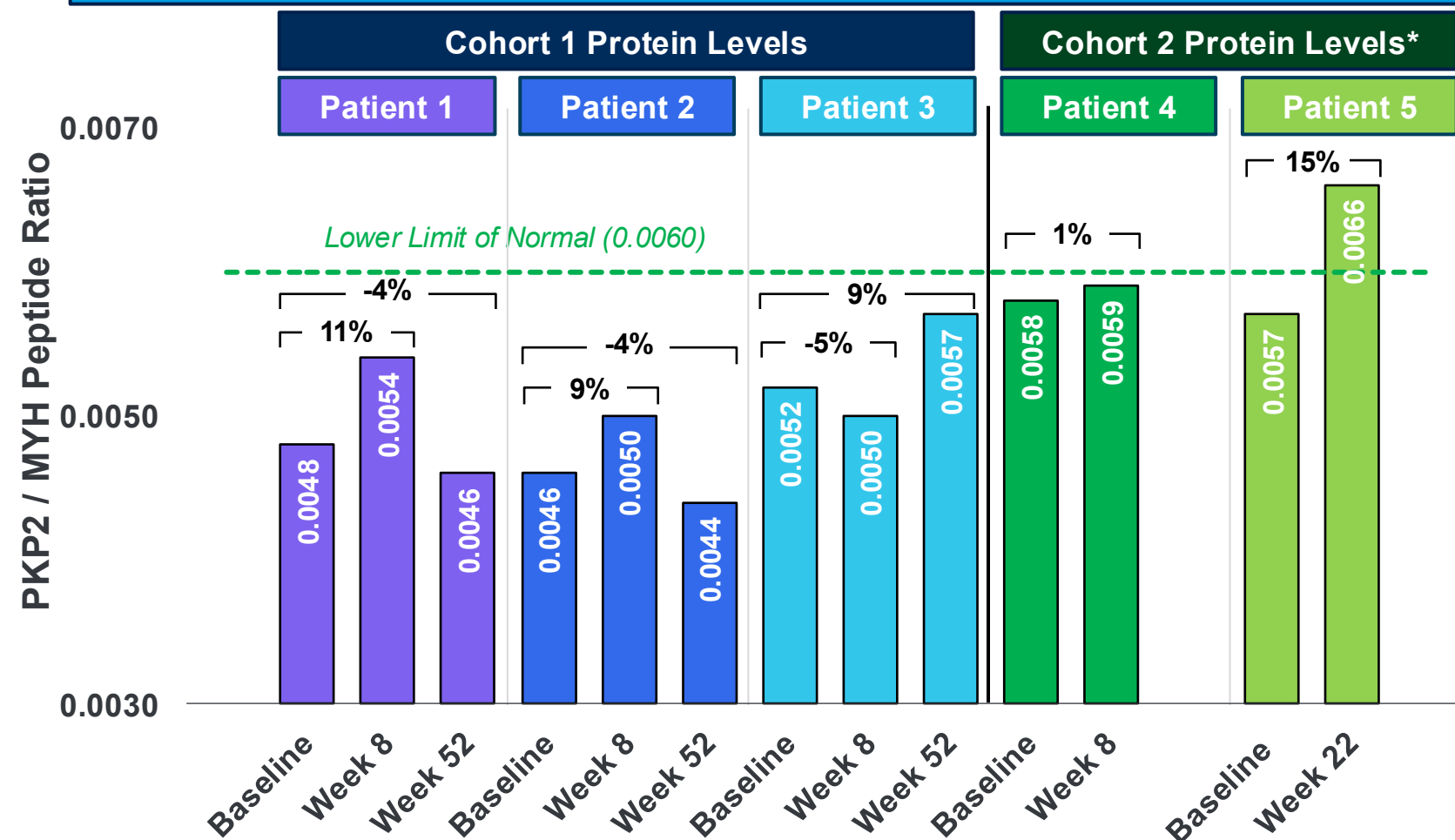


- Assay for TN-401 RNA is specific to TN-401 (vs. endogenous)
- TN-401 promoter drives **expression in cardiomyocytes**
- TN-401 RNA **undetectable at baseline as expected**
- **Durable expression** 52 weeks after single dose of TN-401 for all Cohort 1
- **Increasing RNA expression** in 2 of 3 patients in Cohort 1
- **TN-401 transgene expression clearly observed in target cell**, though results subject to variable cellular composition in small biopsies

