**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, DC 20549**

# FORM 8-K

**CURRENT REPORT**
**Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): September 30, 2022

# Rocket Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

| **Delaware** | **001-36829** | **04-3475813** |
|---|---|---|
| (State or other jurisdiction of incorporation) | (Commission File Number) | (IRS Employer Identification No.) |

| **9 Cedarbrook Drive, Cranbury, NJ** | **08512** |
|---|---|
| **(**Address of principal executive offices) | (Zip Code) |

Registrant's telephone number, including area code: (646) 440-9100

**Not applicable**
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common stock, $0.01 par value | RCKT | The Nasdaq Global Market |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 8.01 Other Events**

On September 30, 2022, Rocket Pharmaceuticals, Inc. (the "Company") announced positive clinical updates from its Phase 1 Danon Disease Trial for RP-A501 through an oral poster session at the Heart Failure Society of America (HFSA) Annual Scientific Meeting 2022. This included updated safety and efficacy data from patients in the pediatric and adult cohorts which demonstrate that RP-A501 was generally well tolerated and conferred clinical benefit.

**Safety Profile of the First Pediatric Cardiomyopathy Gene Therapy Trial: RP-A501 (AAV9:LAMP2B) for Danon Disease and Extended Results from Phase 1**

The data described in this oral poster presentation (data cut-off September 27, 2022 for pediatric patients, and August 19, 2022 for adult patients, with source data verification through July 11, 2022) and in this report are from the ongoing first-in-human Phase 1 clinical trial evaluating a single intravenous infusion of RP-A501, the Company's investigational gene therapy for the treatment of Danon Disease. The presentation includes early efficacy data with updated safety data from the low-dose ($6.7 \times 10^{13}$GC/kg; n=2) pediatric cohort, as well as updated efficacy and safety data from young adult and adolescent patients in the low-dose ($6.7 \times 10^{13}$ GC/kg; n=3) and high-dose ($1.1 \times 10^{14}$ GC/kg; n=2) cohorts.

- Early pediatric efficacy data were consistent with initial improvements observed in adult patients at a similar timeframe of up to nine months follow-up and sustained clinical benefit across biomarker, clinical and functional parameters in currently enrolled adult patients at 24 to 30 months of follow-up.
    - **Gene expression**: In the pediatric cohort, *LAMP2B* gene expression by immunohistochemistry was 21.1% in patient 1008 at six months and 34.7% in patient 1009 at three months. Evidence of durable and meaningful cardiac *LAMP2B* protein expression as read at a centralized core lab was achieved in all patients across pediatric and adult cohorts at three months and sustained through six to nine months in the pediatric cohort and 24 months in the adult cohorts in patients with a closely monitored immunomodulatory regimen.
- The following assays were performed and reported for patients with at least six months of follow-up.
    - **Vacuolar area**: In the first pediatric patient, vacuolar area as assessed by an automated method in representative biopsy samples was found to have decreased by 77% at six months. Six-month biopsy results were not yet available for the second pediatric patient. All adult patients showed meaningful decreases in vacuolar area ranging from 26% to 74% at most recent available timepoints.
    - **Brain natriuretic peptide (BNP)**: In the pediatric cohort, BNP, a key marker of heart failure, decreased from a pretreatment baseline by 78% in patient 1008 at nine months and by 62% in patient 1009 at six months. The majority of patients in the pediatric and adult cohorts showed stabilization or meaningful decreases in BNP, with the most dramatic decreases observed in patients with higher baseline BNP (90% for patient 1002 in the adult cohort at 30 months and 78% for patient 1008 in the pediatric cohort at nine months). The four currently enrolled adult patients demonstrated reduction in BNP of greater than 75% from mean pretreatment baseline compared to mean values at 18 to 24 month timepoints.
    - **Troponin**: The pediatric patients, despite a more limited six and nine months of follow-up, were observed to have meaningful decreases in high sensitivity troponin I (hsTnI), a protein in the blood showing signs of cardiac injury, of 90% and 85%, respectively. Patients in the adult cohorts demonstrated significant decreases in hsTnI. Notably, the two adult patients were observed to have a reduction in troponin of greater than 75% from mean pretreatment baseline to mean values at 18 to 24 months that was sustained in the two adult patients who are currently 30 to 36 months post-treatment.
    - **New York Heart Association (NYHA) Class**: In the pediatric cohort, an improvement (from Class II to I) in NYHA class, a measure of the symptoms and functional limitations resulting from heart failure, was observed in both patients. In the adult cohorts, all three patients treated with a closely monitored immunomodulatory regimen showed improvement in NYHA class. Stabilization of NYHA class was observed in one adult patient treated at the low dose without a closely monitored regimen.

- **Kansas City Cardiomyopathy Questionnaire (KCCQ)**: Patients in the pediatric cohort showed significant improvement in KCCQ Overall Score, a measure (0-100) of physical and social limitations, symptoms and quality of life in patients with heart failure. Specifically, patient 1008 demonstrated improvement from a pretreatment baseline of 50 to 93 at nine months and patient 1009 demonstrated improvement from a pretreatment baseline of 52 to 81 at three months. All patients treated in pediatric and adult cohorts with a closely monitored immunomodulatory regimen showed improvements ranging between three and 43 points when comparing baseline to the most recent available timepoint.
- **Left ventricular (LV) wall thickness**: In the pediatric cohort, patient 1008 demonstrated reduction in maximum LV wall thickness by 3% from treatment baseline after six months of follow-up. In the adult cohort, three patients demonstrated a reduction of greater than 15% and greater than 15% from mean baseline in both LV posterior wall thickness in diastole and maximum LV wall thickness, respectively, compared to mean values at 18 to 24 months, which represents improvement of the ventricular hypertrophy.

