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Preliminary Data from Phase 1 Trial of RP-A601

May 2025

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Various statements in this presentation concerning Rocket's future expectations, plans and prospects that involve risks and uncertainties, as well as assumptions that, if they do not materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this release are forward-looking statements. You should not place reliance on these forward-looking statements, which often include words such as "believe," "expect," "anticipate," "intend," "plan," "will give," "estimate," "seek," "will," "may," "suggest" or similar terms, variations of such terms or the negative of those terms. These forward-looking statements include, but are not limited to, statements concerning Rocket's expectations regarding the safety and effectiveness of product candidates that Rocket is developing to treat Fanconi Anemia (FA), Leukocyte Adhesion Deficiency-I (LAD-I), Pyruvate Kinase Deficiency (PKD), Danon Disease (DD) and other diseases, the expected timing and data readouts of Rocket's ongoing and planned clinical trials, the expected timing and outcome of Rocket's regulatory interactions and planned submissions, Rocket's plans for the advancement of its DD program, including its planned pivotal trial, and the safety, effectiveness and timing of related pre-clinical studies and clinical trials, Rocket's ability to establish key collaborations and vendor relationships for its product candidates, Rocket's ability to develop sales and marketing capabilities or enter into agreements with third parties to sell and market its product candidates and Rocket's ability to expand its pipeline to target additional indications that are compatible with its gene therapy technologies. Although Rocket believes that the expectations reflected in the forward-looking statements are reasonable, Rocket cannot guarantee such outcomes. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Rocket's dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, the outcome of litigation, unexpected expenditures, Rocket's competitors' activities, including decisions as to the timing of competing product launches, pricing and discounting, Rocket's ability to develop, acquire and advance product candidates into, enroll a sufficient number of patients into, and successfully complete, clinical studies, Rocket's ability to acquire additional businesses, form strategic alliances or create joint ventures and its ability to realize the benefit of such acquisitions, alliances or joint ventures, Rocket's ability to obtain and enforce patents to protect its product candidates, and its ability to successfully defend against unforeseen third-party infringement claims, as well as those risks more fully discussed in the section entitled "Risk Factors" in Rocket's Annual Report on Form 10-K for the year ended December 31, 2024, filed February 27, 2025 with the SEC and subsequent filings with the SEC including our Quarterly Reports on Form 10-Q. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and Rocket undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

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PKP2-ACM (Plakophilin 2-Arrhythmogenic Cardiomyopathy)

PKP2-ACM is an inherited, autosomal dominant progressive arrhythmogenic cardiomyopathy (ACM)[1,2]

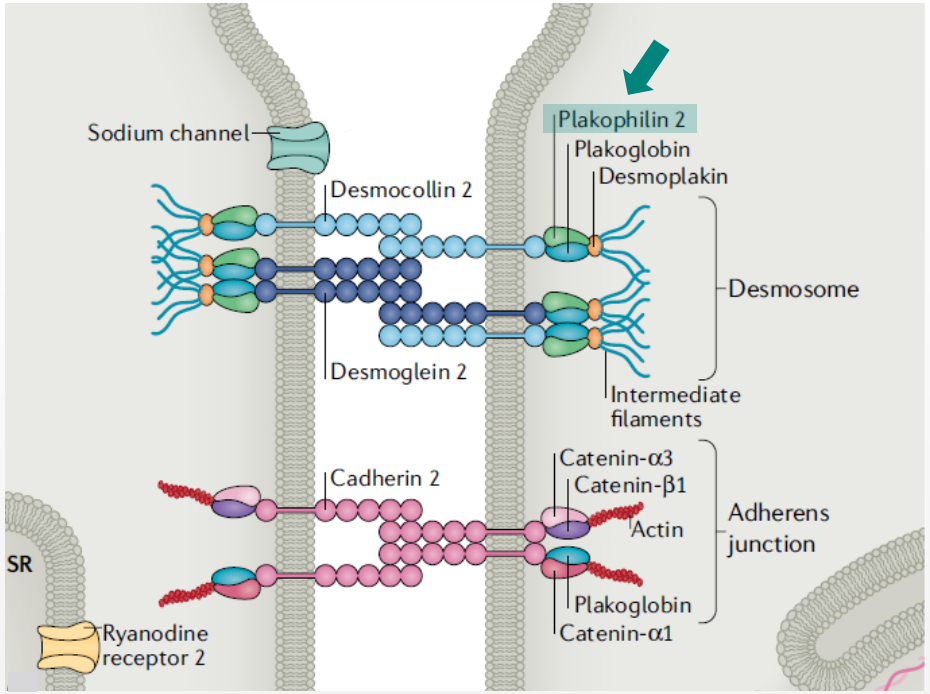
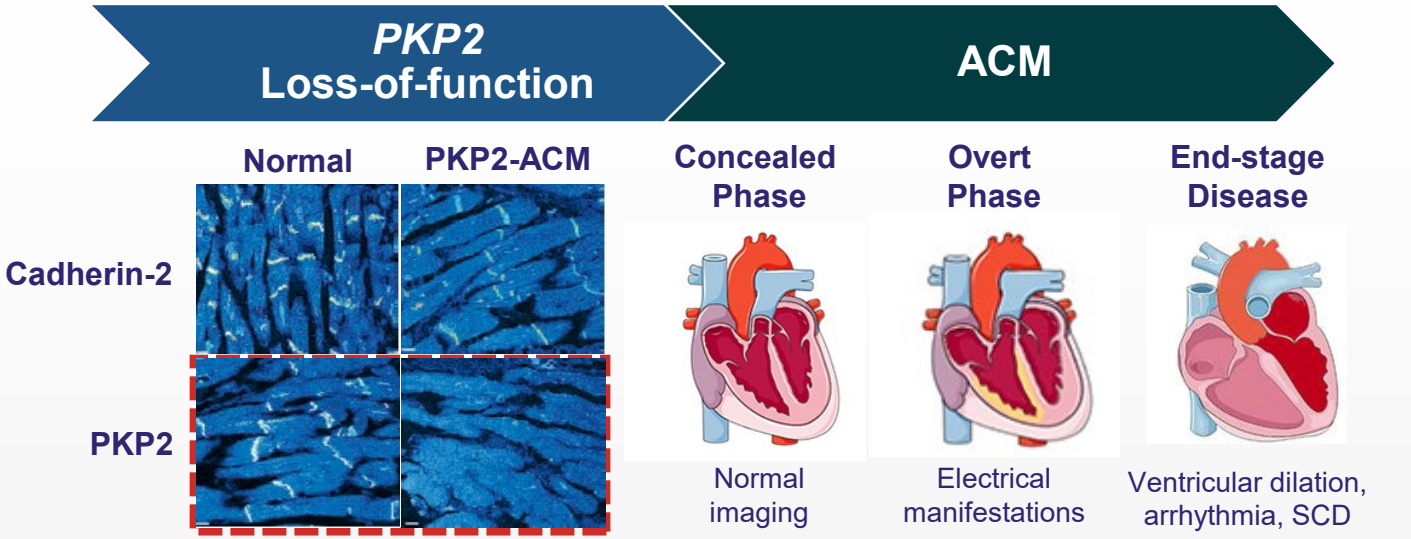


