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SEEKING GENE THERAPY CURES

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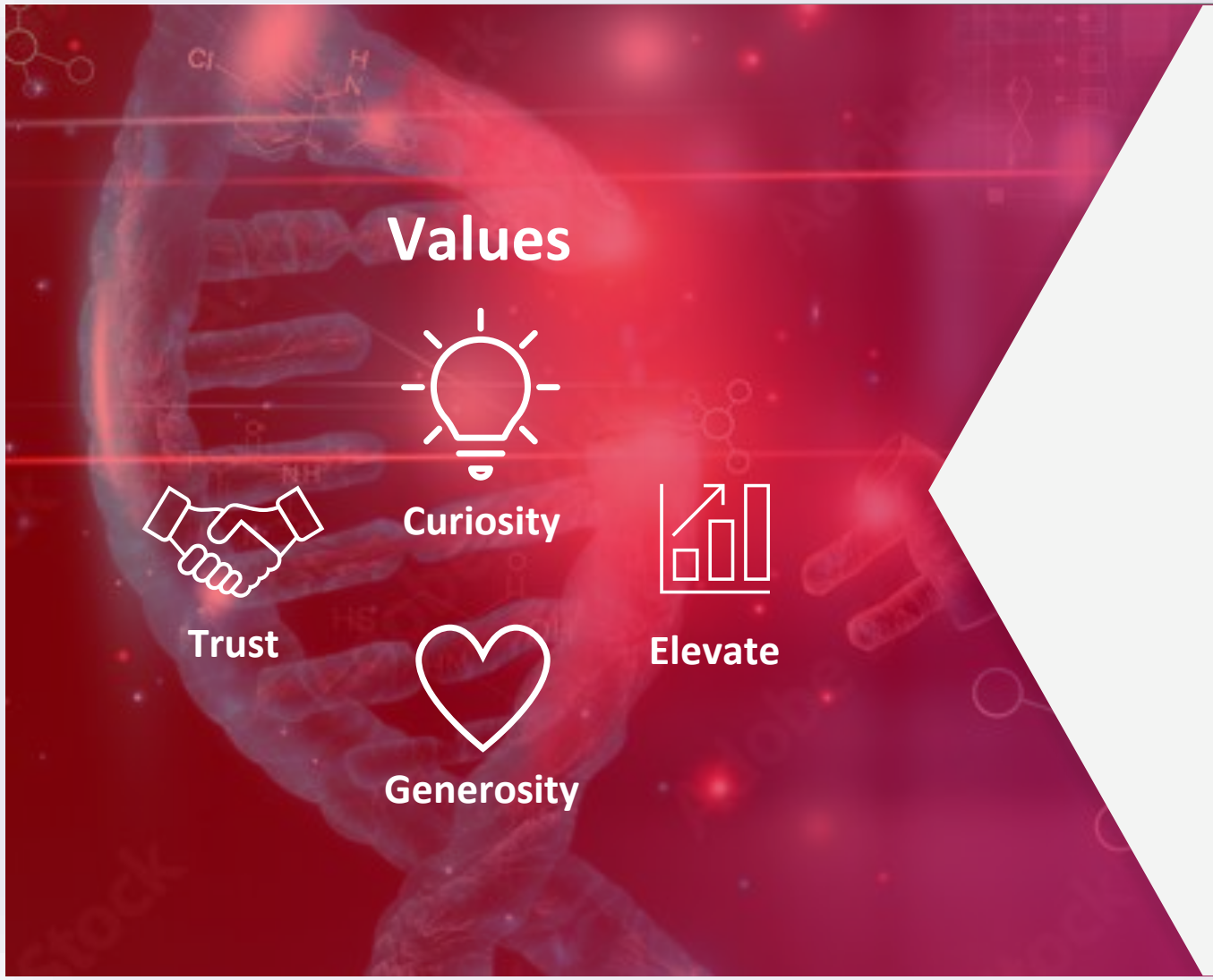
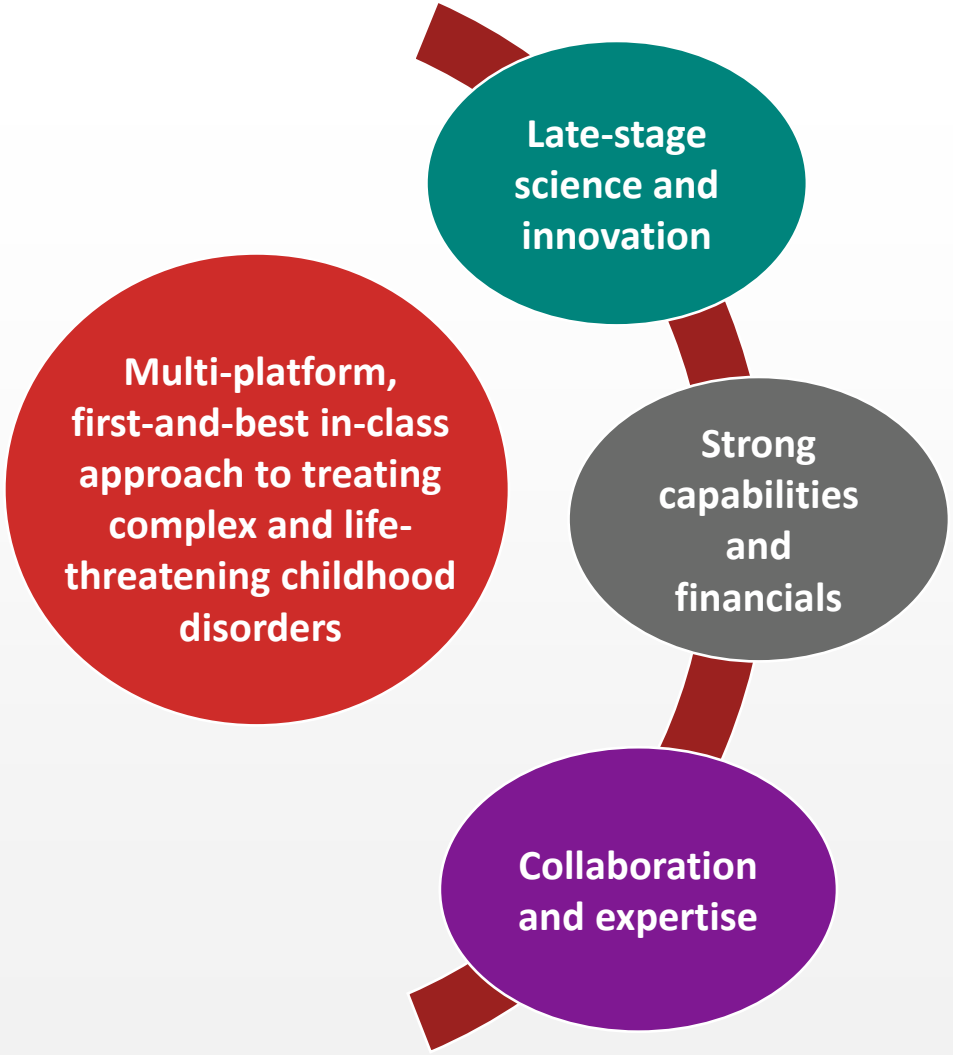
# **Vision:** Seeking Gene Therapy Cures