- RP-A501 was observed to be generally well tolerated at the low dose with a manageable tolerability profile across pediatric and adult cohorts.
  - In the pediatric cohort, RP-A501 was well tolerated in both patients with six to eleven months follow-up. The patients were observed to have normal-range platelets, minimal complement activation and no complement-related adverse events. The two patients received a modified immunomodulatory regimen to mitigate adverse events. No significant immediate or delayed toxicities, significant skeletal myopathy, or late transaminase elevations have been observed to date.
- Taken together, RP-A501 has been generally well tolerated in adult and pediatric cohorts in Danon Disease.
  - Phase 1 enrollment and treatment are complete.
  - RP-A501 together with the enhanced immunomodulatory regimen appears generally well tolerated and has mitigated adverse events in the pediatric cohort.
  - In the adult cohort, RP-A501 stabilizes and potentially improves Danon Disease cardiomyopathy.
  - Early pediatric data are encouraging and consistent with improvements at similar or earlier timepoints compared to the adult cohorts.
  - Findings are supportive of Phase 2 evaluation of RP-A501 in Danon Disease.

**Rocket Cautionary Statement Regarding Forward-Looking Statements**

Various statements in this report concerning Rocket's future expectations, plans and prospects, including without limitation, Rocket's expectations regarding its guidance for 2022, the safety and effectiveness of RP-A501 for the potential treatment of Danon Disease, trends for RP-A501 safety and efficacy based on the adult patients treated to date, the expected timing and outcome of Rocket's regulatory interactions and planned submissions, including in connection with the potential advancement toward a Phase 2 pivotal study for RP-A501, Rocket's plans for the advancement of its Danon Disease program 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 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 Annual Report on Form 10-K for the year ended December 31, 2021, filed February 28, 2022 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.

In connection with this announcement, the Company utilized a slide presentation which is substantially in the form attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
| --- | --- |
| 99.1 | Presentation of Rocket Pharmaceuticals, Inc. |
| Exhibit 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document). |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: October 3, 2022

**Rocket Pharmaceuticals, Inc.**

By: /s/ Gaurav Shah, MD
Name: Gaurav Shah, MD
Title: Chief Executive Officer and Director

Exhibit 99.1


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Update from Phase 1 Trial of
RP-A501 Gene Therapy
Treatment for Danon Disease
September 30, 2022

# DISCLAIMER

Various statements in this release concerning Rocket's future expectations, plans and prospects, including without limitation, Rocket's expectations regarding its guidance for 2022, the safety and effectiveness of RP-A501 for the potential treatment of Danon Disease, trends for RP-A501 safety and efficacy based on the adult patients treated to date, the expected timing and outcome of Rocket's regulatory interactions and planned submissions, including in connection with the potential advancement toward a Phase 2 pivotal study for RP-A501, Rocket's plans for the advancement of its Danon Disease program 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 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 Annual Report on Form 10-K for the year ended December 31, 2021, filed February 28, 2022 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.

# Danon Disease (DD): Serious Condition with Unmet Medical Need

**Addressable Market – US and EU**
Prevalence of **15,000 to 30,000** individuals
Annual incidence of **800 to 1,200** individuals

## Disease Etiology

- X-linked, dominant, monogenic disease
- Loss-of-function mutations in *LAMP-2B*

## Therapeutic Challenges

- Standard of care:
  - Heart transplant (HTx)
- Limitations:
  - Considerable morbidity and mortality
  - Only ~20% of patients receive HTx
  - Not curative of extracardiac disease

## Clinical Manifestations

**Impaired autophagy**
- Prominent autophagic vacuoles
- Myocardial disarray

**Other clinical manifestations**
- Skeletal myopathy
- CNS manifestations
- Ophthalmologic manifestations

**Severe cardiomyopathy**
- Mortality secondary to heart failure or arrhythmia
- Males: Aggressive disease course, median overall survival: 19 years
- Females: Delayed median presentation (~20 years later) due to additional X chromosome, highly morbid and fatal disorder



CNS, central nervous system; LAMP-2B, lysosome-associated membrane protein 2B.
Boucek D et al. *Genet Med*. 2011;13(6):563-568. Brambatti M et al. *Int J Cardiol*. 2019;286:92-98.

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# RP-A501: Prospect of Direct Benefit

