Danon Disease Phase 1 Clinical Trial Interim Results

December 8, 2020

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SEEKING GENE THERAPY CURES

Important Information

Cautionary Statement Regarding Forward-Looking Statements

Various statements in this release concerning Rocket's future expectations, plans and prospects, including without limitation, Rocket's expectations regarding its guidance for 2020 in light of COVID-19, the safety, effectiveness and timing of product candidates that Rocket may develop, to treat Fanconi Anemia (FA), Leukocyte Adhesion Deficiency-I (LAD-I), Pyruvate Kinase Deficiency (PKD), Infantile Malignant Osteopetrosis (IMO) and Danon Disease, and the safety, effectiveness and timing of related pre-clinical studies and clinical trials, may constitute forward-looking statements for the purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995 and other federal securities laws and are subject to substantial risks, uncertainties and assumptions. 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. 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 ability to monitor the impact of COVID-19 on its business operations and take steps to ensure the safety of patients, families and employees, the interest from patients and families for participation in each of Rocket’s ongoing trials, our expectations regarding when clinical trial sites will resume normal business operations, our expectations regarding the delays and impact of COVID-19 on clinical sites, patient enrollment, trial timelines and data readouts, our expectations regarding our drug supply for our ongoing and anticipated trials, actions of regulatory agencies, which may affect the initiation, timing and progress of pre-clinical studies and clinical trials of its product candidates, Rocket's dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the section entitled "Risk Factors" in Rocket’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed November 6, 2020 with the SEC. 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.

Danon Disease Background

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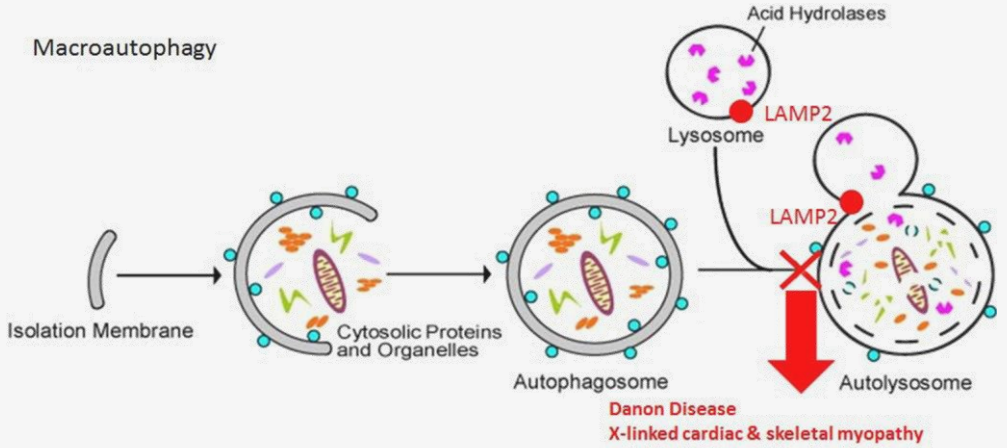
Danon Disease and RP-A501 AAV-Based Therapy

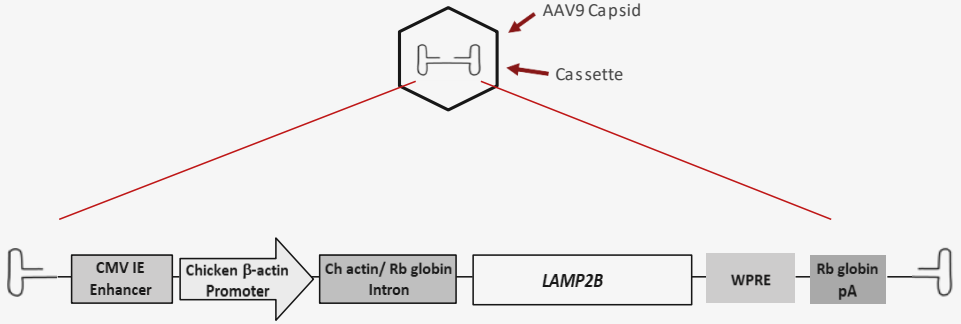
THE DISEASE

- ***Monogenic, X-linked*** dominant disorder
- ***LAMP2*** gene mutation results in impaired autophagy and cardiac hypertrophy
- 95% of patients develop severe cardiomyopathy
  - Progressive heart failure with high early mortality
- Other clinical manifestations
  - Skeletal Myopathy
  - CNS manifestations
- Heart transplant not curative and associated with considerable morbidity and mortality