Figure used with permission from Austin KM, et al. *Nat Rev Cardiol*. 2019;16(9):519-537.



Figures used with permission from Asimaki A, et al. *N Engl J Med*. 2009;360(11):1075-1084 and Tadros HJ, et al. *Appl Clin Genet*. 2023;16:181-203.

Mean age at presentation: 35 ± 18 years[1]
Estimated prevalence: 50,000 (US+EU)[3-5†]

†Utilizing the conservative ACM prevalence of 1 in 5000 and the aggregated mean of 32.9% PKP2 mutation frequency in ACM calculated based on 2,572 ACM patients assessed from 13 publications.
ACM, arrhythmogenic cardiomyopathy; ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

1. Bhonsale A, et al. *Eur Heart J*. 2015;36(14):847-855. 2. Tadros HJ, et al. *Appl Clin Genet*. 2023;16:181-203. 3. Peters S, Trümmel M, Meyners W. *Int J Cardiol*. 2004;97(3):499-501. 4. McKenna WJ, Judge DP. *Nat Rev Cardiol*. 2021;18(1):22-36. 5. Data on file. Rocket Pharmaceuticals.

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ACM: High-Risk of Arrhythmias and Sudden Cardiac Death

No Currently Available Curative Treatment Options

Associated Risks[1]

In a study population of 439 index-patients, who fulfilled 2010 Task Force Criteria for ARVD/ARVC:

>70% Index patients experienced **sustained ventricular arrhythmias**

>80% Index patients receive **ICD placement**

~11% Index patients experience **sudden cardiac death** (SCD) or resuscitated SCD

Susceptibility[2]

- Frequent and/or endurance exercise are associated with increased likelihood of ACM diagnosis and severity; patients are often advised to avoid strenuous activity

Therapeutic Challenges[1,3-5]

- Current standard of care includes beta-blockers, anti-arrhythmic agents, ICD, and ablation
- Current therapeutic options do not alter pathophysiology or disease progression
- ICD firings are lifesaving but highly traumatic events
- Disease progression may lead to heart failure, premature death, or transplant

ACM, arrhythmogenic cardiomyopathy; ARVC, arrhythmogenic right ventricular cardiomyopathy; ARVD, arrhythmogenic right ventricular dysplasia; ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

1. Groeneweg JA, et al. *Circ Cardiovasc Genet.* 2015;8(3):437-446. 2. James CA, et al. *J Am Coll Cardiol.* 2013;62(14):1290-1297. 3. Bhonsale A, et al. *Eur Heart J.* 2015;36(14):847-855. 4. Towbin JA, et al. *Heart Rhythm.* 2019;16(11). doi:10.1016/j.hrthm.2019.05.007. 5. Hermida A, et al. *Eur J Heart Fail.* 2019;21(6):792-800.