## Mission

To develop **first-in-class** and **best-in-class curative gene therapies** for patients with devastating diseases

# A Fully Integrated Commercial Stage Gene Therapy Company




**Promising top-line clinical data** designed to facilitate **US and European registration and launch** with potential for expansion into Asian markets and beyond

**Therapeutic area focus:**
**Heart and bone marrow**
Only company with safety and efficacy data for gene therapy targeting the **heart**

**~100,000 sq ft**
US-based in-house facility dedicated to AAV cGMP manufacturing

Well capitalized to develop full pipeline of assets with approximately
**$437M[1]**
in cash and cash equivalents; **sufficient to fund operations into 2026**

Leadership team with proven track record of
**20+**
US and ex-US drug approvals and launches

**World-class scientific experts, commercial acumen** and partners learning from and closely collaborating with **patient communities, HCPs and Payors**



[1]Cash balance as of November 6, 2023.

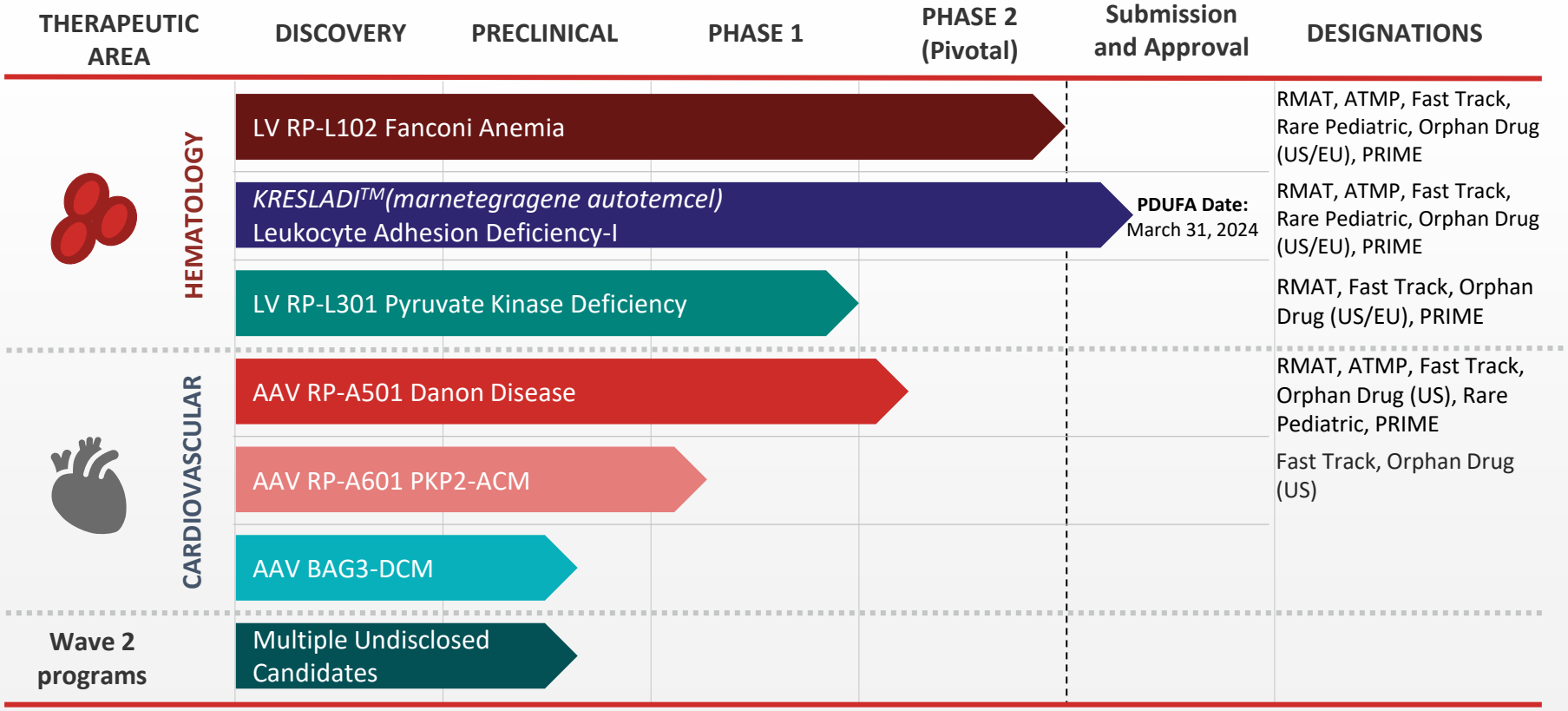
# Strong Science, Carefully-selected Assets and Smart Execution

## 6 Disclosed programs with compelling clinical evidence and significant commercial potential

### Criteria used to select programs

- First-, best- and/or only-in-class
- On-target MOA; clear endpoints
- Sizeable market to maximize patient impact

### 6+ programs with 2 programs fast approaching regulatory filing and launch




AAV, adeno-associated virus; ATMP, advanced therapy medicinal product; BLA, Biologics License Application; LV, lentiviral vector; MAA, Marketing Authorisation Application; MOA, mechanism of action; PRIME, Priority Medicines; RMAT, regenerative medicine advanced therapy. PKP2: plakophilin 2; ACM: Arrhythmogenic Cardiomyopathy; BAG3: BLC2-associated athanogene 3 DCM: Dilated Cardiomyopathy
Data on file. Rocket Pharmaceuticals. 2023.