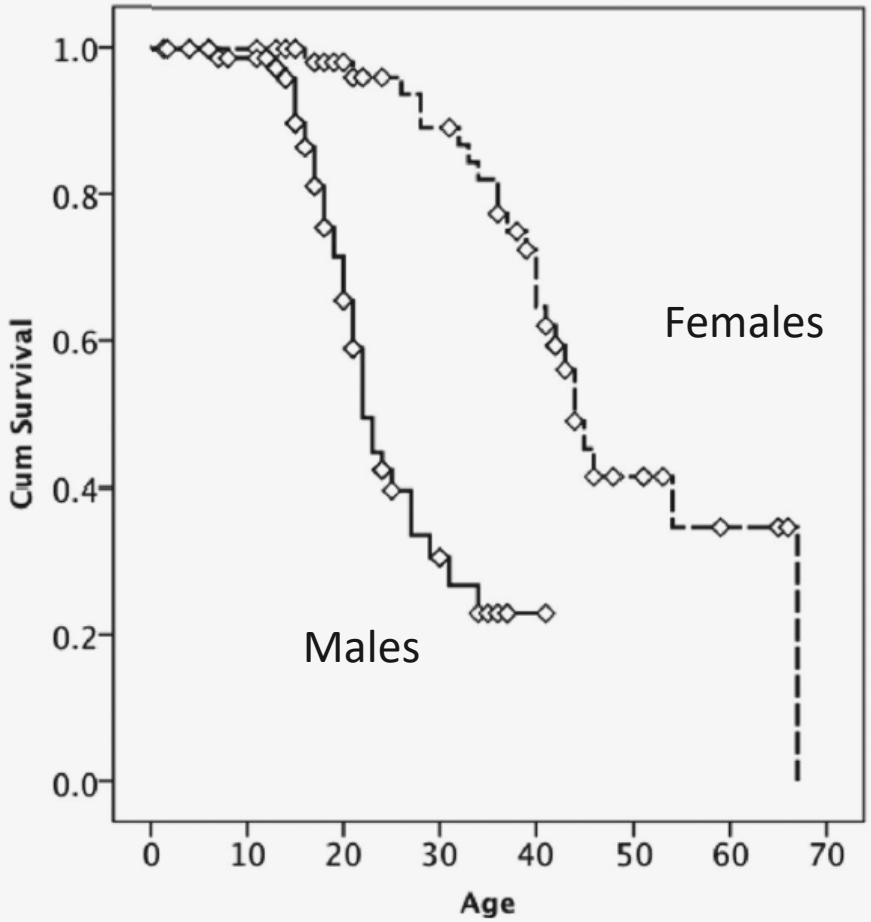
MECHANISM OF ACTION



RP-A501 VECTOR / TRANSGENE



Gender Specific Clinical Presentation of Danon Disease



Males:

- More *aggressive* and predictable disease course – childhood presentation with advanced progression during adolescence
- Frequent triad of disease involvement:
  1. Cardiomyopathy: Early onset, rapid progression to heart transplant and/or death
  2. Skeletal myopathy
  3. Mild cognitive impairment – may be the first manifestation of DD
- Elevated transaminases in male pts predominantly due to myopathy

Females:

- More *variable* presentation due to additional X chromosome
- Cardiomyopathy not limited to HCM but also includes dilated cardiomyopathy (DCM)
- Isolated cardiomyopathy common; does not often present with extra-cardiac manifestations

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Boucek D, Jirikowic J, Taylor M. Genet Med 2011; 13(6):563-68

Danon Disease: Epidemiology and Market Opportunity

Hypertrophic Cardiomyopathy (HCM)

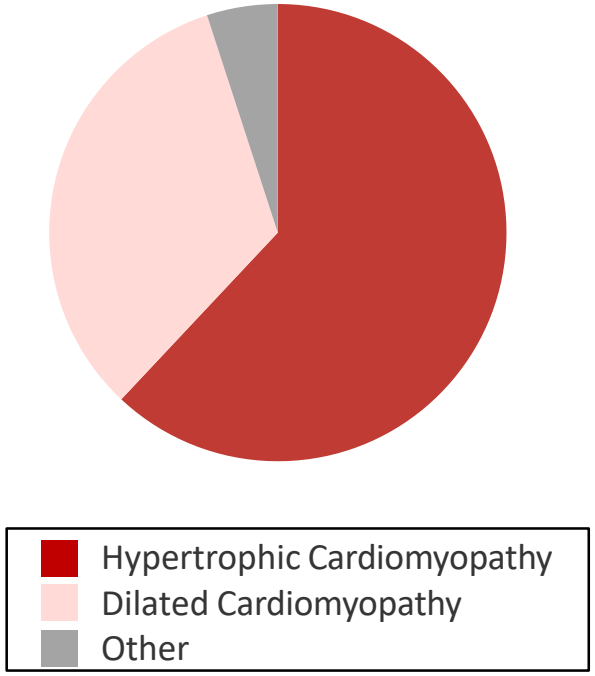
- US HCM Prevalence: 600K-1MM+*
- 1-4% of HCM patients consistently identified with LAMP2 mutations in multiple studies with >1000 subjects evaluated**
- Danon Disease Patients with HCM: ***
  - 85% of males
  - 30% of females

Dilated Cardiomyopathy (DCM)

- Danon Disease Patients with DCM ***
  - 15% of males
  - 50% of females

US+EU Prevalence:

~15,000-30,000



* J Am Coll Cardiol. 2015 Mar 31;65(12):1249-1254.