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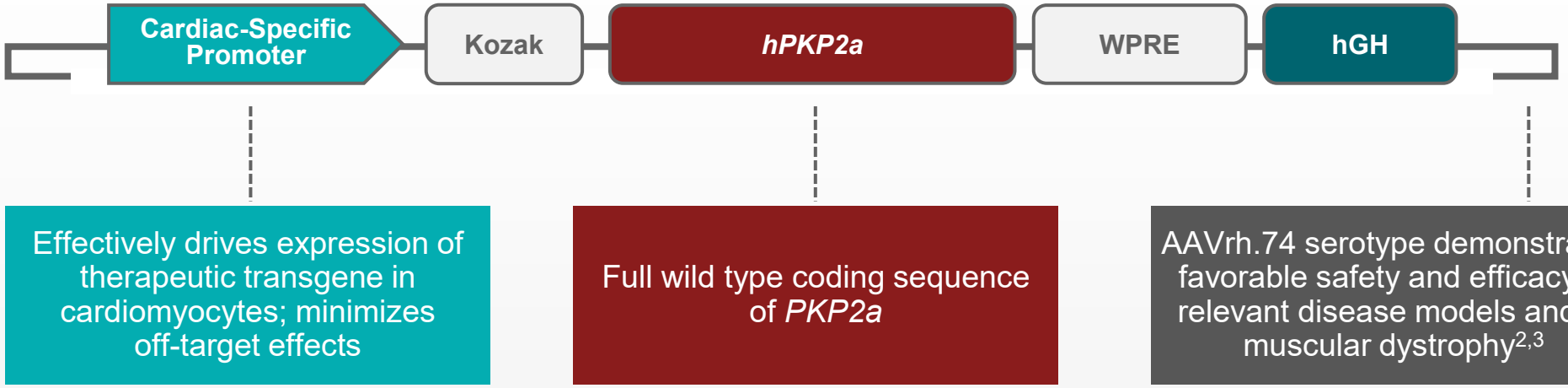
AAV Gene Therapy for PKP2-ACM: RP-A601

RP-A601 (AAVrh.74-PKP2a): recombinant adeno-associated viral (AAV) vector containing the coding sequence of human *PKP2a*[1]



A single RP-A601 infusion demonstrated cardiotropism, extended survival, and mitigated ISO-induced PVCs and arrhythmia in a conditional *PKP2a*-KO mouse model[4,5]

hGH, human growth hormone; ISO, isoproterenol; KO, conditional knock-out; PVC, premature ventricular contractions; WPRE, woodchuck hepatitis virus post-transcriptional regulatory element.

1. Herzog CD, et al. Preclinical Efficacy and Safety of AAVrh.74-PKP2a (RP-A601): Gene Therapy for PKP2-associated Arrhythmogenic Cardiomyopathy. ESGCT Congress 2023. 2. Rodino-Klapac LR, et. al. Safety, β-Sarcoglycan Expression, and Functional Outcomes From Systemic Gene Transfer of rAAVrh74.MHCK7.hSGCB in LGMD2E/R4. MDA Conference 2022. 3. Mendell J, et. al. A Phase 2 clinical trial evaluating the safety and efficacy of delandistrogene moxeparvovec (SRP-9001) in patients with Duchenne muscular dystrophy. MDA Conference 2022. 4. Cerrone M, et al. *Nat Commun.* 2017;8(1):106. doi:10.1038/s41467-017-00127-0. 5. van Opbergen CJM, et al. *Circ Genom Precis Med.* 2024;17(1):e004305. doi:10.1161/CIRCGEN.123.004305.

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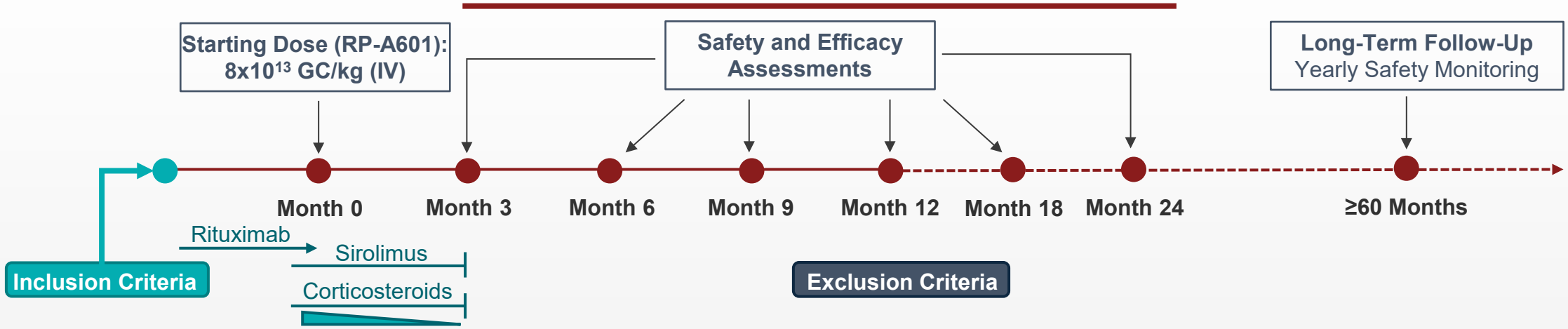
Phase 1 Study Overview

First-in-Human, Phase I, Open-label, Dose Escalation Trial of RP-A601 in Adult Patients with PKP2-ACM

Primary Endpoints: Safety
- Incidence of TEAEs
- Incidence of SAEs
- Identification of dose limiting toxicities

Secondary Endpoints: Efficacy
- Change in PKP2 protein expression
- Change in frequency of clinical markers of life threatening arrythmias
- Cardiac biomarkers