# Rocket Offers **Multi-platform Gene Therapy Expertise**

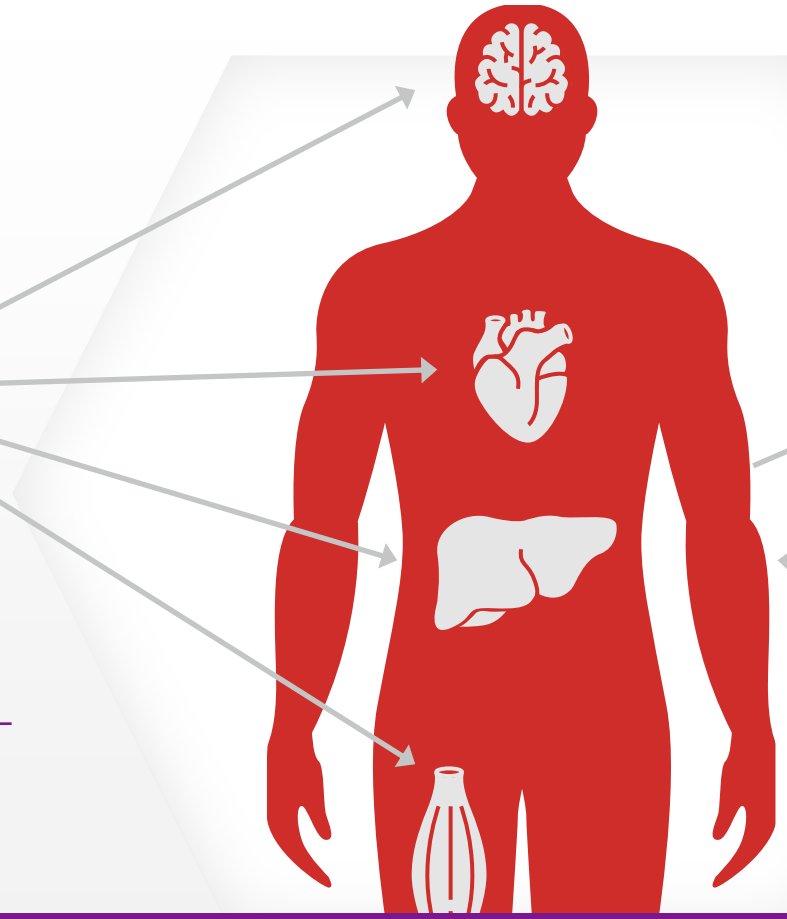
## IN VIVO platform

Laboratory-produced AAV

Therapeutic AAV

Direct intravenous injection

**RP-A501**: Danon Disease
**RP-A601:** PKP2-ACM
**AAV** BAG3-DCM



## EX VIVO platform

Remove cells and isolate patient HSCs

Laboratory-produced LV

Therapeutic LV

Infusion of modified HSCs

Gene-modified HSCs

**RP-L102**: Fanconi Anemia
**RP-L201**: Leukocyte Adhesion Deficiency-I
**RP-L301**: Pyruvate Kinase Deficiency

***All Rocket therapies transfer full (non-truncated) coding sequence to target tissue***

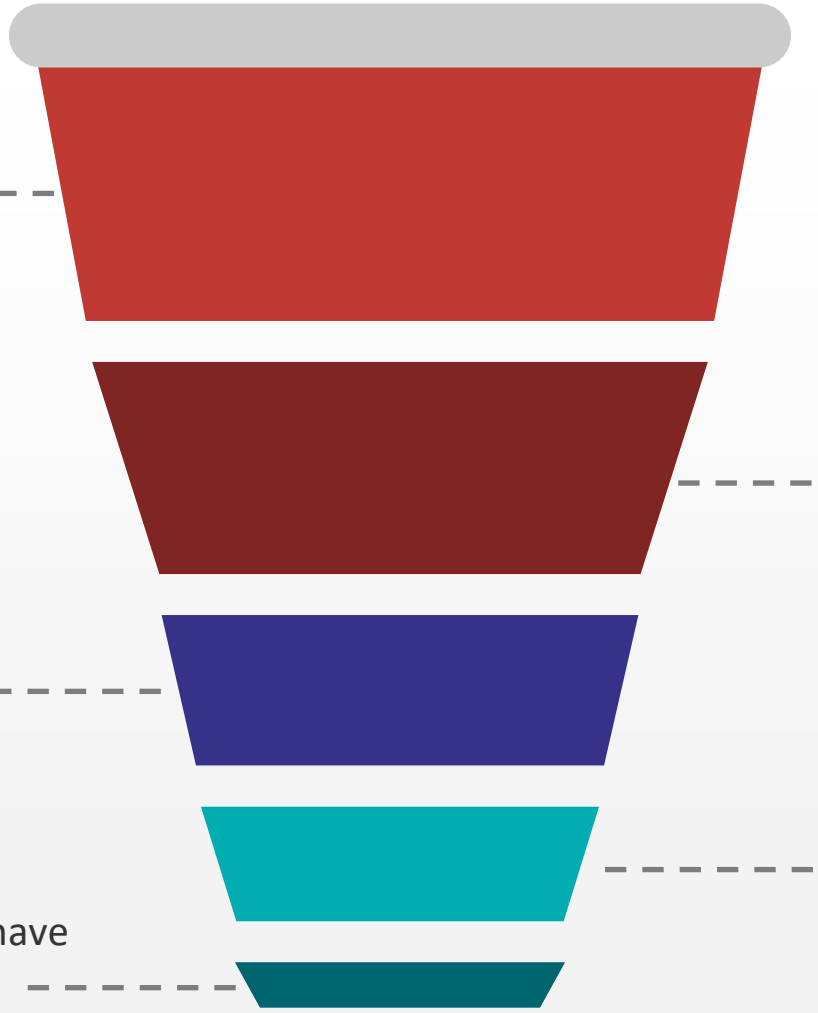


AAV, adeno-associated virus; HSC, hematopoietic stem cell; LV, lentiviral vector.
Data on file. Rocket Pharmaceuticals. 2023

# **Rare Diseases** Are Associated With a Reduced Lifespan[1]

**400 million**
**people globally are affected by a rare disease[1]**

Children account for **50%** **of rare disease patients[1]**



**80%** **of rare diseases** have monogenic origins[1]

**3 of 10 children** with a rare disease die before their fifth birthday[1]

**Only about 5%** **of rare diseases** have an FDA-approved drug treatment[1]

FDA, Food and Drug Administration.
1. Global Genes. Accessed April 2022. https://globalgenes.org/rare-disease-facts/