## Trajectory of cardiac pathophysiology and heart failure in male Danon disease patients

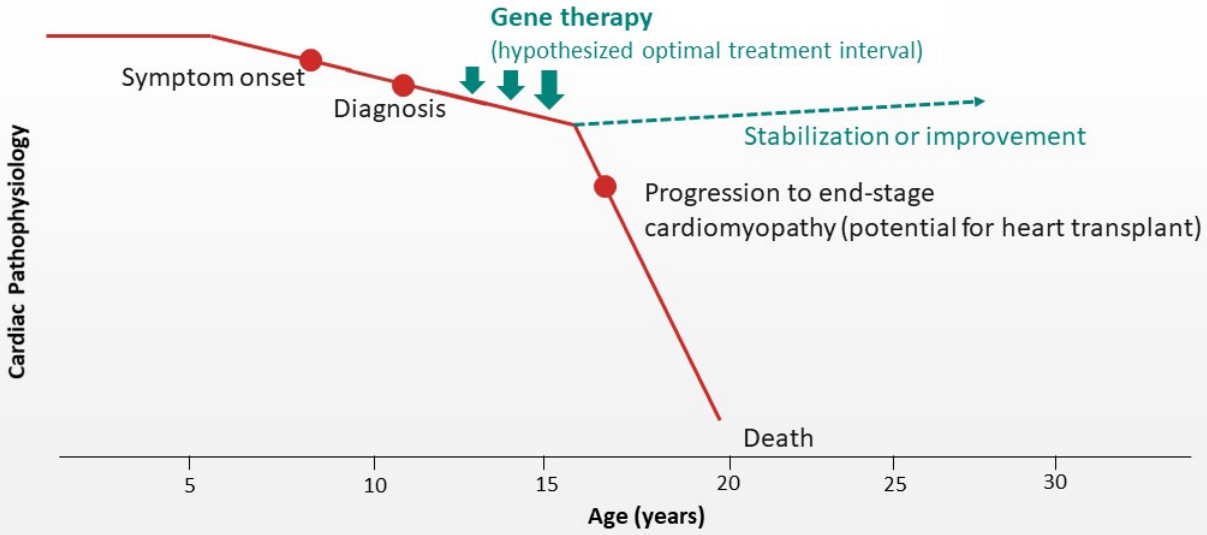
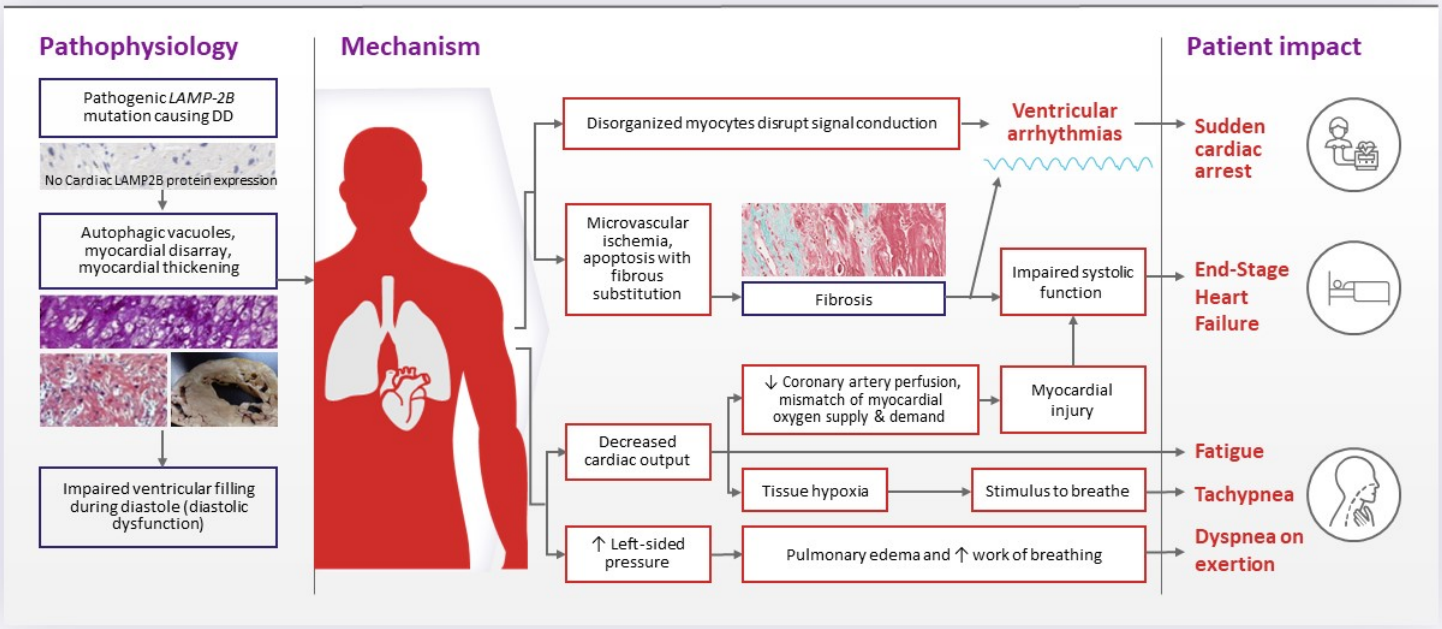





Figure modified from disease progression by age data from Boucek D et al. *Genet Med*. 2011;13(6):563-568 and Brambatti M et al. *Int J Cardiol*. 2019;286:92-98.

# Pathophysiology and Clinical Manifestations of Danon Disease HCM






DD, Danon disease; LAMP2B, lysosome-associated membrane protein 2B; VT, ventricular tachycardia.
Adapted from Jones & Arnold. 2014. Hypertrophic Cardiomyopathy: Pathogenesis and Clinical Findings

# Phase 1 Study: Non-Randomized Open Label

## Non-randomized open label study in male DD patients

### INCLUSION CRITERIA

- Male
- Confirmed *LAMP-2B* mutations
- Cardiac involvement confirmed by imaging or ECG
- NYHA Class II or III
- Able to walk >150 m unassisted during 6-minute walk test (6MWT)

### EXCLUSION CRITERIA

- Anti-AAV9 neutralizing antibody titer >1:40
- Cardiopulmonary instability
- Prior organ transplantation
- LVEF <40% (implemented prior to pediatric cohort)

**Adults (& Adolescents)**
≥15 years
n=5 at UCSD

**Pediatric**
8-14 years
n=2 at CHOP

**Single Intravenous Dose of RP-A501 (AAV9.LAMP2B)**

Low Dose:
6.7 x $10^{13}$ GC/kg

High Dose*:
1.1 x $10^{14}$ GC/kg
*No further enrollment at this dose.

***Enrollment Complete***

**36 months**

### PRIMARY OUTCOMES

- **Early and long-term safety**
- Target tissue transduction & LAMP2B protein expression
- Improved myocardial histology
- Clinical improvement or stabilization

Data Reporting Details
- Pre-dose (baseline) value defined as the mean values from all visits prior to infusion
- Core lab data presented for echocardiographic parameters, cardiac serologies, and cardiac histology
- Data cut September 27, 2022; source data verification through July 11, 2022.



