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RP-A501 Program Update

November 2024

FORWARD LOOKING STATEMENT AND DISCLOSURES

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, 2023, filed February 27, 2024 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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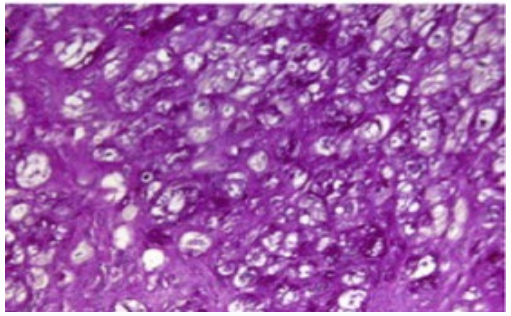
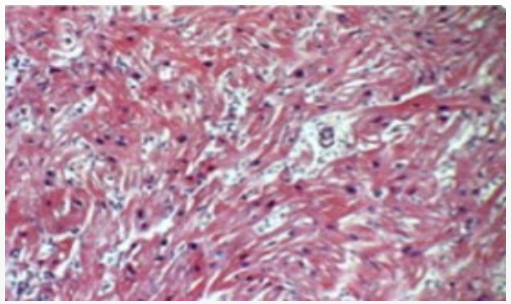
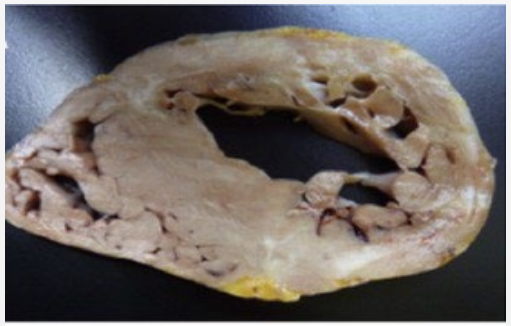
Danon Disease







Figures used with permission from Bottillo I, et al. *Cardiovasc Pathol.* 2016;25(5):423-431.

X-linked monogenic disease[1-8]

- *LAMP2* gene variants
- Impaired autophagy
- Prominent sarcoplasmic vacuoles
- Myofibrillar disarray

Severe Cardiomyopathy[1-3,7]

- Mortality secondary to heart failure or arrhythmia
- **Males:**
  - Hypertrophic phenotype with arrhythmias
  - Left Ventricle (LV) hypertrophy at presentation in >95% of patients
  - Accelerated progression to end-stage disease with death or transplant at an average age of 19-21 years
- **Females:**
  - Dilated/hypertrophic phenotype and arrhythmias
  - Variable age for presentation of cardiac phenotype with mortality generally 2-3 decades later than in males

Other Clinical Features[1,2]

- Skeletal myopathy, CNS, ophthalmic manifestations (predominantly mild-moderate and not life-threatening)

CNS=central nervous system; LAMP2=lysosomal associated membrane protein 2.

Brambatti M, et al. *Int J Cardiol.* 2019;286:92-98. 2. Boucek D, Jirikowic J, Taylor M. *Genet Med.* 2011;13(6):563-568. 3. D'souza RS, et al. *Circ Heart Fail.* 2014; 7(5):843-849..4. Nishino I et al; *Nature* 2000; 406(6798):906-910. 5. Takahashi M, et al. *Ann Neurol.* 2002;52(1):122-125. 6. Endo Y et al; *Acta Neuropathol.* 2015;129(3):391-398. 7. Hedberg Oldfors C et al. *Neuromuscul Disord.* 2015; 25(6):493-501. 8. Bottillo I, et al. *Cardiovasc Pathol.* 2016;25(5):423-431.