- Male or female ≥18 years
- Clinical ACM diagnosis: defined by 2010 revised Task Force Criteria
- Pathogenic or likely pathogenic truncating PKP2 variant
- ICD implantation ≥6 months prior to enrollment
- Anti-AAVrh.74 capsid neutralizing antibody ≤1:40

- Cardiomyopathy related to a genetic etiology other than *PKP2* truncating variant
- Previous participation in a study of gene transfer or gene editing
- Severe right ventricular dysfunction
- Left ventricular ejection fraction by echocardiogram ≤50%
- New York Heart Association Class IV heart failure

Natural history studies are intended to provide context for the Phase 1 trial and additional information on disease progression

Clinicaltrials.gov Identifier: NCT05885412.
ACM, arrhythmogenic cardiomyopathy; GC, genome copies; ICD, implantable cardioverter-defibrillator; IV, intravenous; SAE, serious adverse event; TEAE, treatment emergent event.

Baseline Characteristics of Cohort 1 Patients

Cohort 1 patients received a single intravenous RP-A601 dose: $8x10^{13}$ GC/kg

Patient ID	Sex	Age at Enrollment (y)	Weight at Dosing (kg)	History of Anti-Arrhythmic Agents	KCCQ-12 Score	NYHA Class†	RV Systolic Function (ECHO)
1003	M	55	108.9	Sotalol, Amiodarone,* beta-blocker*	39.6	II	Normal
1011	F	58	58.3	Sotalol, Flecainide, Propafenone, Dronedarone, Amiodarone, beta-blocker	54.2	II	Mild - Moderate Reduced
1010	F	36	77.9	Sotalol, Flecainide,* beta-blocker*	59.4	II	Normal

*Indicates patient still receiving specified agent as of baseline screening visit.
†As assessed on Day -14 pre-infusion.

ECHO, echocardiogram; F, female; GC, genome copies; KCCQ, Kansas City Cardiomyopathy Questionnaire; M, male; NYHA, New York Heart Association RV, right ventricle; y, years.
Data cutoff May 6, 2025.

Most Frequently Reported Treatment Emergent Adverse Events Were Mild or Moderate in Severity*

No dose-limiting toxicities observed – patients received a single intravenous RP-A601 dose: 8x1013 GC/kg

Preferred Term of TEAEs *(Events Observed in ≥2 Patients)*	No. of Patients		
	Grade 1	Grade 2	Grade 3
Alanine aminotransferase increased	2	0	1
Aspartate aminotransferase increased	2	1	0
Complement factor increased	1	2	0
Nausea	2	0	0
Fatigue	2	0	0
Decreased appetite	2	0	0

Serious Adverse Event (SAE)	Grade	No. of Patients (%)
Any SAE		1 (33.33)
Investigations		
Transaminase elevations	3	1 (33.33)
Gastrointestinal disorders		
Acute Pancreatitis†	4	1 (33.33)
Infections and infestations		
Bacteremia†	3	1 (33.33)
Sepsis†	4	1 (33.33)

† Pancreatitis, bacteremia, and sepsis were part of a single SAE

- **All SAEs were experienced by one patient and fully resolved without clinical manifestation, within 2m of treatment**
- No arrhythmia SAEs were identified during the initial 6-12 months of post-treatment follow-up
- No patients developed clinical TMA

Serious adverse events were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.0.; Adverse events were graded using National Cancer Institute Common Terminology Criteria for AEs (NCI-CTCAE) version 5.0.; SAE, Serious Adverse Event; TEAE, treatment-emergent adverse event.; TMA, thrombotic microangiopathy.
Data cutoff May 6, 2025.

RP-A601 VCN and PKP2 RNA Expression in Endomyocardial Biopsy Tissue

RP-A601 Vector Copy Number (DNA Copies Per Diploid Nucleus)		
Patient ID	**Baseline**	**Most Recent Visit***
1003	0	2.89
1011	0	3.81
1010	0	8.23