6MWT, 6-minute walk test; AAV, adeno-associated virus; CHOP, Children's Hospital of Philadelphia; DD, Danon disease; ECG, electrocardiogram; *LAMP-2B*, lysosome-associated membrane protein 2B; LVEF, left ventricle ejection fraction; NYHA, New York Heart Association; UCSD, University of California San Diego.

# RP-A501: Safety Monitoring of Phase 1 Patients

## Cohort 1: Low-dose adult

| Pt | Age | Wt |
|---|---|---|
| 1001[a] | 17.5 | 52.5 |
| 1002 | 20.4 | 89.1 |
| 1005 | 18.3 | 91.8 |

RP-A501 $6.7 \times 10^{13}$ GC/kg

Steroid (prednisone 1mg/kg)

Tacrolimus

**SAEs of Interest**
n=2 grade 3 steroid myopathy

**Platelets**
n=2, Grade 1 decrease (to LLN range)

## Cohort 2: High-dose adult

| Pt | Age | Wt |
|---|---|---|
| 1006 | 21.1 | 82.7 |
| 1007[b] | 20.7 | 96.7 |

RP-A501 $1.1 \times 10^{14}$ GC/kg

Steroid (prednisone 1mg/kg)

Tacrolimus

Rituximab (2 doses)

n=1 grade 4 TMA
n=1 grade 3 steroid myopathy

n=1, Grade 4 decrease

## Cohort 3: Low-dose pediatric

| Pt | Age | Wt |
|---|---|---|
| 1008 | 12.3 | 70.5 |
| 1009 | 11.7 | 55.7 |

RP-A501 $6.7 \times 10^{13}$ GC/kg

*Daily, real-time monitoring of labs & clinical status*

Day -14 | Day 14 | Month 3

Steroid (prednisone 0.5 – 0.8mg/kg); Taper start d 10

Sirolimus (target trough 4-8 ng/mL)

Rituximab (2 doses)

none

Remain in normal range

[a] Corticosteroid compliance uncertain
[b] This patient underwent heart transplant due to DD progression five months post RP-A501 infusion; both because this patient would no longer be eligible for future studies based on revised eligibility criteria and because long-term RP-A501 effect is not evaluable, data for this patient are not shown. He is currently stable.

d, day; LLN, lower limit of normal; Pt, patient; SAE, serious adverse event; TMA, thrombotic microangiopathy; Wt, weight.
Age in years at RP-A501 infusion; weight in kg.



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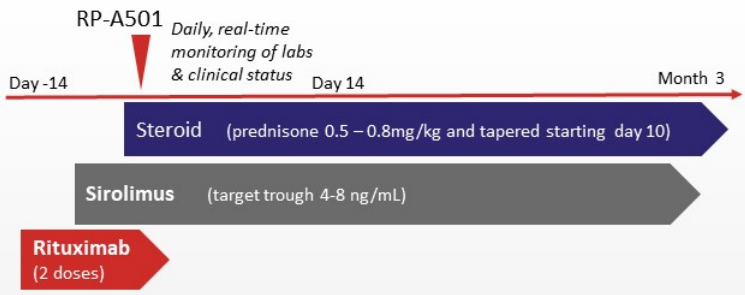
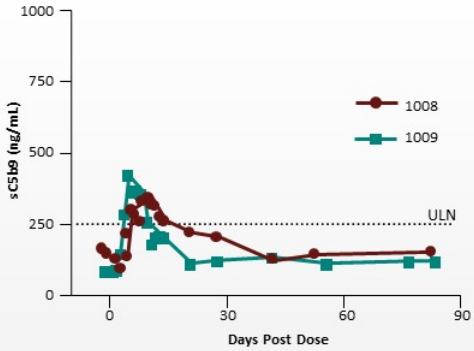
# RP-A501 Was Generally Well Tolerated in Pediatric Cohort on Enhanced Immunomodulation

## All AEs were Transient and Reversible with 6 and 11 month follow up in 1008 and 1009, respectively

### Pediatric immunomodulation protocol




### sC5b9 Evaluation Post RP-A501




**Platelets remained within normal range**

No reported **skeletal myopathy or late transaminitis** with initial steroid dose-reduction and more rapid taper, and introduction of sirolimus

- **Minimal complement activation**
- **No complement-related clinical or laboratory AEs**
- **All AEs were transient and reversible**
- **No treatment-related SAEs**



AE, adverse event; SAE, serious AE; ULN, upper limit of normal.
Data cut-off September 27, 2022 with source data verification through July 11, 2022.

# Early Pediatric Data are Encouraging and Consistent with Adult Efficacy Data at Similar Timeframe

## Patient ID: A501-008-1008

**Baseline Characteristics**

**AGE AT INFUSION**
12.3 years

**MAX LV WALL THICKNESS**
41.9 mm, z-score +32

**ICD** yes[1]

**6MWT**
438 meters

**WPW** yes

9 months

| Variable | Baseline[2] | Most Recent Follow-up |
|---|---|---|
| LAMP2 protein[3] (%) | 0.5 | 21[4] |
| Troponin-I (ng/mL) | 1.89 | 0.28 |
| BNP (pg/mL) | 1837 | 406 |
| KCCQ-overall scale | 50 | 93 |
| NYHA Class | II | I |

## Patient ID: A501-008-1009

**Baseline Characteristics**

**AGE AT INFUSION**
11.7 years

**MAX LV WALL THICKNESS**
19.8 mm, z-score +12

**ICD** no

**6MWT**
553 meters

**WPW** no

6 months

| Variable | Baseline[2] | Most Recent Follow-up |
|---|---|---|
| LAMP2 protein[3] (%) | 2.6 | 35[4] |
| Troponin-I (ng/mL) | 0.67 | 0.07 |
| BNP (pg/mL) | 297 | 113 |
| KCCQ-overall scale | 52 | 81[5] |
| NYHA Class | II | I |