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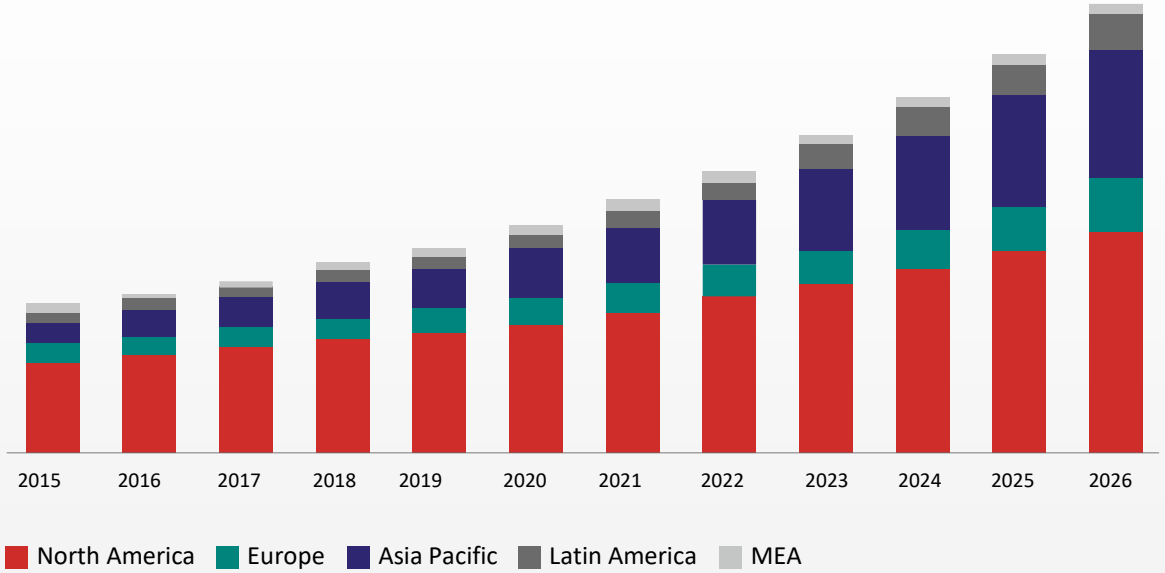
# Market for Rare Disease Treatment Is **Rising**

## Rare disease treatment market by region, 2015-2026 (USD million)[1]




## Rare disease treatment market by drug type, 2019 (USD million)[1]


- Rare disease treatment market is projected to grow from **$161.4 billion in 2020** to **$547.5 billion by 2030**[2]
- CAGR of 13.1% projected by 2030[2]

Orphan drug approvals have increased

**4-fold**[3]

CAGR, compound annual growth rate; CDER, Center for Drug Evaluation and Research; MEA, Middle East and Africa.

**1.** Global Market Insights. Accessed April 2022. https://www.gminsights.com/industry-analysis/rare-disease-treatment-market **2.** Global News Wire. Accessed August 2022. https://www.globenewswire.com/en/news-release/2021/02/24/2181634/0/en/Global-Rare-Disease-Market-is-estimated-to-be-US-547-5-billion-by-2030-with-a-CAGR-of-13-1-during-the-forecast-period-by-PMI.html
**3.** AHIP. Accessed April 2022. https://www.ahip.org/how-big-pharma-makes-big-profits-on-orphan-drugs (increase from 1998 to 2017)