** Heart. 2004 Aug;90(8):842-6. N Engl J Med. 2005 Jan 27;352(4):362-72. Genet Med. 2015 Nov;17(11):880-8. Gene. 2016 Feb 15;577(2):227-35. J Cardiovasc Transl Res. 2017 Feb;10(1):35-46

*** Neurology. 2002 Jun 25;58(12):1773-8. Genet Med. 2011 Jun;13(6):563-8. Rev Esp Cardiol (Engl Ed). 2018 Aug 11.

Natural History of Rapidly Progressing Heart Failure

Cardiac Clinical Features

- Progressive hypertrophic cardiomyopathy/heart failure
- Key Clinical Biomarker Changes
  - Echo:
    - Worsening diastolic parameters
      - ↑ left ventricular end diastolic diameter (LVEDD)
    - ↓ left ventricular fractional shortening (LVFS)
    - ↑ ventricular wall thickness
    - ↓ left ventricular ejection fraction (LVEF) is late event
  - Hemodynamics: Decreasing cardiac output and/or stroke volume
  - Biomarkers: Elevated BNP, CK-MB, troponin

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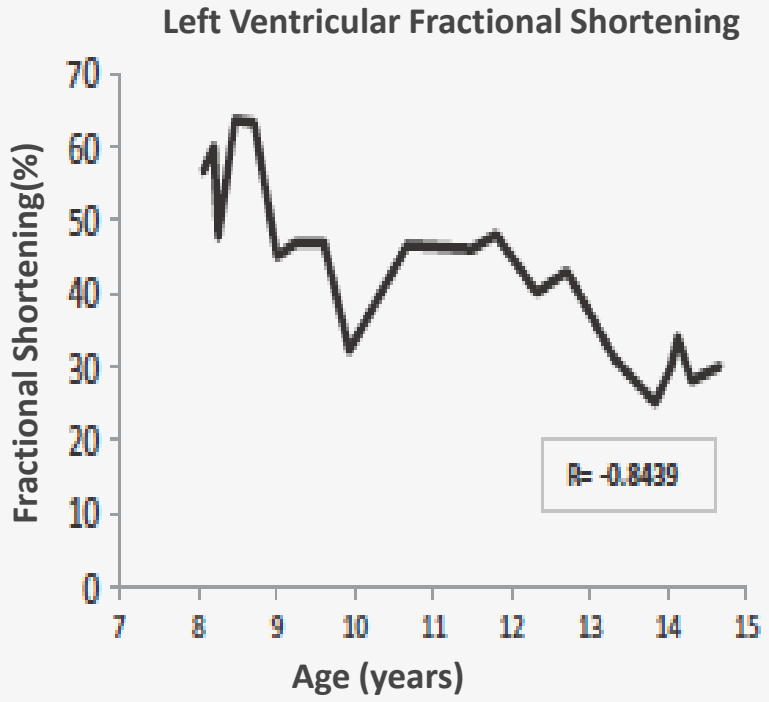
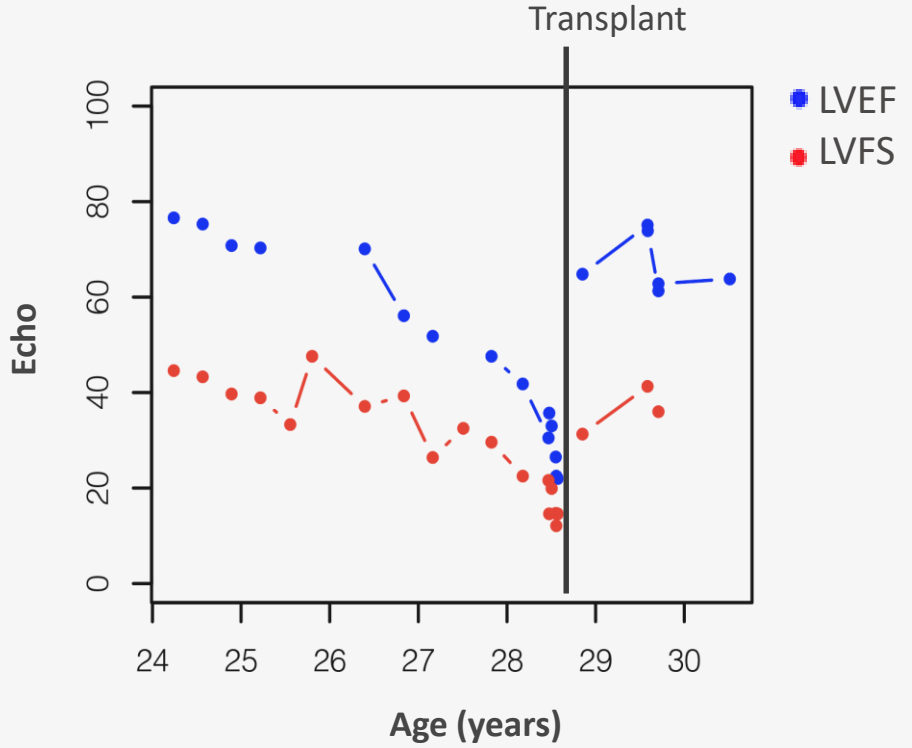
Danon Case Studies Demonstrate Rapidly Progressing Heart Failure



Echo: LVFS in male DD patient Diagnosed at 8 y; Progressive CHF w/ sudden cardiac death at 14 y.[1]