[1] Recommended prior to enrollment; ICD implanted 3 months after RP-A501 infusion
[2] Baseline values for troponin-I and BNP are the mean values from all pre-dose visits
[3] All biopsies stained for LAMP2 were compared to normal controls. Data is quantitated in a blinded fashion from ~3-5 sections
[4] Most recent biopsy data available from 6 month visit for 1008 and 3 month visit for 1009
[5] Most recent KCCQ data available from 3 month visit for 1009

6MWT, 6-minute walk test; BNP, brain natriuretic peptide; ICD, implantable cardioverter defibrillator; KCCQ, Kansas City cardiomyopathy questionnaire; LAMP2, lysosome-associated membrane protein 2; LV, left ventricle; NYHA, New York Heart Association; WPW, Wolff-Parkinson-White syndrome.
Data cut-off September 27, 2022 with source data verification through July 11, 2022.



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# Early Pediatric LAMP2 Expression are Encouraging and Consistent with Adult Data

## Quantified LAMP2 protein expression by immunohistochemistry (IHC)

| Cohort | Patient ID | Initial Biopsy Post Infusion |
|---|---|---|
| **Pediatric - Low Dose** | **1008** | *Month 3:* **18.5%*** |
| | **1009** | *Month 3:* **34.7%** |
| Adult - Low Dose | 1001 | *Month 2:* 7.3% |
| | 1002 | *Month 2:* 36.9% |
| | 1005 | *Month 2:* 17.6% |
| Adult - High Dose | 1006 | *Month 2:* 5.0% |
| | 1007 | *Month 2:* 6.9% |

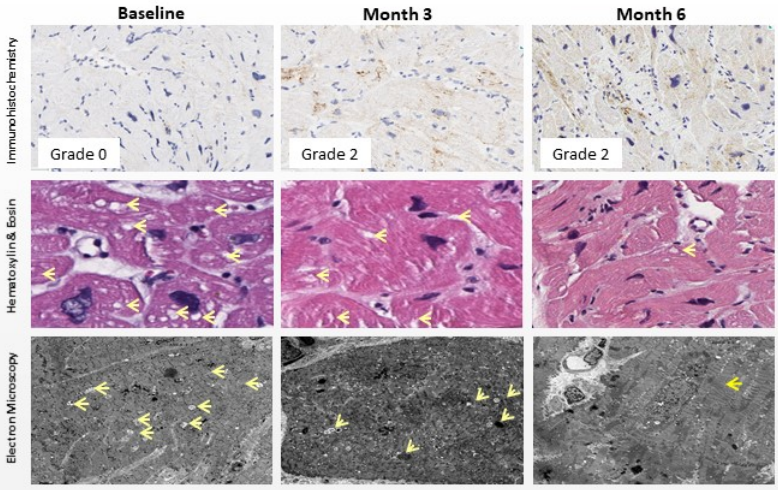
All biopsies stained for LAMP2 were compared to normal control samples. Data is quantitated in a blinded fashion from ~3-5 sections.
* 1008 Month 6 biopsy: 21% as noted in previous slide



LAMP2, lysosome associated membrane protein 2.
IHC, immunohistochemistry.

# LAMP2 Myocardial Protein Expression and Histologic Improvement in the Pediatric Cohort

## A501-008-1008 Endomyocardial Biopsy (EMB) Images




**LAMP2 protein expression assessed (relative to normal human controls) by core lab in a blinded fashion of entire tissue sample**

- Percentages reflect estimated extent of LAMP2 staining
  - Grade 0 negative staining
  - Grade 1 ≤25%
  - Grade 2 26%-50%
  - Grade 3 51%-75%
  - Grade 4 >75%
- H&E images captured at 20x magnification, presented digitally zoomed
- Arrows indicate autophagic vacuoles
- Similar findings on EMB from patient 1009 at Baseline and Month 3

EMB, endomyocardial biopsy; H&E, hematoxylin & eosin stain; LAMP2, lysosome associated membrane protein 2.



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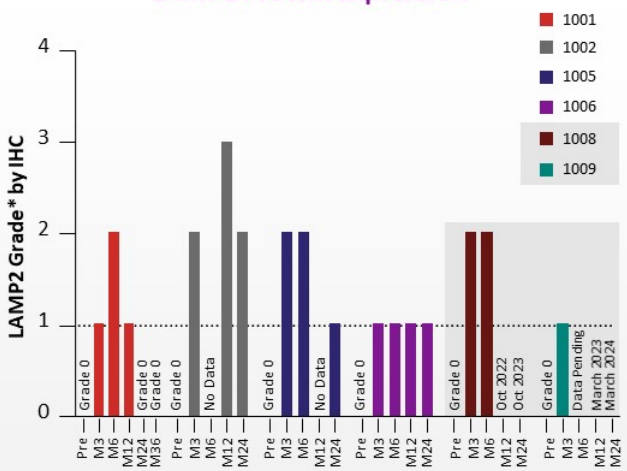
# Pediatric LAMP2 Protein and DNA Suggests Durable Expression As Demonstrated in Adult Cohort

## LAMP2 Protein Expression




*LAMP2 protein expression assessed (relative to normal human controls) by core lab in a blinded fashion of entire tissue sample; Percentages reflect estimated extent of LAMP2 staining: Grade 0=negative staining; Grade 1 ≤25%; Grade 2 =26%-50%; Grade 3 =51%-75%; Grade 4 >75%.