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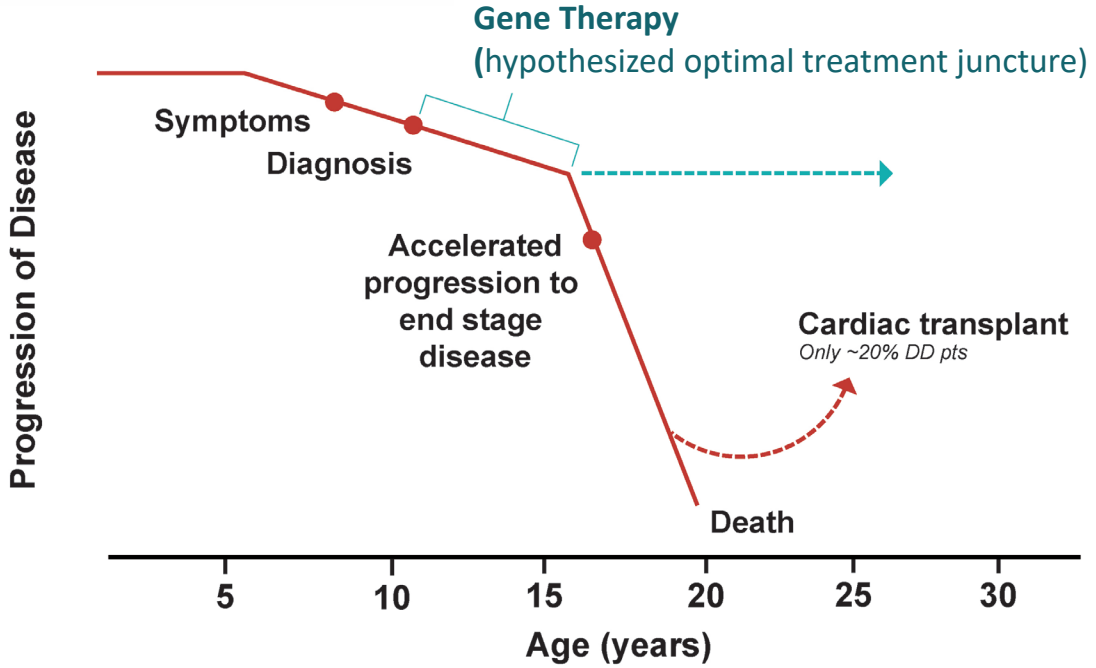
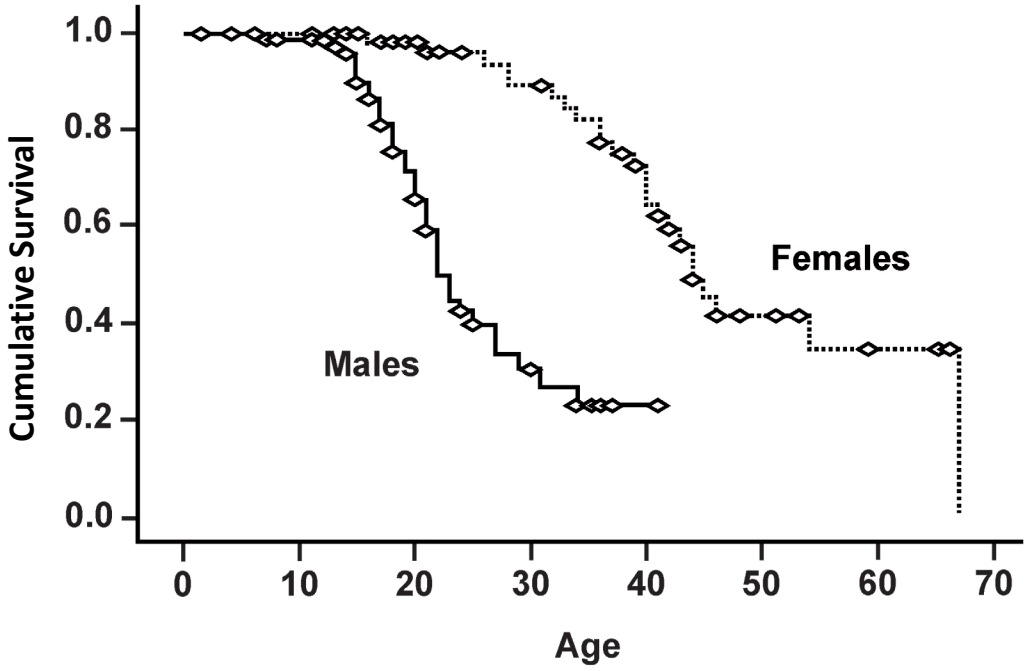
Rapidly Progressive Cardiomyopathy with Early Mortality in Males

Males: Critical interval in childhood/ early adolescence precedes rapid decline[1,2]



Limited Overall Survival[1]*



- ***Rapid decline in second decade of life (male patients)***
- ***Guideline-directed heart failure therapies do not alter disease course/prognosis***
- ***Heart transplant is the only current definitive intervention***

*Figures used with permission from Boucek D, Jirikowic J, Taylor M. *Genet Med.* 2011;13(6):563-568.

1. Boucek D, Jirikowic J, Taylor M. *Genet Med.* 2011;13(6):563-568.
2. Brambatti M et al. *Int J Cardiol.* 2019;286:92-98.

AAV Gene Therapy for Danon Disease: RP-A501

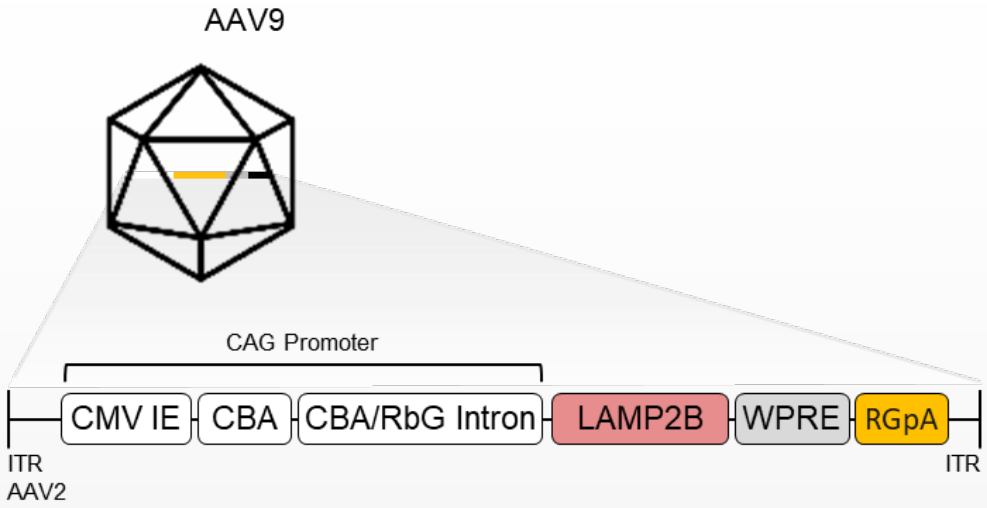
Goal

- Restore LAMP2B protein expression
- Restore autophagy
- Normalize myocardial structure and function