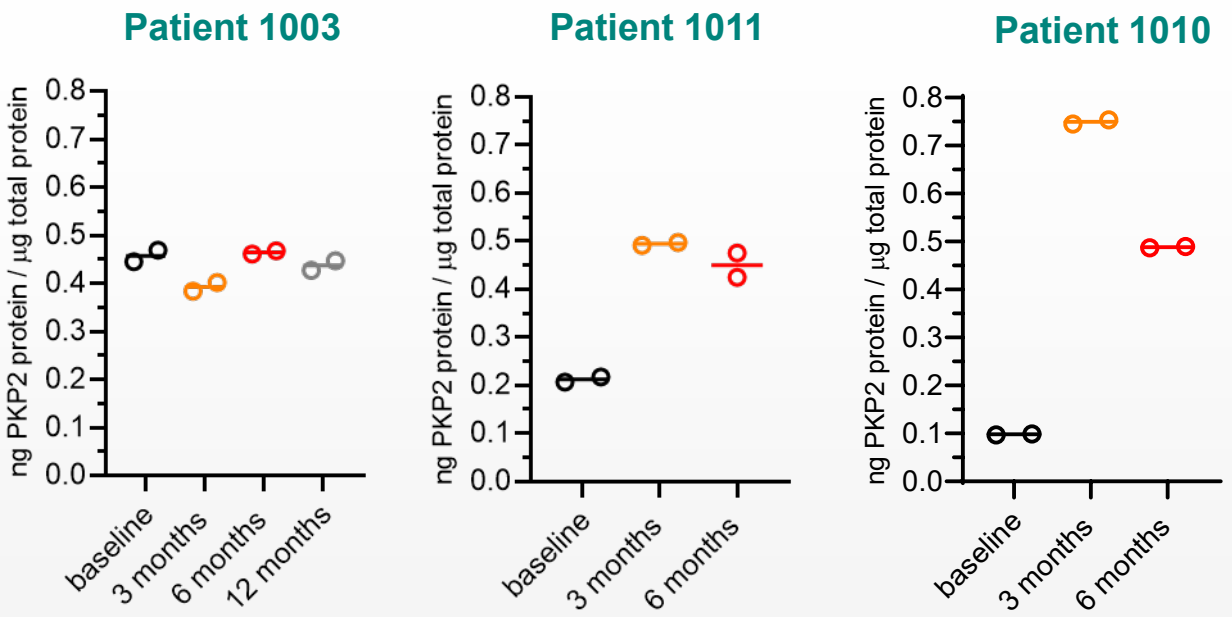
PKP2 Exogenous mRNA (Copies Per µg Nucleic Acid)			
Patient ID	**Baseline**	**Month 3**	**Most Recent Visit***
1003	0	5.56E+04	5.84E+04
1011	0	9.19E+04	2.75E+05
1010	0	4.78E+05	1.07E+05

*Month 12 data for Patient 1003, and Month 6 data for Patients 1011 and 1010.

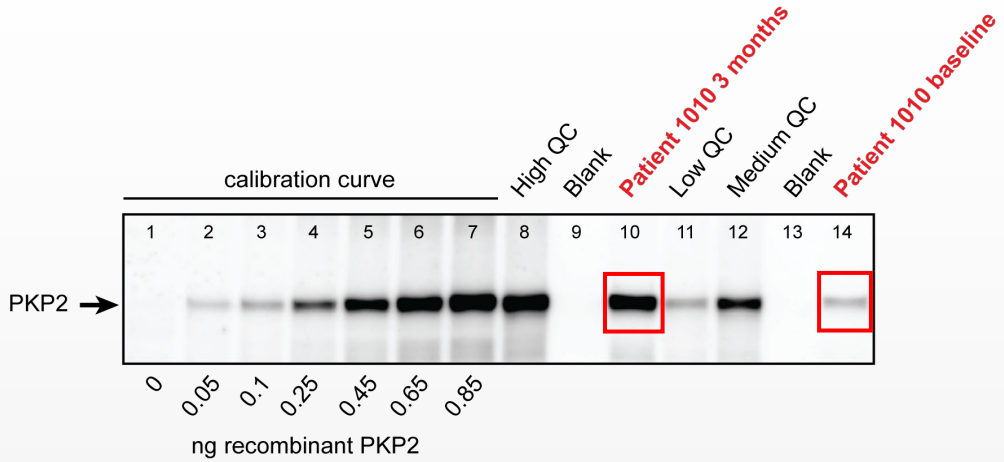
VCN, Vector Copy Number
Data cut of April 2025.

RP-A601 Increased PKP2 Protein Expression at 3 and 6 Months

PKP2 Protein Expression
Western Blot Quantification



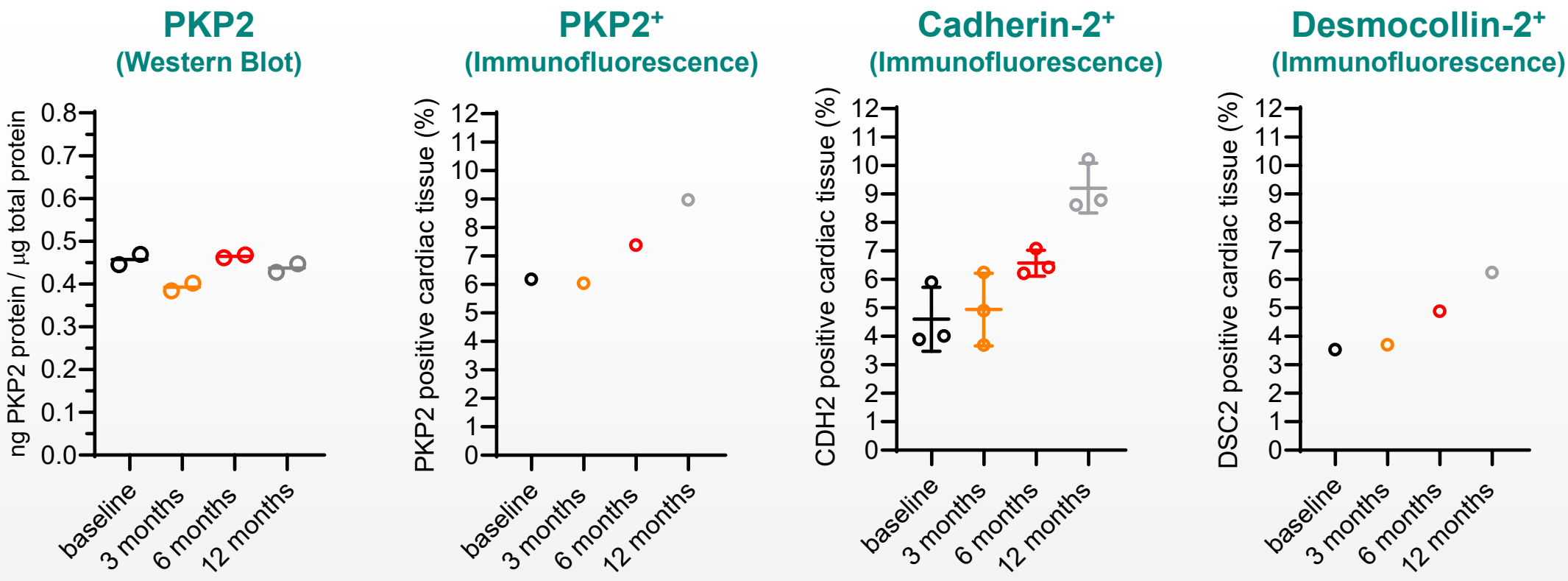
PKP2 Protein Expression
Western Blot Image