*Patient 6 RNA analysis not completed by April 2026 data cut

ASSESSMENT OF TN-401 PROTEIN EXPRESSION COMPLICATED BY BIOPSY SAMPLE VARIABILITY

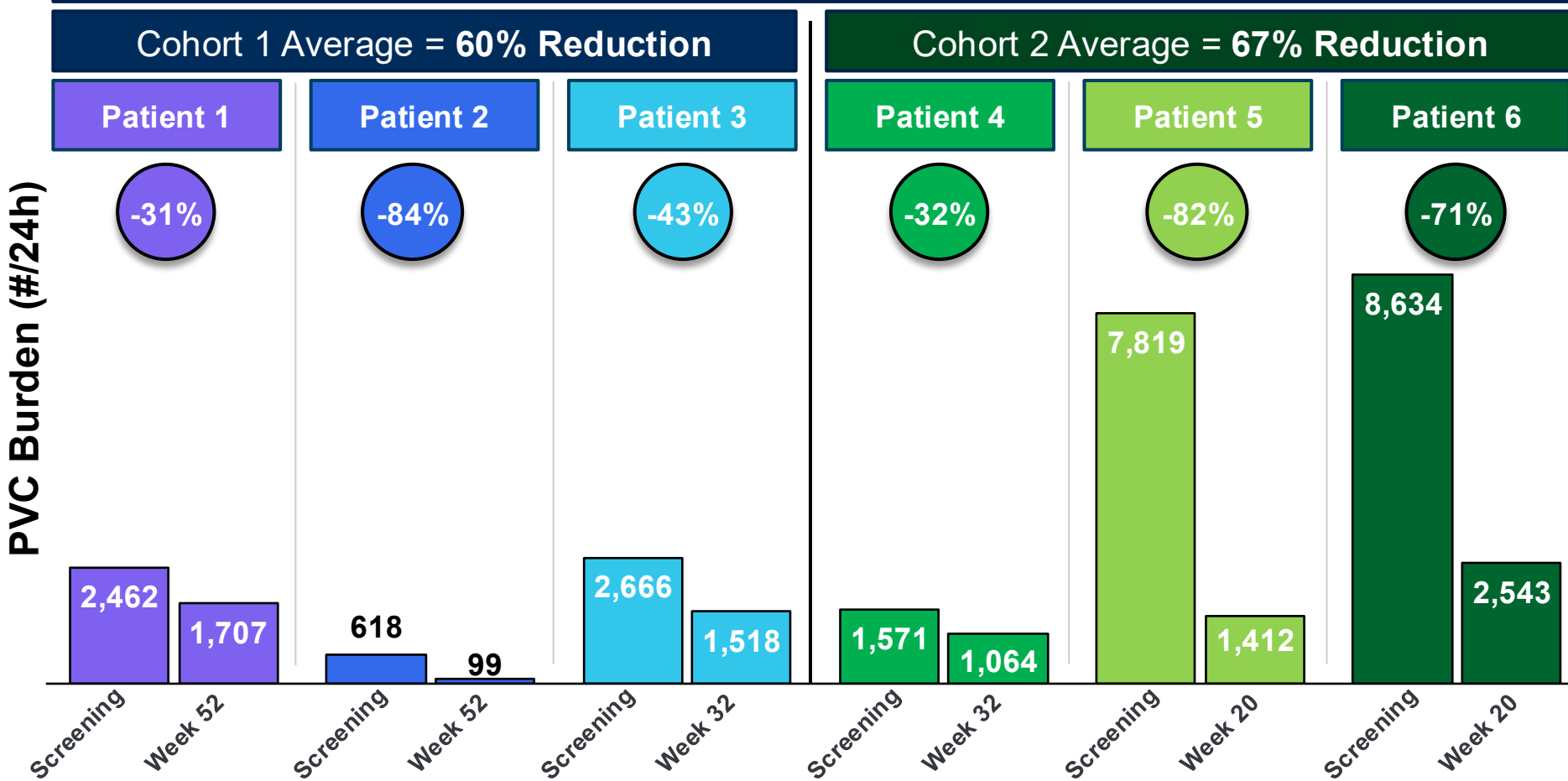
PKP2 Protein Levels Over Time in Cohorts 1 and 2



- LC-MS assay quantifies total PKP2 protein level, normalized to a cardiomyocyte protein (myosin, MYH)
- PKP2 protein from endogenous gene and TN-401 are indistinguishable
- PKP2 varies ~20% across healthy hearts, complicating assessment of TN-401 on PKP2 protein levels¹
- Variability is exacerbated across and within patients due to extent of fibrofatty infiltrate in myocardium
- **Totally of biopsy data**, including transduction, expression, and localization (not shown), **support TN-401 pharmacodynamic effect**

ALL PATIENTS HAD CLINICALLY MEANINGFUL REDUCTIONS IN PVC BURDEN POST-TN-401

Change in Daily PVC Rate from Screening to Most Recent Visit



- PVCs assessed by 7-day continuous ECG
- **Consistent reductions** in PVCs over time
- Cohort 1 reductions **remain durable** ≤1 year
- Cohort 2 reductions more **dramatic and rapid**, potentially a dose effect
- 5 of 6 had **completed IS** at most recent assessment
- PVC reduction **associated with 55% lower VA odds**¹