Intravenous administration of RP-A501

- RP-A501: rAAV9 capsid with DNA encoding full-length LAMP2B protein
- AAV9: demonstrated myocardial tropism
- In non-dividing, terminally differentiated cardiomyocytes, dilution of the vector DNA is unlikely

Schematic Representation of RP-A501 (AAV9.LAMP2B)



Potential toxicities related to treatment with systemic AAV9 therapies[1-5]

- Acute complement-mediated TMA
- Hepatotoxicity due to AAV liver transduction and T cell-mediated immunity
- Myocarditis
- Adverse events related to immunosuppression including steroid induced skeletal myopathy, infection

AAV=adeno-associated virus; CBA=chicken beta-actin; CMV IE=cytomegalovirus immediate early; ITR=inverted terminal repeat; LAMP2B=lysosomal-associated membrane protein 2B; rAAV=recombinant adeno-associated virus; RbG=rabbit globin introns; RGpA=rabbit globin poly-adenylation signal; TMA=thrombotic microangiopathy; WPRE=woodchuck hepatitis virus post-transcriptional regulatory element.

1. Kishimito TK, Samulski RJ. *Expert Opin Biol Ther.* 2022;22(9):1067-1071. 2. Ertl HCJ. *Front Immunol.* 2022;13:975803. doi:10.3389/fimmu.2022.975803. 3. Mendell JR et al; *Mol Ther.* 2021;29(2):464-488. 4. Day JW et al; *Drug Saf.* 44 (10):1109-1119. 5. Silver E, et al. *Int J Cardiol.* 2024;398:131617. doi:10.1016/j.ijcard.2023.131617.

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Phase 1 Study Overview

Safety and Preliminary Efficacy Follow-up for RP-A501 Out to 24-54 Months †

Inclusion Criteria

- Males age ≥8 years
- *LAMP2* variant
- Cardiac involvement (imaging or ECG)
- NYHA Class II or III

Exclusion Criteria

- Anti-AAV9 neutralizing antibody >1:40
- LVEF<40%
  - Implemented prior to pediatric cohort

†Safety data are presented for all 7 patients treated; efficacy data are presented for the 6 evaluable patients in follow-up. Patient 1007 had LV systolic dysfunction (LVEF <40%) at enrollment and had progressive heart failure requiring transplantation 5m following RP-A501 treatment; this patient is currently stable 3 years post-transplant..

AAV=adeno-associated virus; ECG=electrocardiogram; LAMP2=lysosomal-associated membrane protein 2; LVEF=left ventricular ejection fraction; m=month(s); NYHA=New York Heart Association; Steroid: predominantly prednisone.

Data cut-off: April 19, 2024.

Baseline Characteristics

Marked LV Hypertrophy, Elevated Biomarkers and Symptoms of Disease

	6.7×10^{13} GC/kg Adult/adolescent, N=3			1.1×10^{14} GC/kg Adult/adolescent, N=2[a]		6.7×10^{13} GC/kg Pediatric, N=2	
Clinical Characteristics							
Patient	1001	1002	1005	1006	1007	1008	1009
Age at infusion, y	17.5	20.4	18.3	21.1	20.7	12.3	11.7
ICD history	No	Yes	Yes	No	Yes	No[†]	No
Imaging Parameters[b]							
LVEF, %	57	55	65	62	32	74	77
LV mass, g	311	989	438	315	966	605	232
LVMI, g/m$^{2.7}$	85.0	260.2	98.2	68.6	168.3	141.5	82.0
IVSd (mm), z Score	19.8, +13	60.1, +46	30.9, +25	18.0, +9	32.8, +19	42.4, +32	18.5, +12
LVPWd (mm), z Score	18.8, +14	39.1, +34	32.1, +25	24.0, +18	19.1, +10	22.8, +17	14.9, +10
Biomarkers							
BNP, ng/L	NA	NA	NA	123	674	1629	297
NT-proBNP, ng/L	336	5119	841	720	NA	NA	1912
cTnI, ng/mL	0.60	1.46	0.28	0.47	0.86	1.78	1.08
Symptoms & Quality of Life							
NYHA class	II	II	II[‡]	II	II	II	II
KCCQ-12 score	44	64	77	79	67	50	52

[a]Patient 1007 had LV systolic dysfunction (LVEF <40%) at enrollment and had progressive heart failure requiring transplantation 5m following RP-A501 treatment; this patient is currently stable 3 years post-transplant.
[b]Centrally evaluated (blinded) MRI data were utilized for LVMI when available at most recent visit (patients 1006 and 1009). All other measurements of cardiac structure and function reflect centrally evaluated (blinded) echocardiogram data. [†]ICD implanted 3 months after RP-A501 infusion (recommended prior to enrollment). [‡]Class III 6 months prior to enrollment.
Central laboratory assessment of BNP, brain natriuretic peptide; cTnI, cardiac troponin I; ECHO, echocardiogram; GC, genome copies; ICD, implantable cardioverter defibrillator; IVSd, interventricular septum at end-diastole; KCCQ-12, Kansas City Cardiomyopathy Questionnaire; LV, left ventricle; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; LVPWd, left ventricular posterior wall at end-diastole; MRI, magnetic resonance imaging; NT-Pro-BNP, N-terminal pro–B-type natriuretic peptide; NA, not available; NYHA, New York Heart Association.