- Cardiac biopsies (n=2 of 3) show increased PKP2 protein expression following RP-A601 treatment
  - ~2.1X (110%) change from baseline to 6 months in Patient 1011
  - ~5X (398%) change from baseline to 6 months in Patient 1010
  - Patient 1003 shows increased PKP2, Cadherin-2 (CDH2), and Desmocollin-2 (DSC2) at the desmosome/intercalated disc shown on following slides

Data cutoff April 2025.

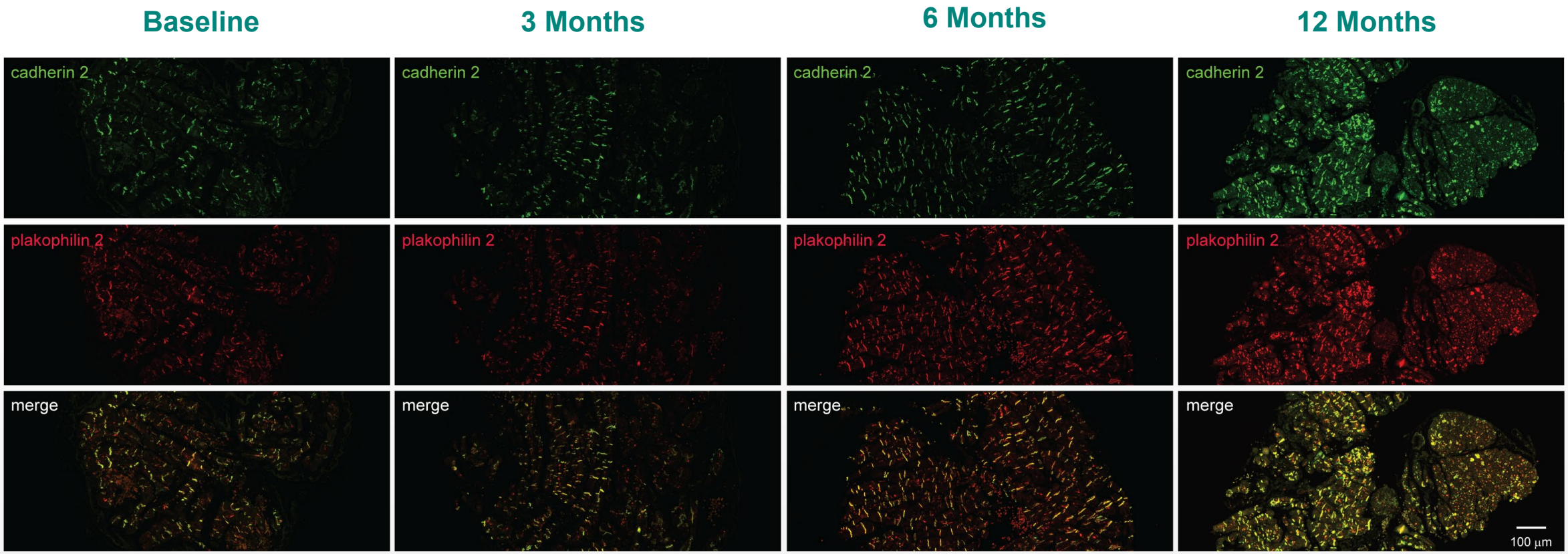
RP-A601 Increases Expression of Desmosomal Proteins & Cadherin-2 at 6 and 12 Months in Patient 1003



RP-A601 promotes PKP2, Cadherin-2 (CDH2), and Desmocollin-2 (DSC2) expression

Data cutoff April 2025.

Immunofluorescence Shows RP-A601 Increased PKP2 & Cadherin-2 Expression at 6 and 12 Months in Patient 1003



- RP-A601 promotes PKP2 and Cadherin-2 expression at 6 and 12 months
- RP-A601 promotes increased co-distribution of PKP2 and Cadherin-2 at cell-cell junctions at 6 and 12 months
- These findings suggest improved desmosome structure and cardiomyocyte intercellular adhesion

Data cutoff April 2025.