# **Costs** Associated With Rare Diseases Have Increased Exponentially[1]

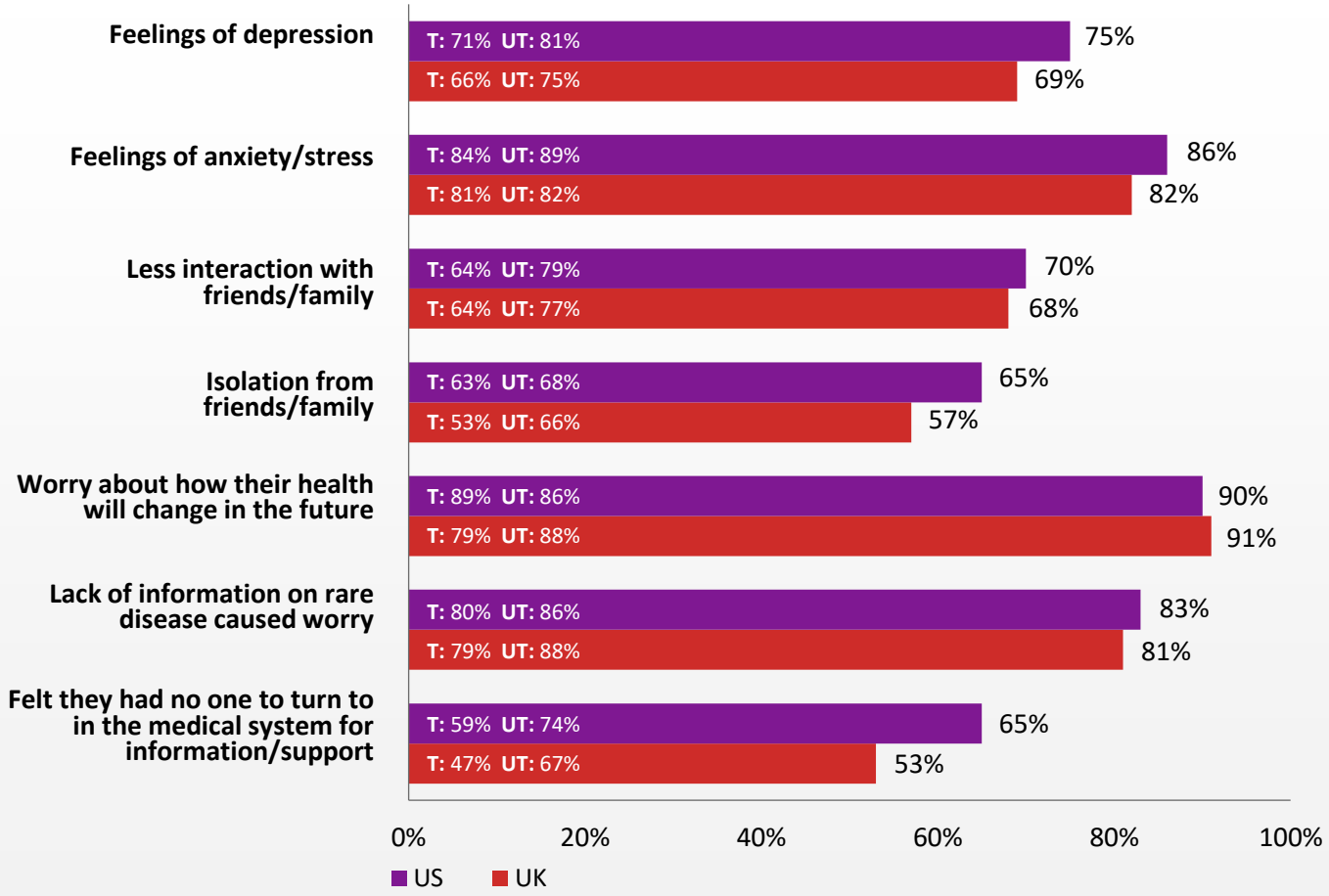
## Economic impact[1]

**26-fold** increase in average per-patient annual cost for orphan drugs* compared to doubled costs for specialty and traditional drugs[1]

**Patients with rare diseases** or their **caregivers** are **often compelled to leave the workforce**[2]

Cost of **bone marrow** and **heart transplants & maintenance** is high

## Emotional impact[4]




*An orphan drug is a pharmaceutical agent developed to treat medical conditions, which, because they are so rare, would not be profitable to produce without government assistance.
T, treatable; UT, untreatable.

**1.** AHIP. Accessed April 2022. https://www.ahip.org/news/press-releases/drug-prices-for-rare-diseases-skyrocket-while-big-pharma-makes-record-profits (increase from 1998 to 2017)
**2.** Every Life Foundation for Rare Diseases. Accessed April 2022. https://everylifefoundation.org/wpcontent/uploads/2021/02/The_National_Economic_Burden_of_Rare_Disease_Study_Summary_Report_February_2021.pdf
**3.** Data on file. Rocket Pharmaceuticals. 2022. **4.** Global Genes. Accessed April 2022. https://globalgenes.org/wp-content/uploads/2013/04/ShireReport-1.pdf



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