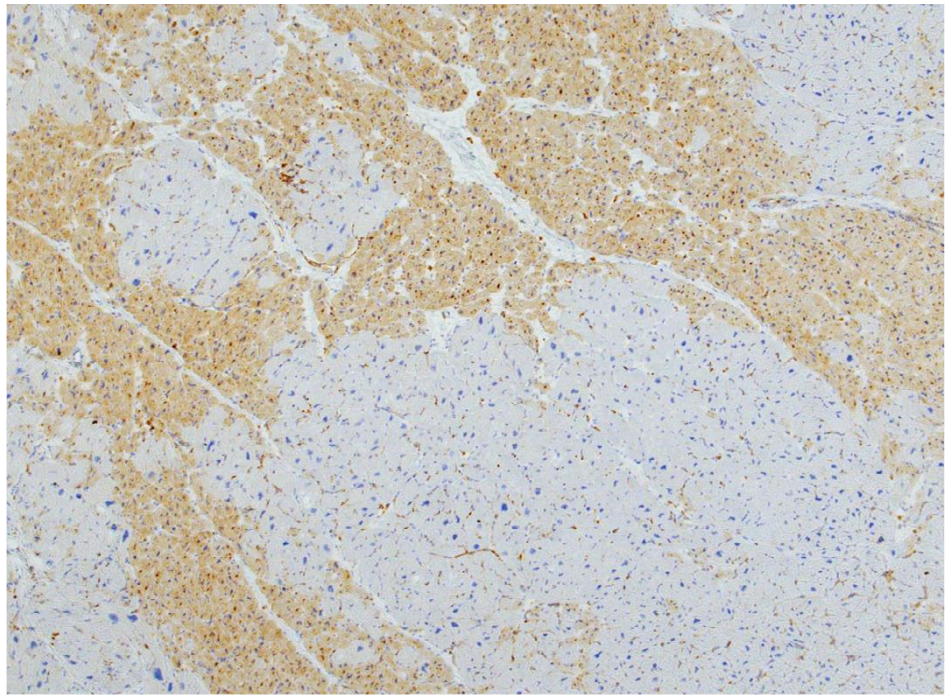


Echo: Parameters for male DD patient prior/post heart transplant. Courtesy of UCSD/U Colorado

1. D'souza. J Com Hosp Int Med Persp 2017; 7:107-14

Female Danon Cardiac Histology Suggests Broad LAMP2 Expression Important for Reversal of Phenotype

- Immunohistochemistry (IHC) from Danon female patients with severe disease display large patches negative for LAMP2 expression
- Broad expression of LAMP2 is likely the key to correcting phenotype rather than overall protein levels
- Based on this data, IHC demonstrating broad and ***homogeneous cardiac expression may be the best predictor of long-term efficacy***



Cardiac IHC Staining in Female Danon Patient Requiring Transplant at 10 y[1]

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1. *Oldfors et al 2015*

RP-A501: Clinical Update

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RP-A501 Phase 1 Danon Disease Clinical Trial Overview

Study Design

- Phase 1 open label study in male Danon patients
- Two age cohorts
  - Adolescent/Adult (>15 y)
  - Pediatric (8-14 y)
- Treatment doses
  - Low 6.7 x 10^{13} GC/kg
  - Higher 1.1 x 10^{14} GC/kg[1]

Primary Outcomes

Assessment of:

- Safety at all doses
- Target tissue transduction & LAMP2B expression
- Effect on cardiomyocyte histology
- Clinical stabilization or improvement via cardiac imaging, serology and exercise testing

Inclusion Criteria

- Male
- Danon disease including molecular confirmation of LAMP2 mutation
- Cardiac involvement confirmed by imaging or ECG
- NYH Class II/III or Class I with decreased 6MWT
- Able to walk >150 meters unassisted during 6MWT
- AST/ALT $\leq$ 10 X ULN; GGT < 2 X ULN;
  BR $\leq$ 1.5 X ULN; no liver cirrhosis by U.S.

1. IND enables doses up to 2.0 x 10^{14} GC/kg
https://clinicaltrials.gov/ct2/show/NCT03882437?cond=danon+disease&draw=2&rank=2

RP-A501: Subject Characteristics & AAV Vector Dose

Patient ID	Age at Treatment	Dosing Weight	Cohort Dose	Total Dose
1001	17 y	52.2 kg	6.7×10^{13} GC/kg	3.25×10^{15} GC
1002	20 y	89.1 kg	6.7×10^{13} GC/kg	5.97×10^{15} GC
1005	18 y	97.8 kg	6.7×10^{13} GC/kg	6.08×10^{15} GC
1006	21 y	82.7 kg	1.1×10^{14} GC/kg	9.10×10^{15} GC
1007	20 y	96.7 kg	1.1×10^{14} GC/kg	1.06×10^{16} GC

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Safety / Tolerability

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RP-A501 Demonstrated a Manageable Safety Profile

- In Low-dose cohort, RP-A501 was generally well tolerated with manageable safety profile
  - ***Transient*** and ***reversible*** decline in platelets
  - ***Transient*** and ***reversible*** transaminase elevation

- In Higher-dose cohort, a single patient experienced drug-related SAE related to complement activation
  - Patient with enhanced risk due to high weight & vector dose and pre-existing AAV immunity
  - Anticipated SAE of atypical hemolytic-uremic syndrome (aHUS) resulting in reversible thrombocytopenia and acute kidney injury (AKI)
  - AKI required supportive care including eculizumab and transient hemodialysis with full return to baseline kidney function within 2-3 weeks
- ***All patients have fully recovered from immune-related sequelae***

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Data as of November 2020

RP A-501: Gene Expression and Efficacy Endpoints
Low Dose (n=3) $6.7x10^{13}$ GC/kg

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RP-A501: Low Dose Subject Characteristics & Drug Product Metrics