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Treatment-Emergent Severe Adverse Events

Preferred term	6.7×10^{13} GC/kg Adult/adolescent N=3 Patients, n (%)	1.1×10^{14} GC/kg Adult/adolescent N=2* Patients, n (%)	6.7×10^{13} GC/kg Pediatric N=2 Patients, n (%)
Grade ≥3 serious TEAEs	**3 (100)**	**1 (50)**	**1 (50)**
Myopathy[a]	2 (66.7)[b]	1 (50)	0
Acute cardiac failure	0	1 (50)	0
Palpitations	0	0	1 (50)
Ventricular tachycardia	0	1 (50)	0
Chest pain	1 (33.3)	0	0
Deep vein thrombosis[a]	0	1 (50)	0
Thrombocytopenia[c]	0	1 (50)	0
Thrombotic microangiopathy[c]	0	1 (50)	0
Acute kidney injury[c]	0	1 (50)	0
Renal failure[c]	0	1 (50)	0
Nausea[a,c]	1 (33.3)	0	0
Vomiting[c]	1 (33.3)	0	0
Increased ALT[c]	1 (33.3)	0	0
Increased AST[c]	1 (33.3)	0	0
Pyrexia[c]	1 (33.3)	0	0
Salmonella sepsis	1 (33.3)	0	0

Favorable Safety Profile with Enhanced Immunomodulation Protocol

Low Dose Adult/Adolescent Cohort:

- One instance each of AST/ALT elevation, pyrexia and nausea/vomiting related to drug product administration
- 2 steroid related SAEs (myopathy)

High Dose Adult/Adolescent Cohort:

- One instance of reversible TMA and one instance of steroid myopathy

Low Dose Pediatric Cohort:

- No RP-A501 administration-related SAEs

All SAEs were observed within initial 2-4 months following dosing and reversible with supportive care

*Patient 1007 had LV systolic dysfunction (LVEF <40%) at enrollment and had progressive heart failure requiring transplantation 5m following RP-A501 treatment; this patient is currently stable 3 years post-transplant.
GC, genome copies; TEAE, treatment-emergent adverse event.
[a]Assessed as related to steroids. [b]A total of 6 myopathy events were reported in 2 patients. [c]Assessed as related to RP-A501.
Data cut-off: April 19, 2024.

Sustained LAMP2 Expression in Endomyocardial Biopsies

Durable myocardial LAMP2 protein expression seen in all patients

Myocardial LAMP2 Protein Expression

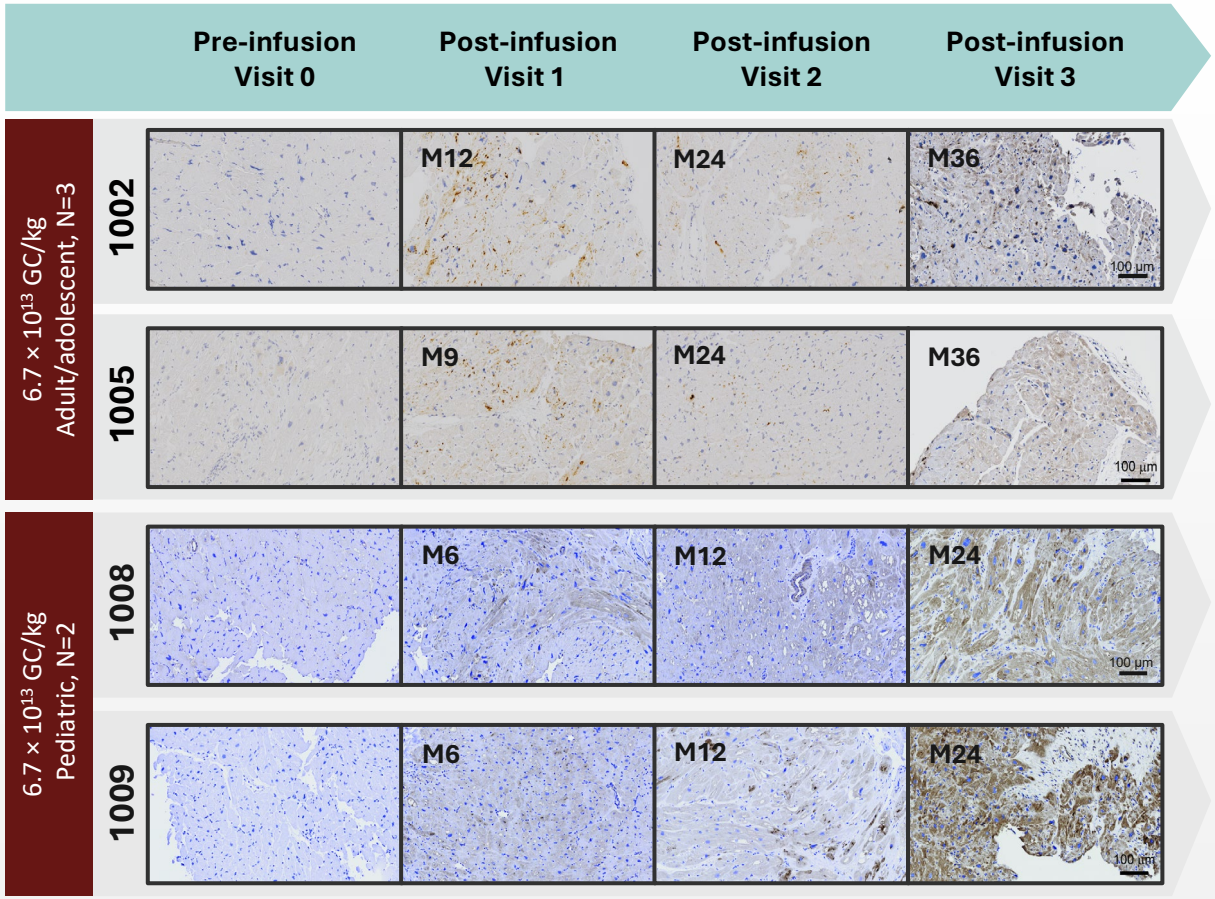
Cohort	Patient	BL	M6	M12	M18	M24	M30	M36	M60‡
6.7 × 10^{13} GC/kg Adult/adolescent	1001	0	++	+	NP	NP	0*	0*	+++‡
	1002	0	NP	+++	++	++	++	++	
	1005	0	NP	++†	NP	+	+	+	
1.1 × 10^{14} GC/kg Adult/adolescent[a]	1006	0	+	+	+	+	NP	+++	
6.7 × 10^{13} GC/kg Pediatric	1008	0	++	+	NP	++	Visits Pending		
	1009	0	+	++	NP	+++			