**Market Opportunity – 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 *LAMP2*

## 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, Jirikowic J, Taylor M. Natural history of Danon disease. Genet Med. 2011;13(6):563-568.
Brambatti M, Caspi O, Maolo A, et al. Danon disease: Gender differences in presentation and outcomes. Int J Cardiol. 2019;286:92-98.

# **Phase 1 Data:** Benefit Observed Across All Key Clinical Parameters

## Early LAMP2, BNP, TnI changes associated with sustained clinical improvement and guided Phase 2 endpoint selection

| Cohort | Patient ID | Follow-up (months) | Myocardial LAMP2 Grade (≤M12) | TnI Δ (≤M12) | BNP Δ (≤M12) | LV mass Δ (g) | LV Mass Index Δ (g/m^2.7) | Max LV Wall Thickness Δ (mm) | NYHA class Δ | KCCQ score Δ |
|---|---|---|---|---|---|---|---|---|---|---|
| Low dose adult/ adolescent | 1001 (17.4 aai) | 36 | 1 | -75% (M18) | -36% | 311 ⇢ 212 | 85 ⇢ 57 | 25 ⇢ 23 | II ⇢ II | 44 ⇢ 49 |
| | 1002 (20.3 aai) | 36 | 3 | -79% | -76% | 989 ⇢ 511 | 260 ⇢ 129 | 64 ⇢ 38 | II ⇢ II | 64 ⇢ 81 |
| | 1005 (18.3 aai) | 30 | 2 (M9) | -57% (M9) | -64% (M9) | 438 ⇢ 375 | 98 ⇢ 76 | 33 ⇢ 24 | II ⇢ I | 77 ⇢ 85 (M24) |
| High dose adult/ adolescent | 1006 (21.1 aai) | 24 | 1 | -47% | -70% | 410 ⇢ 300 | 90 ⇢ 63 | 22 ⇢ 18 | II ⇢ I | 79 ⇢ 82 |
| Low dose pediatric | 1008 (12.3 aai) | 12 | 1 | -86% | -83% | 605 ⇢ 447 | 140 ⇢ 96 | 42 ⇢ 39 | II ⇢ I | 50 ⇢ 82 |
| | 1009 (11.7 aai) | 6 | 1 | -90% | -62% | 234 ⇢ 185 | 83 ⇢ 63 | 20 ⇢ 20 | II ⇢ I | 52 ⇢ 78 |