## Cardiac LAMP2 DNA by qPCR (vector copies per diploid nucleus)

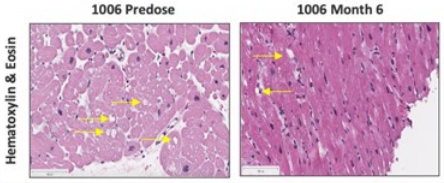
| Patient ID | Predose | Month 6 | Month 12 | Month 36 |
|---|---|---|---|---|
| **1001**[a] | 0 | 0.384 | 0.197 | 0.120 |
| **1002** | 0 | ND | 0.575 | 0.590[c] |
| **1005** | 0 | 0.583 | ND | 1.228[c] |
| **1006** | 0 | 2.693 | 1.131 | - |
| **1007** | 0 | RV: 6.77[b]<br>LV: 9.15[b] | Post heart transplant | |
| **1008** | 0 | 0.492 | - | - |
| **1009** | 0 | Data pending | - | - |

LV, Left ventricle and RV, Right ventricle at 5 months from explanted heart; ND. not done, -, visit pending.
[a] Corticosteroid compliance uncertain. [b] Assessment from explanted heart tissue at 5 months. [c] Month 30 visit.

LAMP2, lysosome associated membrane protein 2; M, month.

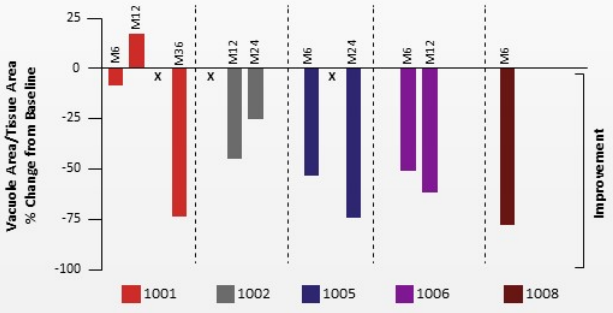
# Restored Autophagy Sustained Following RP-A501

## *Restored autophagy indicated by attenuation of vacuolar area*

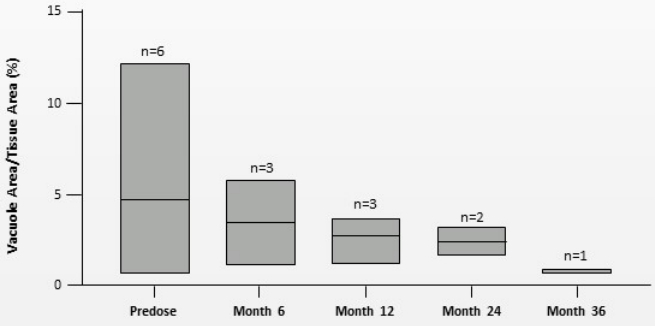



Light microscopy images at 20X;
Autophagic vacuoles are depicted by yellow arrows.

### A. Vacuolar Area of Endomyocardial Tissue




### B. Vacuolar Area Decreases with Treatment




M, month; X, data not assessed

Bars denote minimum and maximum range, and line within each bar represents the mean value within study population.



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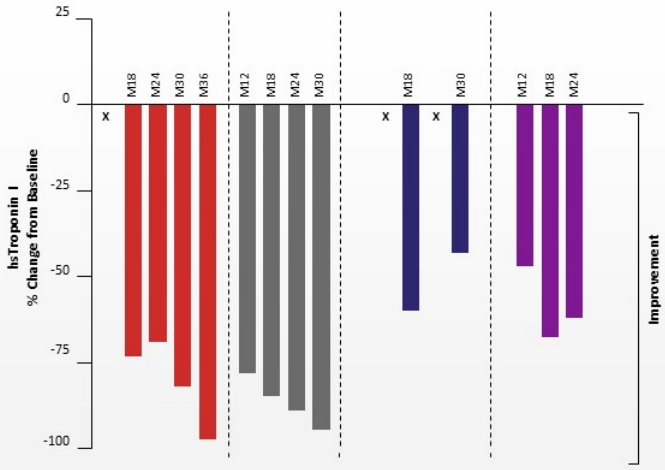
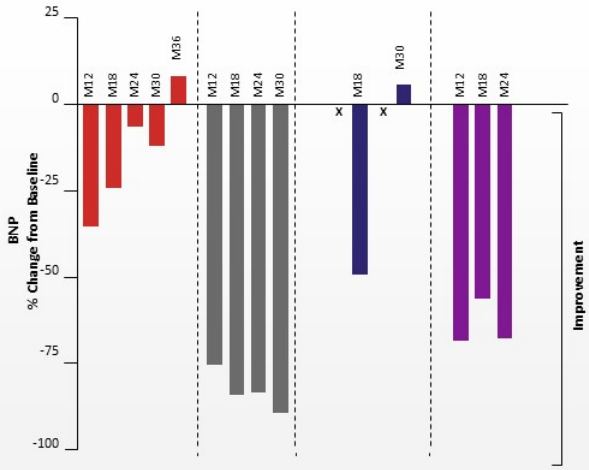
# Sustained Improvement or Stabilization of Biomarkers of Myocardial Injury and Stress Following RP-A501