†Reflects patient 1005 9M visit biopsy as 12M biopsy not performed
‡ Preliminary assessment of biopsy from 1001 Y5 visit with updated IHC assay

Legend: IHC Staining Grade (% Positive Cardiomyocytes)

0 = no staining	+ = 1 (≤25%)	+++ = 3 (51%–74%)
NP = not performed	++ = 2 (26%–50%)	++++ = 4 (≥75%)

Representative LAMP2 IHC Images



a. Patient 1007 had LV systolic dysfunction (LVEF <40%) at enrollment and had progressive heart failure requiring transplantation 5m following RP-A501 treatment; this patient is currently stable 3 years post-transplant.
Note: Grading of LAMP2 protein expression by IHC was done by a board-certified pathologist in a blinded fashion. The semi-quantitative grading reflects the extent of LAMP2 protein expressing cardiomyocytes in the entirety of biopsy sample according to the scale: Grade 0, negative staining; Grade 1 = < 25%; Grade 2 = 26%-50%; Grade 3 = 51%-74%; Grade 4 = >75%.
IHC=immunohistochemistry; LAMP2=lysosome-associated membrane protein 2; M=month(s); VCN=vector copy number.
*Patient 1001 demonstrated Grade 0 LAMP2 protein IHC staining at the 30- and 36- month assessments, however, patient 1001's LAMP2B vector RNA and DNA (VCN) levels have persisted through 36 months of follow-up.

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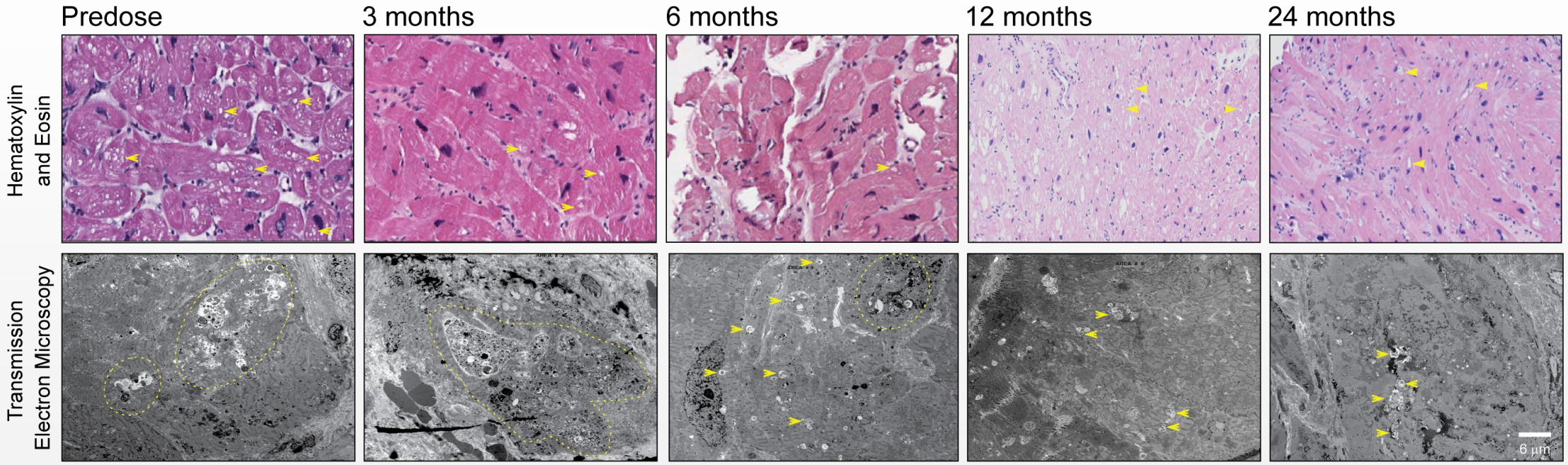
Reduction in Autophagic Vacuoles