***All specified parameters either improved or stabilized (none deteriorated)***

Improved Stabilized Worsened



Does not include pt 1007 in Ph1 trial who had advanced HF with EF<40% at enrollment and received HTx 5M following tx due to pre-existing advanced HF. Patient is currently stable.
aai, age at infusion, BNP, brain natriuretic peptide; hsTnI, high-sensitivity troponin I; KCCQ, Kansas City Cardiomyopathy Questionnaire; LAMP2, lysosome-associated membrane protein 2; LV, left ventricle; NYHA, New York Heart Association. Data cut-off Oct 6, 2022; Grade 0=negative staining; Grade 1 ≤25%; Grade 2 =26%-50%; Grade 3 =51%-75%; Grade 4 >75%. Low dose = 6.7x1013 GC/kg, high dose = 1.1x1014 GC/kg

# Latest Phase 1 Pediatric Data Shows Sustained Improvements in Biomarkers, Symptoms, and Function

## Subject ID: A501-008-1008

**Baseline Characteristics**

**AGE AT INFUSION**
12.3 years
**ICD** yes[1]
**WPW** yes

**MAX LV WALL THICKNESS**
41.9 mm, z-score +32
**6MWT**
438 meters

18 months

| Variable | Baseline[2] | Most Recent Follow-up |
|---|---|---|
| LAMP2 protein[3] | 0 | 1 (M12) |
| Troponin-I (ng/mL) | 1.89 | 0.30 (-84%) |
| BNP (pg/mL) | 1837 | 328 (-82%) |
| NYHA Class | II | I |
| LV Mass Index | 140 | 96 (-31%)[4] |

## Subject ID: A501-008-1009

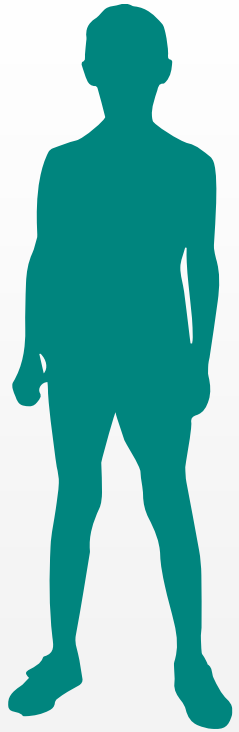
**Baseline Characteristics**

**AGE AT INFUSION**
11.7 years
**ICD** no
**WPW** no

**MAX LV WALL THICKNESS**
19.8 mm, z-score +12
**6MWT**
553 meters

12 months

| Variable | Baseline[2] | Most Recent Follow-up |
|---|---|---|
| LAMP2 protein[3] | 0 | 1 (M6) |
| Troponin-I (ng/mL) | 0.67 | 0.08 (-88%) |
| BNP (pg/mL) | 297 | 163 (-45%) |
| NYHA Class | II | I |
| LV Mass Index | 83 | 60 (-28%)[4] |



[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] Extent of LAMP2 expression grading: Grade 0 = negative staining, Grade 1 < 25%, Grade 2 = 26-50%, Grade 3 = 51-75%, Grade 4 > 75%. [4]M12 Note: All data preliminary, not yet validated.
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.