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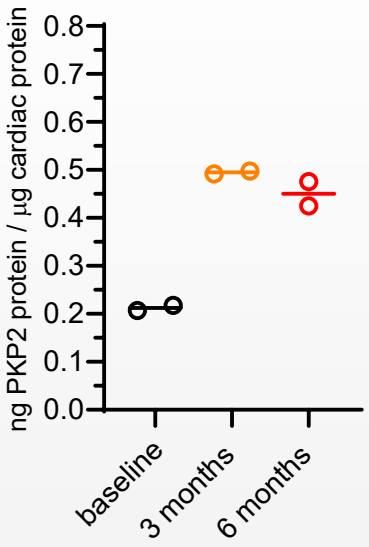
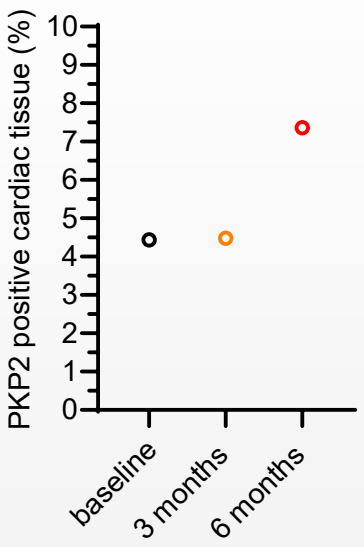
RP-A601 Increases Expression of Desmosomal Proteins & Cadherin-2 at 6 Months in Patient 1011

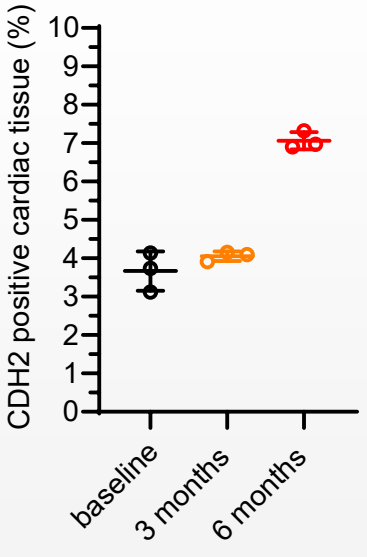
PKP2 (Western Blot)



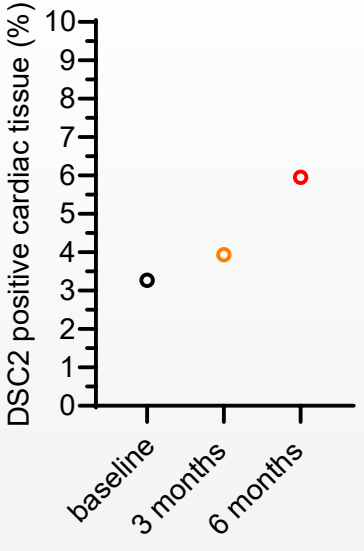
PKP2⁺ (Immunofluorescence)



Cadherin-2⁺ (Immunofluorescence)



Desmocollin-2⁺ (Immunofluorescence)

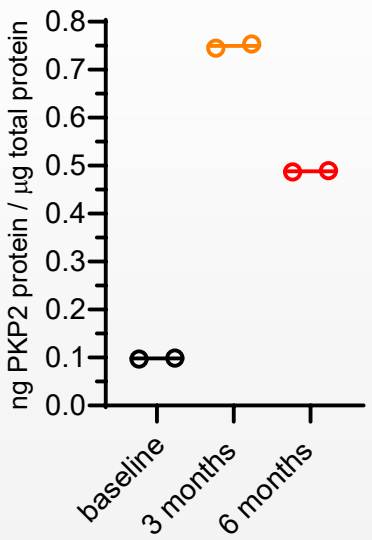


RP-A601 promotes PKP2, Cadherin-2 (CDH2), and Desmocollin-2 (DSC2) expression

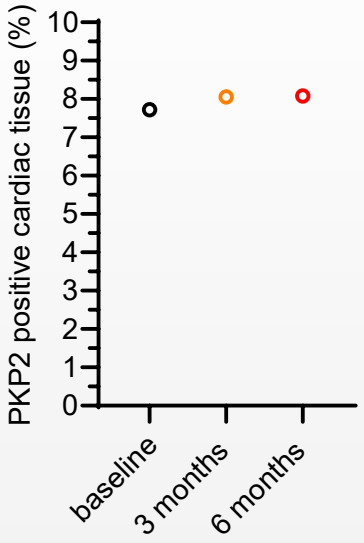
Data cutoff April 2025.

RP-A601 Increases Expression of Desmosomal Proteins & Cadherin-2 at 3 and 6 Months in Patient 1010

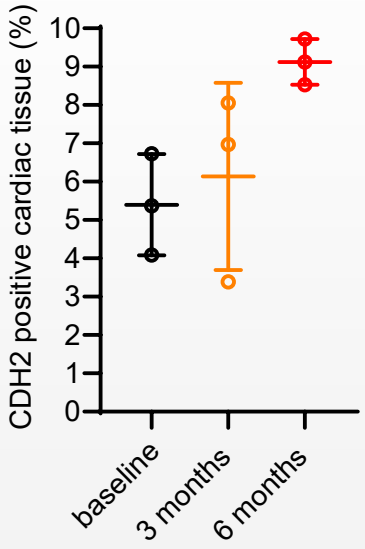
PKP2 (Western Blot)