Representative H&E Staining and EM Images from Endomyocardial Biopsies

Representative Images from the Endomyocardial Biopsy of Patient 1008



Dashed yellow lines mark myocardial regions with high densities of phagocytic vacuoles. Yellow arrowheads mark small clusters or individual phagocytic vacuoles

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Improvement or Stabilization from Baseline in Key Efficacy Parameters

Cohort	Patient	Age at Most RV (y)	Most Recent Visit (mo)	LVEF BL to RV (%)	Δ LVMI,* BL to RV ($g/m^{2.7}$)	Δ IVSd, BL to RV (mm)	Δ LVPWd, BL to RV (mm)	Δ NT-proBNP, BL to RV (ng/L)	Δ cTnI,† BL to RV (ng/mL)	Δ NYHA Class	Δ KCCQ-12 OS, BL → RV
1: Low Dose Adult/ Adolescent	1001	22.3	54	57 to 64	-33%, 85 to 56.9	-6%, 19.8 to 18.6	-20%, 18.8 to 15	-17%, 336 to 279	-99% 0.6 to 0.01	II to I	+52, 44 to 96
	1002	24.9	54	55 to 66	-48%, 260.2 to 135.3	-52%, 60.1 to 28.6	-49%, 39.1 to 19.8	-93%, 5119 to 351	-96%, 1.46 to 0.06	II to I	+27, 64 to 91†
	1005	21.8	42	65 to 59	-11%, 98.2 to 87.3	-10%, 30.9 to 27.8	-27%, 32.1 to 23.4	+16%, 841 to 975	-33%, 0.28 to 0.19	II to I	+7, 77 to 84
2: High Dose Adult/ Adolescent	1006	23.9	36	62 to 51	-7%, 68.6 to 63.6	+5%, 18.0 to 19.0	-27%, 24.0 to 17.4	-65%, 720 to 249	-39%, 0.47 to 0.29	II to I	+9, 79 to 89
3: Low Dose Pediatric	1008	14.4	24	74 to 78	-38%, 141.5 to 87.8	-19%, 42.4 to 34.2	+1%, 22.8 to 23.1	-78%, 1629‡ to 360‡	-85%, 1.78 to 0.27	II to I	+27, 50 to 77
	1009	13.7	24	77 to 77	-13%, 82.0 to 71.2	+12%, 18.5 to 20.8	-3%, 14.9 to 14.4	-48%, 1912 to 998	-82%, 1.08 to 0.20	II to I	+30, 52 to 82

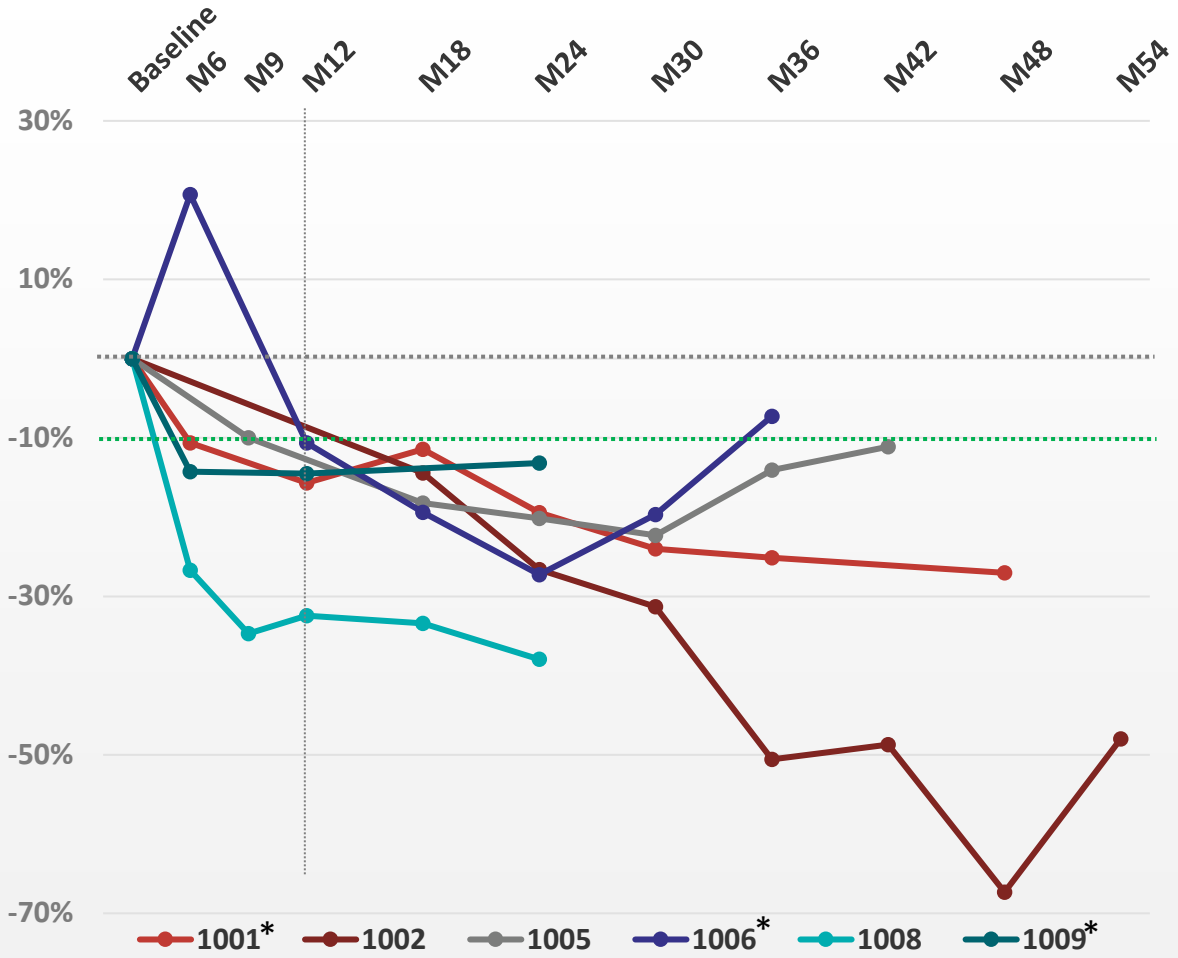
* Centrally evaluated (blinded) MRI data were utilized for LVMI when available. All other measurements of cardiac structure and function reflect centrally evaluated (blinded) echocardiogram data.
† Central laboratory assessment of cTnI were performed on cryopreserved and non-cryopreserved samples. Values for cTnI from high-sensitivity and earlier tests. high-sensitivity and earlier assay are expressed in ng/mL.