Subject Characteristics

Patient	Age at Treatment	Dosing Weight	Cohort Dose	Total Dose
1001	17 y	52.2 kg	6.7×10^{13} GC/kg	3.25×10^{15} GC
1002	20 y	89.1 kg	6.7×10^{13} GC/kg	5.97×10^{15} GC
1005	18 y	97.8 kg	6.7×10^{13} GC/kg	6.08×10^{15} GC

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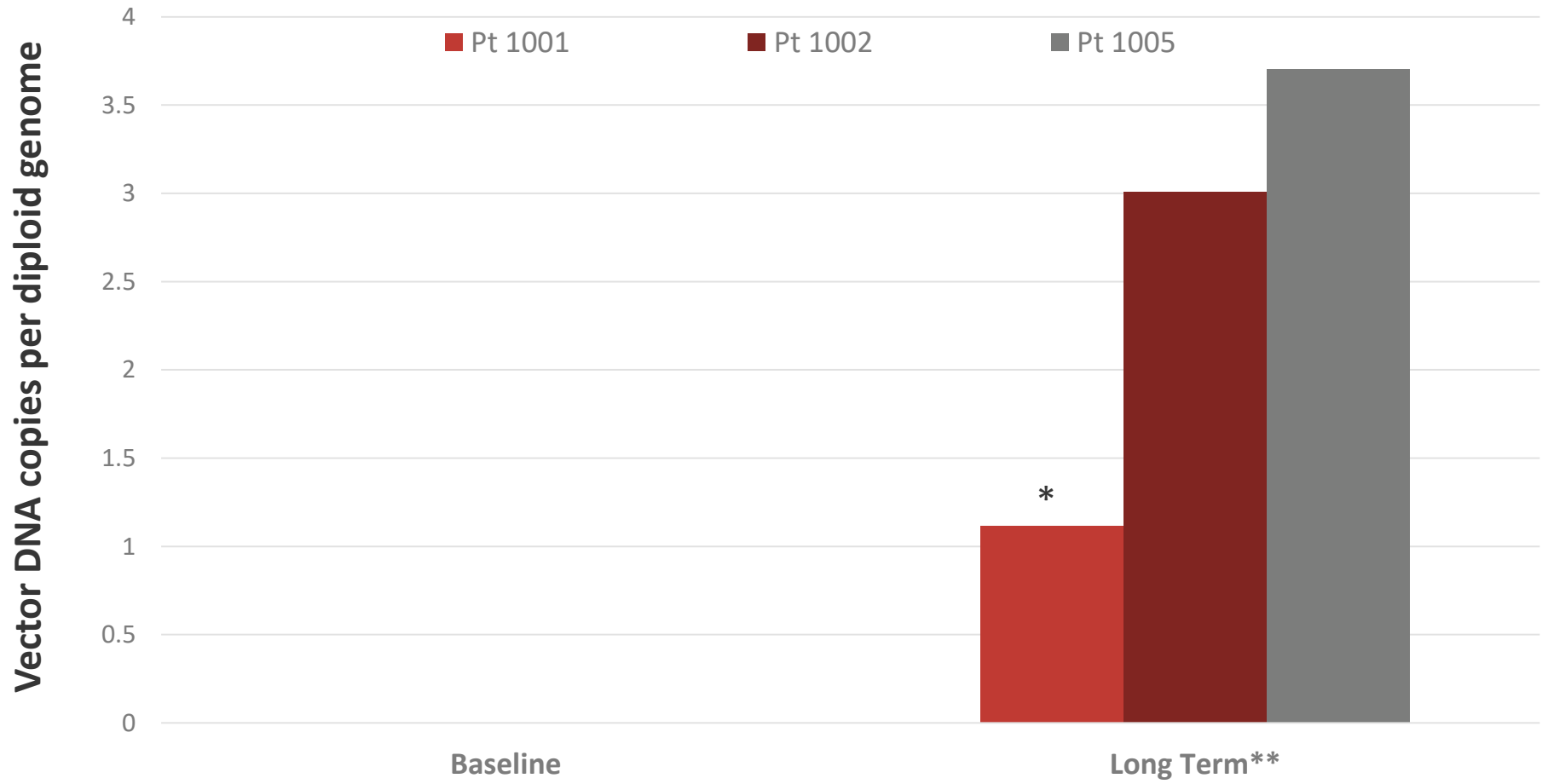
RP-A501 Low Dose: DNA Vector Copy Number



** Clinical course and VCN drop suggest apparent poor compliance with steroid regimen*
*** 1001 and 1002 Month 12; 1005 Month 9*

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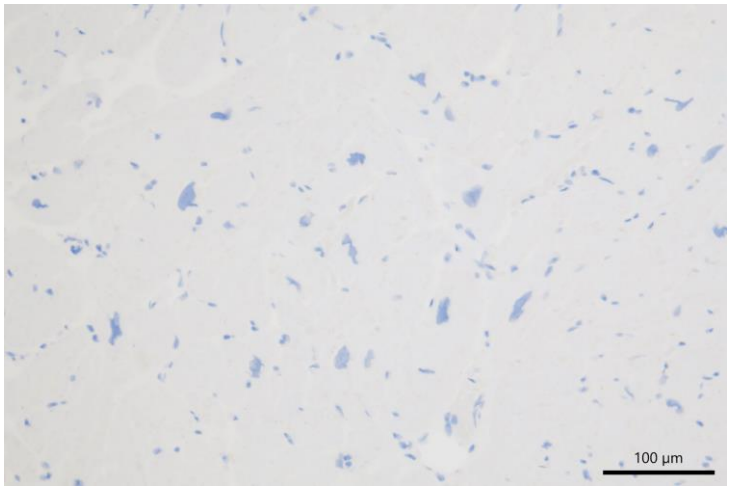
RP-A501 Low Dose Cohort Demonstrates Robust Cardiac Expression as Measured by LAMP2 Immunohistochemistry (IHC)