## High Sensitivity Troponin I (hsTnI)




## Brain Natriuretic Peptide (BNP)



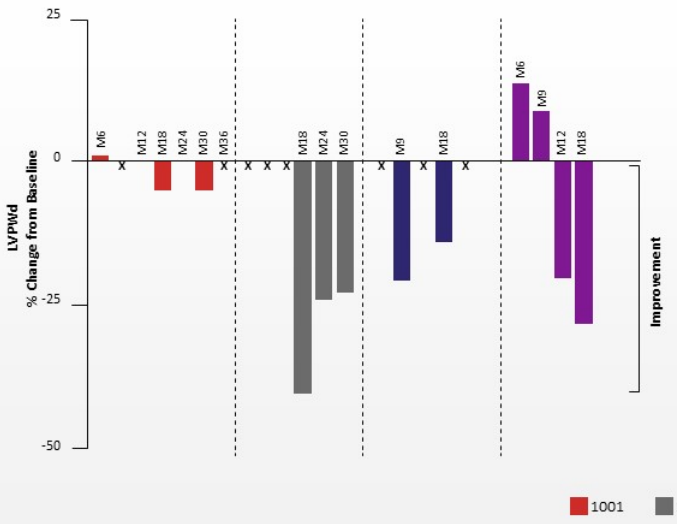

1001 1002 1005 1006



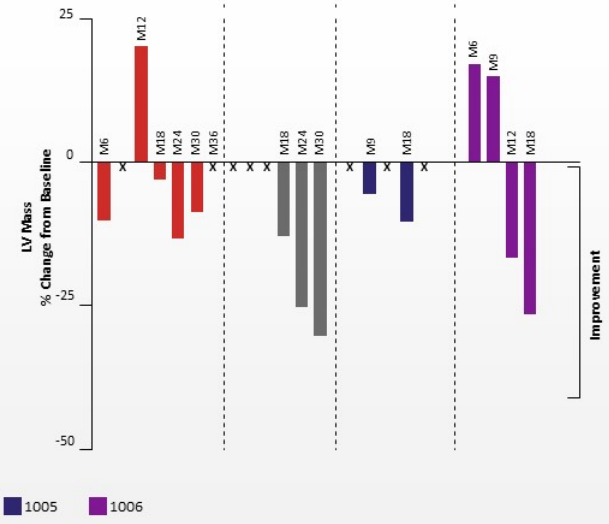
M, month; X, data not assessed

# Sustained Improvement or Stabilization of LV Hypertrophy Following RP-A501

## LV Posterior Wall Thickness




## LV Mass




1001 1002 1005 1006



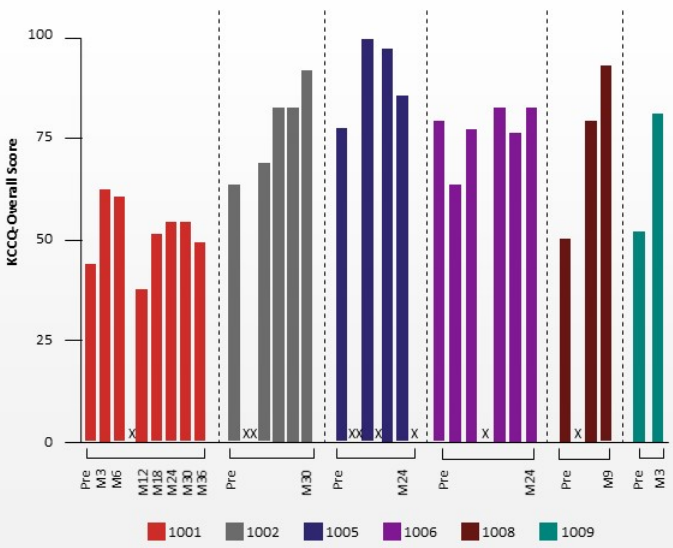
LV, left ventricle; LVPWd, LV posterior wall end diastole; M, month; X, data not assessed
LV hypertrophy is assessed via LV posterior wall at end diastole (LVPWd) and LV mass.

# Sustained Improvement or Stabilization of Functional Cardiac Status Following RP-A501

## New York Heart Association Class

| Cohort | Patient ID | Baseline | Month 12 | Most Recent Follow-up | Time of Most Recent Follow-up |
|---|---|---|---|---|---|
| Low Dose Adult | 1001[a] | II | II | II | 36 months |
| | 1002 | II | III | I | 30 months |
| | 1005 | II | II | I | 30 months |
| High Dose Adult | 1006 | II | I | I | 24 months |
| Low Dose Pediatric | 1008 | II | October 2022 | I | 9 months |
| | 1009 | II | March 2023 | I | 6 months |

## Kansas City Cardiomyopathy Questionnaire Overall Score

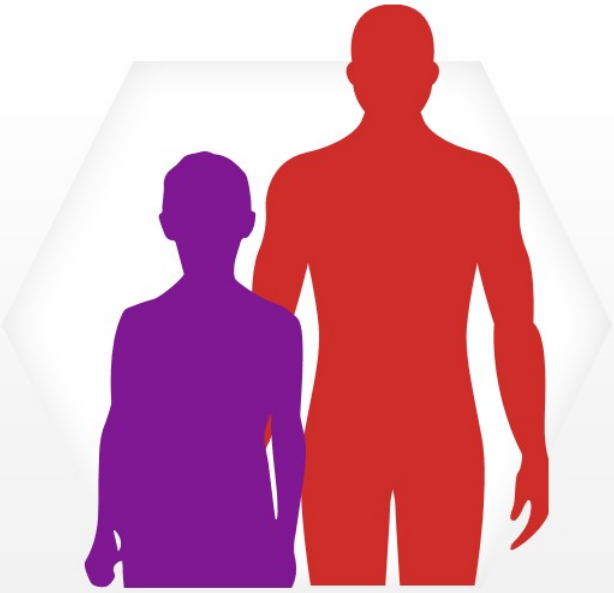



M, month; X, data not assessed.
[a] Corticosteroid compliance uncertain

# Summary of Results

## PEDIATRIC COHORT

- RP-A501 was well tolerated
- No immediate, early or delayed RP-A501 related SAEs observed to date with enhanced immunomodulation
  - Minimal complement activation
  - Platelets remained within normal range
- Absent or limited worsening of skeletal myopathy with reduced steroid dose and more rapid taper, and introduction of sirolimus
- Increased LAMP2B protein expression was associated with early signals of improved cardiac histology, as well as serological evidence of decreased myocardial injury and stress
- Early improvement in NYHA class and KCCQ for both patients