Improved
Stabilized
Worsened

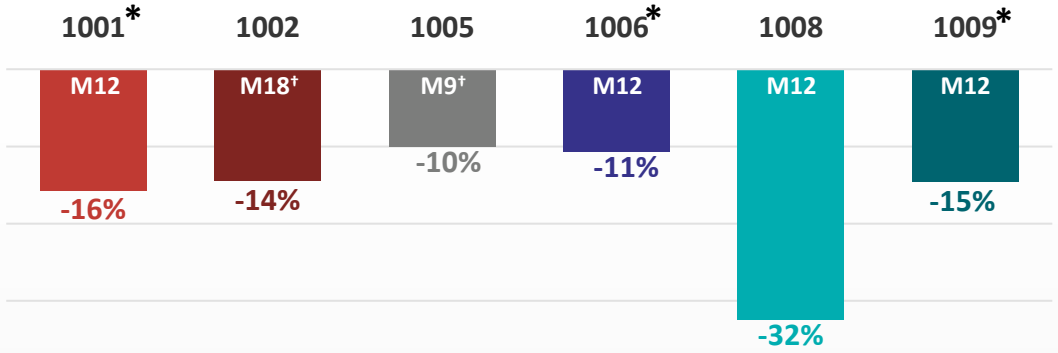
BL=Baseline; BNP=Brain Natriuretic Peptide; cTnI=cardiac troponin I; ICD=Implantable Cardioverter Defibrillator; IVSd=Intraventricular Septum in diastole; KCCQ=Kansas City Cardiomyopathy Questionnaire; NT-Pro-BNP=N-terminal pro–B-type natriuretic peptide; NYHA=New York Heart Association; LV=Left Ventricle; LVEF=Left Ventricular Ejection Fraction; LVMI=Left Ventricular Mass Index, LVPWd=Left Ventricular Posterior Wall in diastole, RV=(Most) Recent Visit.
Data cut-off: April 19, 2024.