Patient	LAMP2B Relative Expression vs. Control*		
	Regimen	Week 8	Long Term
1001	Steroids only (limited compliance)	7.8%	<15%*[1]
1002	Steroids only (local monitoring)	36.9%	67.8%[1]
1005	Steroids → Tacrolimus	17.6%	92.4%[2]

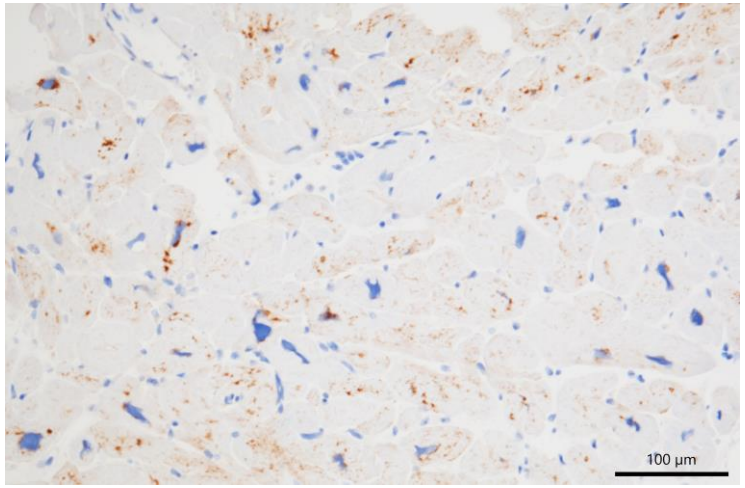
* Endomyocardial biopsies were obtained and stained for LAMP2. Percent area of cell staining was quantitated using software in a blinded fashion and expression compared to normal heart tissue. Values represent average of 3-14 sections. Qualitative assessment reported for samples with high variance.

1. Sample obtained at Month 12
2. Sample obtained at Month 9

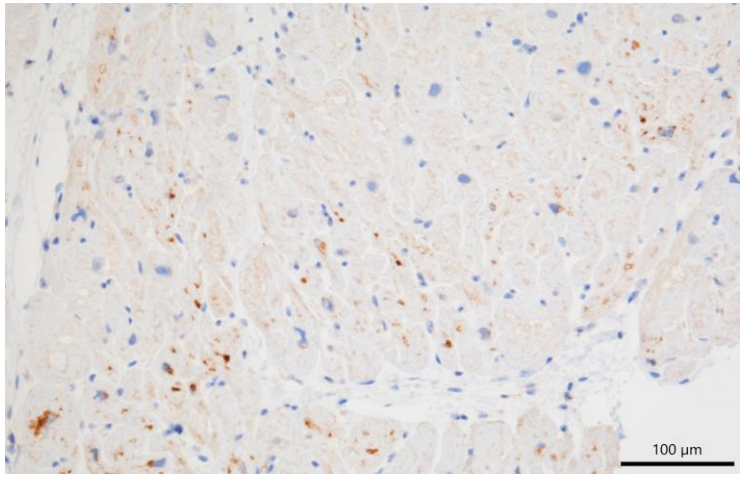
RP-A501 Low Dose: Patients 1002 and 1005 Demonstrate Robust Cardiac Expression of LAMP2 by IHC Through Months 9 and 12, Respectively