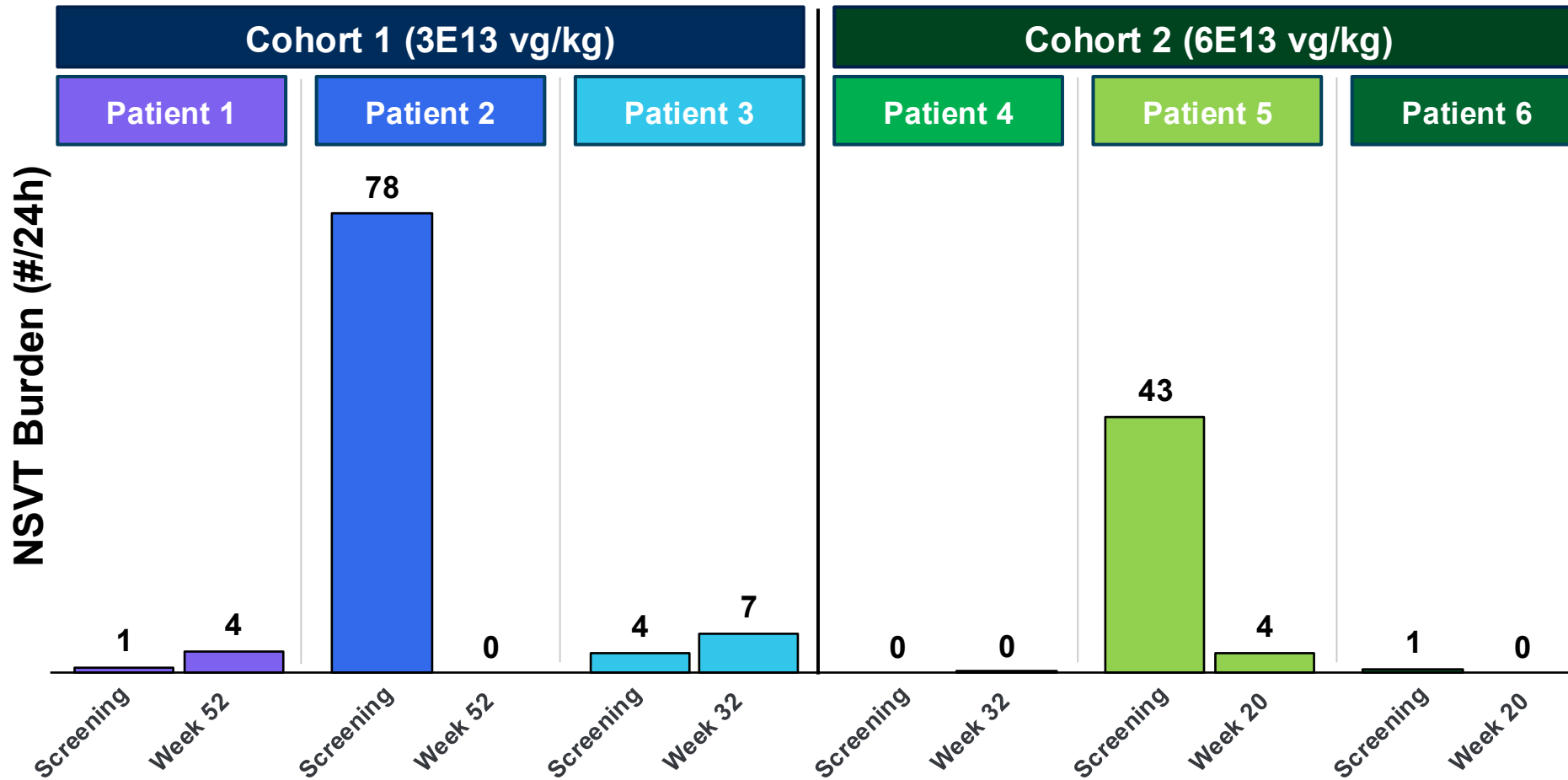
PVC: premature ventricular contraction
VA: ventricular arrhythmia

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

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

PATIENTS WITH HIGH NSVT BURDEN HAD DRAMATIC REDUCTIONS OVER TIME

Change in Daily NSVT Rate from Screening to Most Recent Visit



- 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

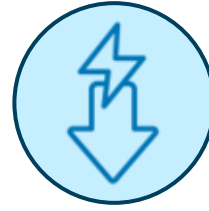
NSVT: non-sustained ventricular tachycardia
ECG: electrocardiogram

Data as of April 2026 data cut

CONCLUSIONS



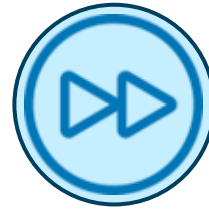
Enrolled patients are **more severe, electrically unstable** than broader *PKP2+* ARVC, despite standard of care



Patients had **clinically meaningful** reductions in PVCs, NSVTs after TN-401 treatment



TN-401 **well tolerated** across 3E13 vg/kg and 6E13 vg/kg doses



These data **support continued development** of TN-401 for *PKP2+* ARVC



TN-401 **transduces and is expressed** in cardiomyocytes at both doses

ACKNOWLEDGMENTS



- RIDGE-1 patients and their families
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