Sustained Improvements in LV Mass Index Observed in All Patients

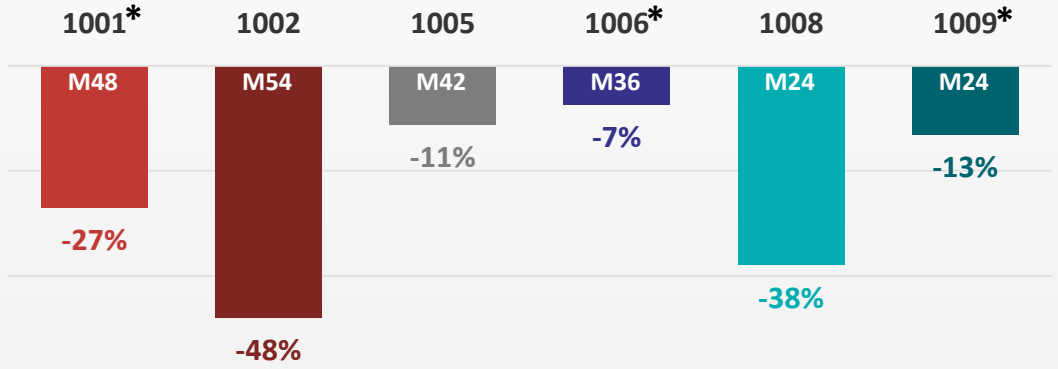
LVMI % Change from Baseline



LVMI % Change: Baseline to 12m†



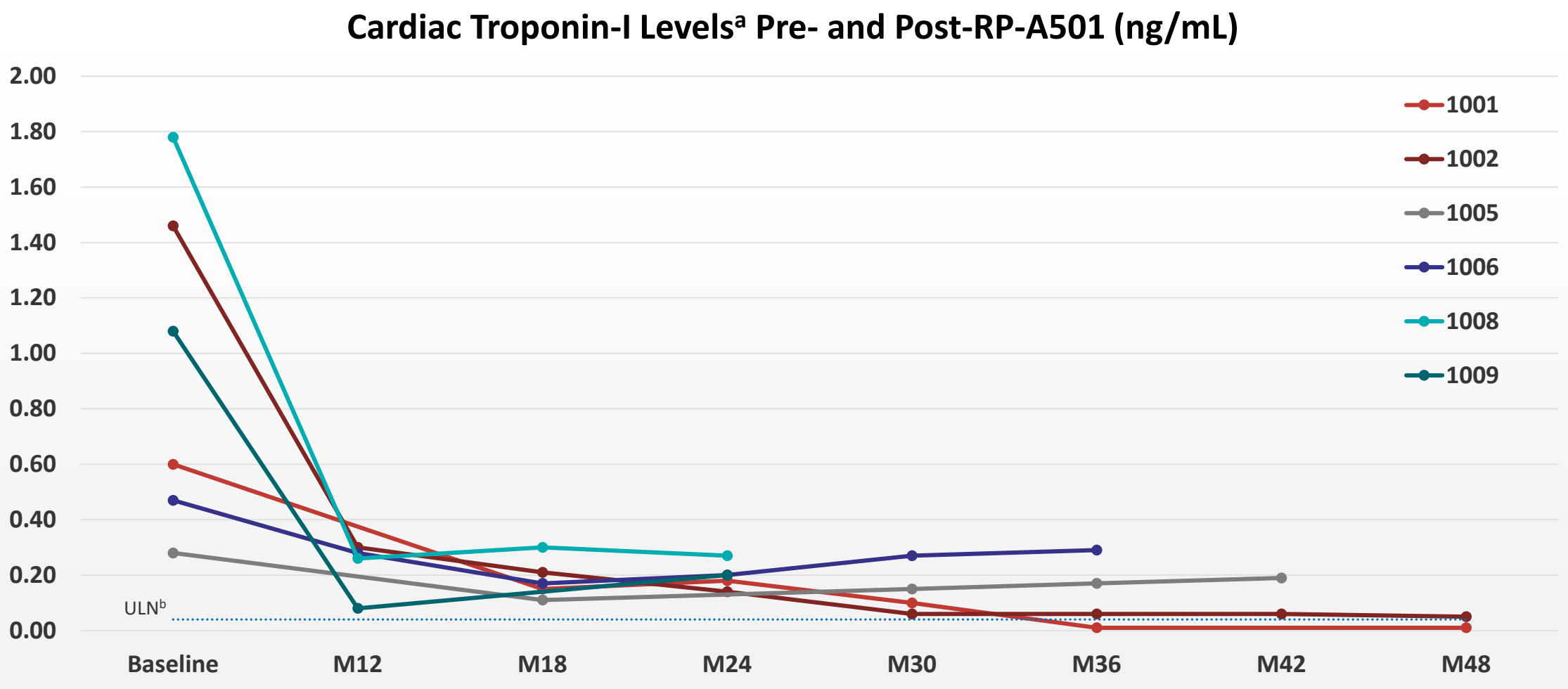
LVMI % Change: Baseline to Most Recent Visit*



All patients showed ≥10% LVMI decrease at ~12m; improved or sustained at most recent visit

* Where possible, cardiac MRI assessments shown (patients 1001, 1006, and 1009); otherwise, echocardiogram data presented. All assessments were conducted by a single reviewer blinded to both patient and timepoint, except for Patient 1001 cardiac MRI data, which includes reads from multiple reviewers. Patient 1001 most recent visit with MRI assessment was at 48m
† Utilized 9m or 18 m data when 12m assessment was not done.
LVMI, left ventricular mass index; MRI, magnetic resonance imaging; m, month(s).
Data cut-off: April 19, 2024.

Sustained Reductions in Circulating Cardiac Troponins



[a]Visits not conducted, and results pending or unavailable at various timepoints; data shown are cTnI levels performed on high-sensitivity and older assays. Values from both assays are expressed in nanograms per milliliter for consistency.
[b]Representative ULN: 0.04 ng/mL.
cTnI, cardiac troponin I; M, month(s); ULN, upper limit of normal.

Phase 1 Study of RP-A501: Summary of Results

Favorable Benefit-Risk Profile for RP-A501

Key Findings

- RP-A501 was generally well tolerated with a transient immunomodulatory regimen of rituximab, sirolimus, and corticosteroids
  - All SAEs were reversible without sequelae, and all patients are alive
- All 6 evaluable patients demonstrated improvement or stabilization across key clinical, biomarker, echocardiographic, and QoL parameters over 24-54 months of follow-up, indicating preliminary evidence of sustained efficacy

Path Forward

- Phase 2 (NCT06092034) pivotal, global, single-arm, multi-center trial evaluating the efficacy and safety of RP-A501 in 12 patients with DD is underway

QoL=quality of life; SAEs=serious adverse events.
Data cut-off: April 19, 2024.

Thank You

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