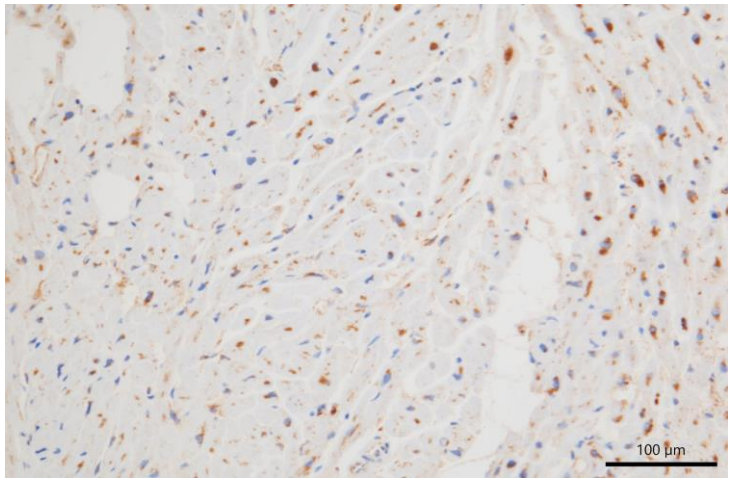
1002 Baseline



1002 Month 12



1005 Month 9



Normal Heart Control

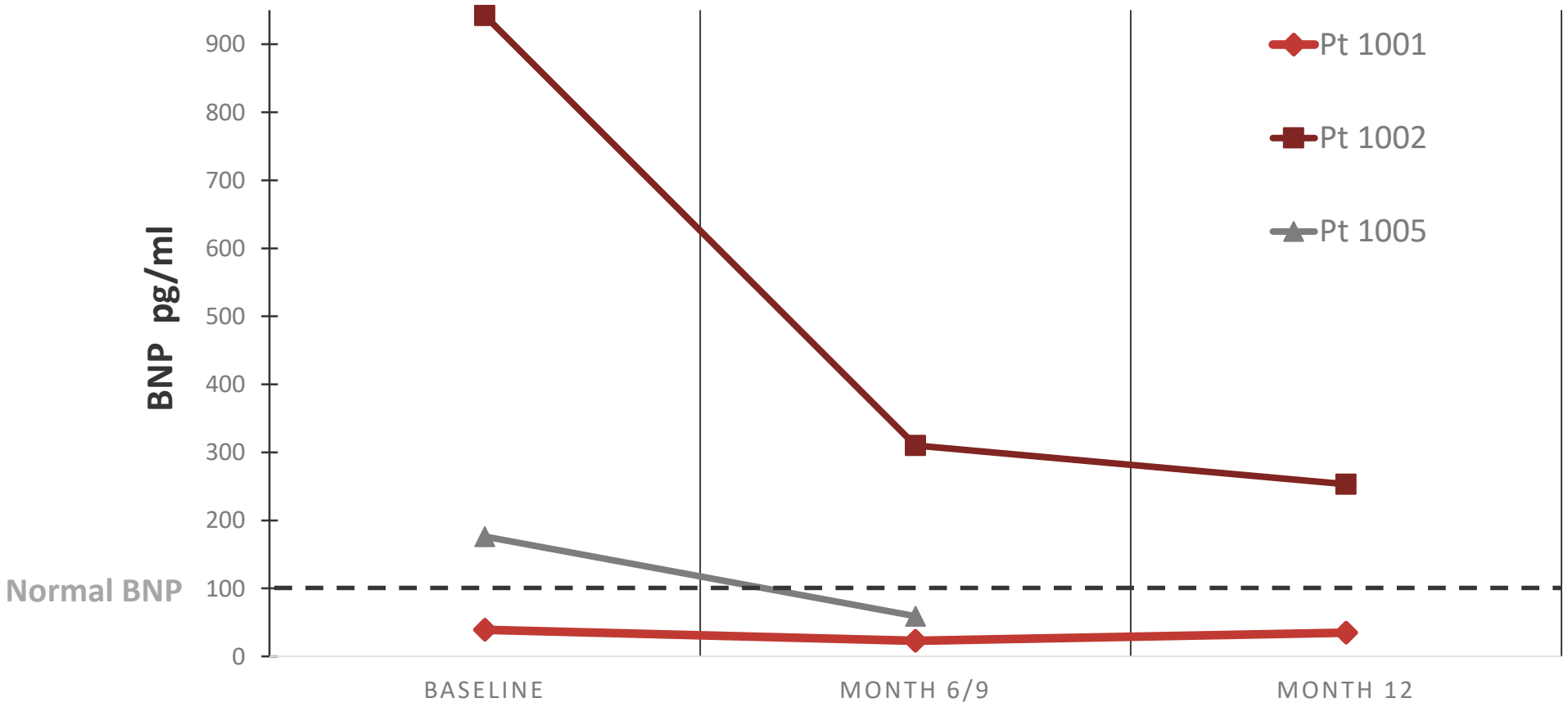
LAMP2 IHC (20x)