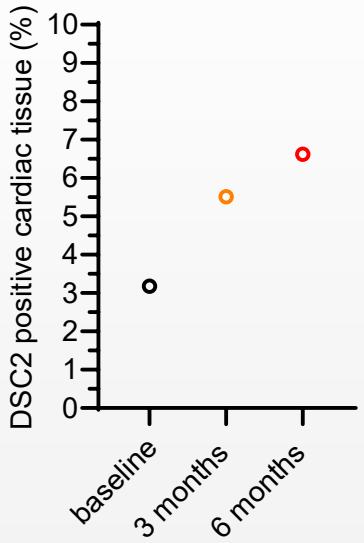
PKP2⁺ (Immunofluorescence)



Cadherin-2⁺ (Immunofluorescence)



Desmocollin-2⁺ (Immunofluorescence)



RP-A601 promotes PKP2, Cadherin-2 (CDH2), and Desmocollin-2 (DSC2) expression

Data cutoff April 2025.

Stabilization or Improvement in RV Function, QoL, and NYHA Class at Most Recent Visit

Patient ID	Age at Enrollment (y)	Most Recent Visit (MRV, mo)	RV Systolic Function (ECHO) BL→ MRV	KCCQ-12 Score BL→ MRV (% change)	NYHA Class BL*→ MRV
1003	55	12	Normal → Normal†	39.6 → 74.0 (+87%)	II → I
1011	58	9	Mild - moderate reduced → Normal	54.2 → 95.3 (+76%)	II → I
1010	36	6	Normal → Normal	59.4 → 59.4 (0%)	II → II

- RV function was stable or improved in all patients
- Patients beyond 6 months follow-up at most recent visit showed:
  - Clinical improvement in KCCQ-12 score (34-41 points; ≥5 point increases considered clinically meaningful in adults)
  - Improved NYHA class

*As assessed on Day-14 pre-infusion.
†Stability of RVEF was corroborated by month 12 cardiac magnetic resonance (CMR) s imaging.

BL, baseline; KCCQ, Kansas City Cardiomyopathy Questionnaire; mo, months; MRV, most recent visit; NYHA, New York Heart Association; QoL, quality of life; RVEF, right ventricular ejection fraction.
Data cutoff April 2025.

Preliminary Indications of Improvement or Stabilization Observed in Clinical Markers of Arrhythmia Burden

Patient ID	Age at Enrollment (y)	Most Recent Visit (MRV, mo)	PVCs per 24h BL → MRV (% change)	NSVT Episodes per 24h BL→ MRV	T-wave inversions (precordial and inferior ECG)
1003	55	12	117* → 43 (-63%)	0 → 0	0 → 0
1011	58	9	2974 → 2713 (-9%)	0 → 0	4 → 4
1010	36	6	2650* → 1057 (-60%)	5* → 0	6 → 2

- Ventricular ectopy, as evident by PVC and NSVT episodes on ambulatory rhythm monitoring decreased or stabilized in all patients
- T-wave inversions in precordial and inferior leads decreased in 1 patient and remained stable in 2 patients

*Ambulatory rhythm monitoring was conducted at baseline for 48 hours. For the specified patients, data from two separate 48-hour rhythm monitoring studies were combined to produce the baseline value. Rhythm monitoring at the most recent visit was conducted for 7 days.
BL, baseline; h, hours; mo, months; MRV, most recent visit; NSVT, non-sustained ventricular tachycardia; PVC, premature ventricular contractions; ECG, electrocardiogram; y, years.
Data cutoff April 2025.

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Summary of Initial Results From Ongoing Phase I Trial

Cohort 1 Patients with PKP2-ACM Treated with RP-A601 Demonstrated

- RP-A601 was generally well-tolerated with no dose-limiting toxicities observed
  - ➢ No TMA or ventricular arrhythmias were observed
- Increased expression and desmosomal localization of PKP2, Desmocollin-2, and Cadherin-2 in all patients
  - ➢ Most evident at ≥ 6 months post-treatment of RP-A601
- Preliminary indications of improvement or stabilization observed in arrhythmia burden, heart function, and quality of life
  - ➢ Decreased/stabilized ventricular ectopy (PVC, NSVT) on rhythm monitoring in all patients
  - ➢ Decreased/stabilized T-wave inversions on ECG in all patients
  - ➢ Improved/stabilized RV function
  - ➢ Improved quality-of-life and NYHA Class in patients followed beyond 6 months

ECG, electrocardiogram; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association Functional classification; PVC, premature ventricular contractions; RV, right ventricular; TMA, thrombotic microangiopathy

Key Findings and Path Forward

Key Findings

- RP-A601 was generally well tolerated in all 3 patients SAEs were reversible without clinical manifestations, no dose-limiting toxicities observed
- All 3 patients in Cohort 1 demonstrated cardiac transduction with localized myocardial protein expression that was maintained or increased up to 12-months post-infusion
- Initial efficacy in all patients showed early signs of disease modification across multiple clinical parameters with up to 12-months of follow-up
- **Based on the Phase 1 trial, 8.0e13 GC/kg considered final dose**

Path Forward

- Phase 1 (NCT05885412) is a dose-finding trial to evaluate the safety of RP-A601
- With no further dose escalation, Rocket plans to design and execute a potential pivotal trial to further evaluate the efficacy and safety of RP-A601

Thank You

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