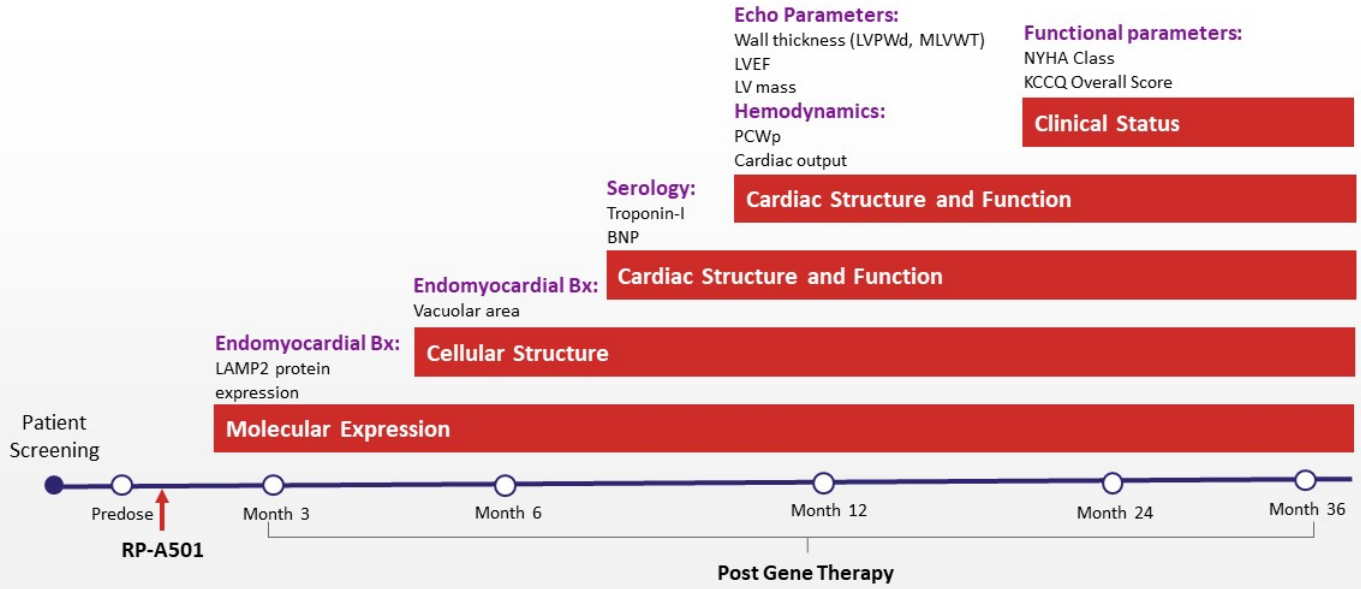
## ADULT COHORT

- Low-dose continues to be generally well tolerated at 2-3 years post-treatment
- Increased LAMP2B protein expression was associated with durable disease improvement or stabilization including clinical status (NYHA class, KCCQ), LV hypertrophy (LV wall thickness and mass), biomarkers of myocardial injury and stress (hsTroponin I and BNP), and cardiac histology
- All patients are alive in their early 20s, whereas median survival in DD males is 19 years old*



BNP, brain natriuretic peptide; hs, high sensitivity; KCCQ, Kansas City cardiomyopathy questionnaire; LAMP2B, lysosome-associated membrane protein 2B; LV, left ventricle; NYHA, New York Heart Association; SAE, serious adverse event.
*Except for patient 1007 who received a heart transplant at 5 months due to Danon Disease progression. He is currently stable. Brambatti M et al. *Int J Cardiol*. 2019;286:92-98
Data cut-off September 27, 2022 with source data, verification through July 11, 2022.

# Connecting Surrogate Endpoints to Functional Outcomes for Pivotal Study*






BNP, brain natriuretic peptide; Bx, biopsy; KCCQ, Kansas City cardiomyopathy questionnaire; LAMP2, lysosome-associated membrane protein 2; LV, left ventricle; LVEF, LV ejection fraction; LVPWd, LV posterior wall end diastole; MLVWT, maximal LV wall thickness; NYHA, New York Heart Association; PCWp, pulmonary capillary wedge pressure.
*Pending regulatory feedback

# Summary of Results

Phase 1 enrollment and treatment are **complete**

- ✓ The enhanced immunomodulatory regimen **was generally well tolerated and has mitigated adverse events** in the pediatric cohort, who are currently 6 and 11 months post treatment
- ✓ The **early LAMP2 expression data from the pediatric cohort are encouraging and consistent** with that seen in the adult patients at the same timepoints
- ✓ The **early clinical trends for the pediatric cohort are encouraging and consistent** with the **sustained clinical responses seen in the adults at 24-36 months**
- ✓ **Study design and endpoints have been identified** for the planned Phase 2 pivotal study* and **endorsed by an International Scientific and Clinical Advisory Board**; FDA discussion planned at the end of this year



*Pending regulatory feedback

# Development Plan

## Moving toward pivotal Phase 2 study

**CURRENT**

- Phase 1 treatment completed in males
- Orphan Drug, Rare Pediatric and Fast Track designations in the US (eligible for PRV, if approved)
- Initiated in-house manufacturing to support Phase 2 product

**PLANNED**

- Expanded natural history study
- End of Phase 1 regulatory meeting with FDA
- Initiate Phase 2 global pivotal study activities
- Initiate female study

**PLANNED GLOBAL REGISTRATIONAL PHASE 2 STUDY**



FDA, Food and Drug Administration; H2, second half of the year; PRV, priority review voucher.
Data on file. Rocket Pharmaceuticals. 2022.