RP-A501 Low Dose: Endocardial LAMP2B Protein Expression

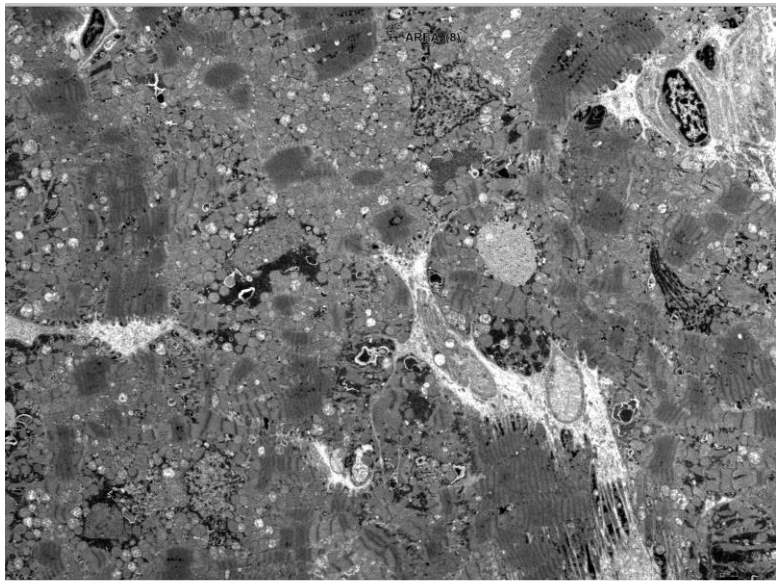
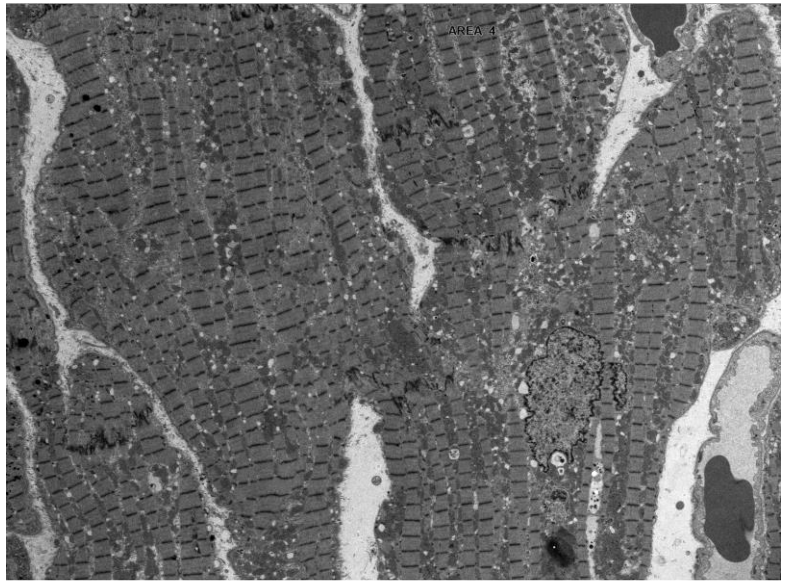
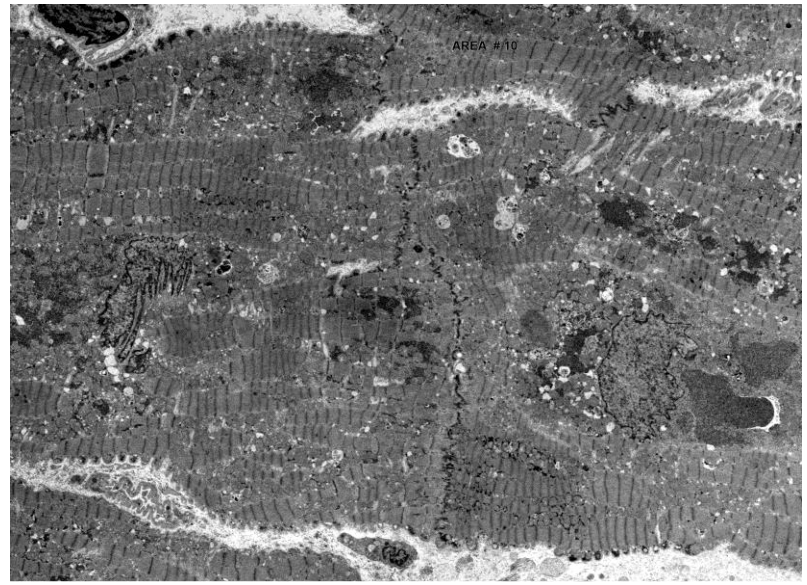
Patient	Relative LAMP2B Expression vs. Normal By Western Blot	
	Week 8	Long Term
1001	20.7%	17.9%[1]
1002	27.3%	-
1005	42.8%	61.1%[2]

1. Sample obtained at Month 6
2. Sample obtained at Month 9

RP-A501 Low Dose Improves or Stabilizes Key Cardiac Marker of Heart Failure: B-type Natriuretic Peptide (BNP)



RP-A501 Electron Microscopy of Cardiac Myocytes Demonstrates Marked Decrease in Vacuolar Pathology: Patient 1005

Baseline	Week 8	Month 9
		

RP-A501 Low Dose Confers Improvement in Cardiac Output Based on Invasive Hemodynamics in Patients 1002 and 1005

Cardiac Output (L/min)

Patient	Baseline	Long Term[1]
1001	5.2	4.12[2]
1002	3.58	5.8[2] (**1.62**x **increase**)
1005	4.5	6.08[3] (**1.35**x **increase**)

1. Calculated Stroke Volume: 40% increase in Patient 1002 and 31% increase in Patient 1005

2. Sample obtained at Month 12
3. Sample obtained at Month 9

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RP-A501 Low Dose: Safety & Efficacy Findings (n=3)

- Generally, ***well tolerated*** with manageable safety profile in all low-dose patients
- ***LAMP2B gene expression*** demonstrated in cardiac biopsies from all patients
- ***Enhanced cardiac expression*** by IHC and Western blot in both patients whose compliance with transient immunosuppressive regimen was closely monitored
  - Consistent increases in percentage and level of IHC staining at later (9-12m) timepoints
- ***Positive trends*** in key biomarkers and efficacy endpoints
  - Qualitative improvement of vacuolar pathology
  - Clinical lab markers demonstrated improvement in patients 1002 and 1005
  - Trends towards stabilization and/or improvement in cardiac output
- ***Benefit observed in all three patients*** serves as clinical proof of concept as *Danon disease patients generally do not improve independently*

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Data as of November 2020

Danon Disease: Planned Next Steps

- Treat additional patient in Higher-dose cohort and continue data collection from patients in both cohorts
  - Long-term clinical data in Low-dose cohort
  - Expression and biomarker data in Higher-dose cohort
- Initiate pediatric cohort (8-14 y)
- Engagement with global regulatory agencies to discuss registrational trial design following selection of recommended Phase 2 dose

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