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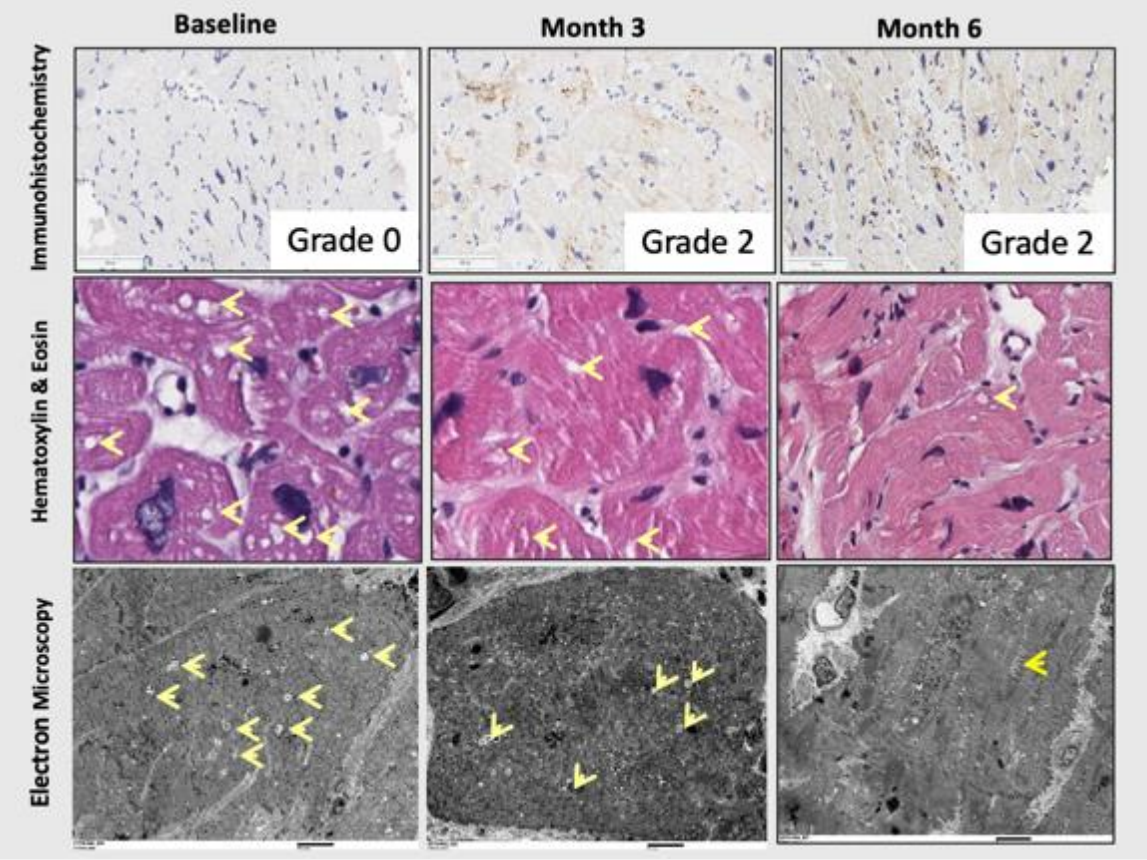
# RP-A501 Increases LAMP2 Protein and Decreases Vacuolization

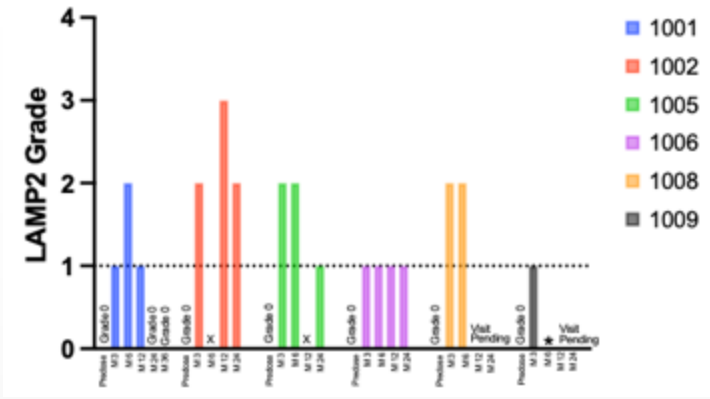
*Enhanced autophagy leads to improved myocardial ultrastructure and clinical phenotype*

## Endomyocardial Biopsy Images

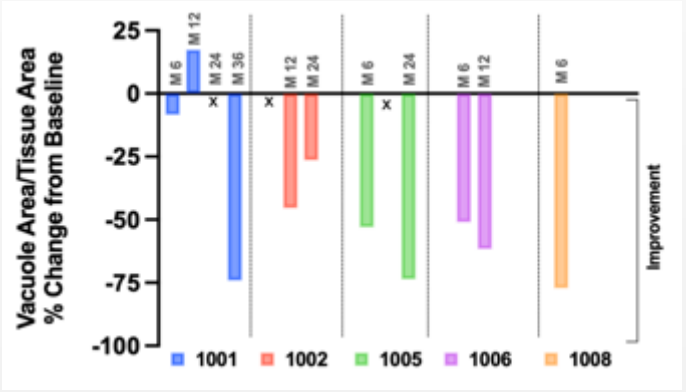
**(Subject 1008, RP-A501 Phase 1 Study)**




## Myocardial LAMP2 Protein Expression




## Vacuolar Area of Endomyocardial Tissue






Rocket AHA 2022 Poster Presentation reflects September 27, 2022 data cutoff. LAMP2, lysosome associated membrane protein 2; M, month. IHC = immunohistochemistry
Grade 0 = negative staining, Grade 1 = ≤25%, Grade 2 = 26%-50%, Grade 3 = 51%-75%, Grade 4 = >75%

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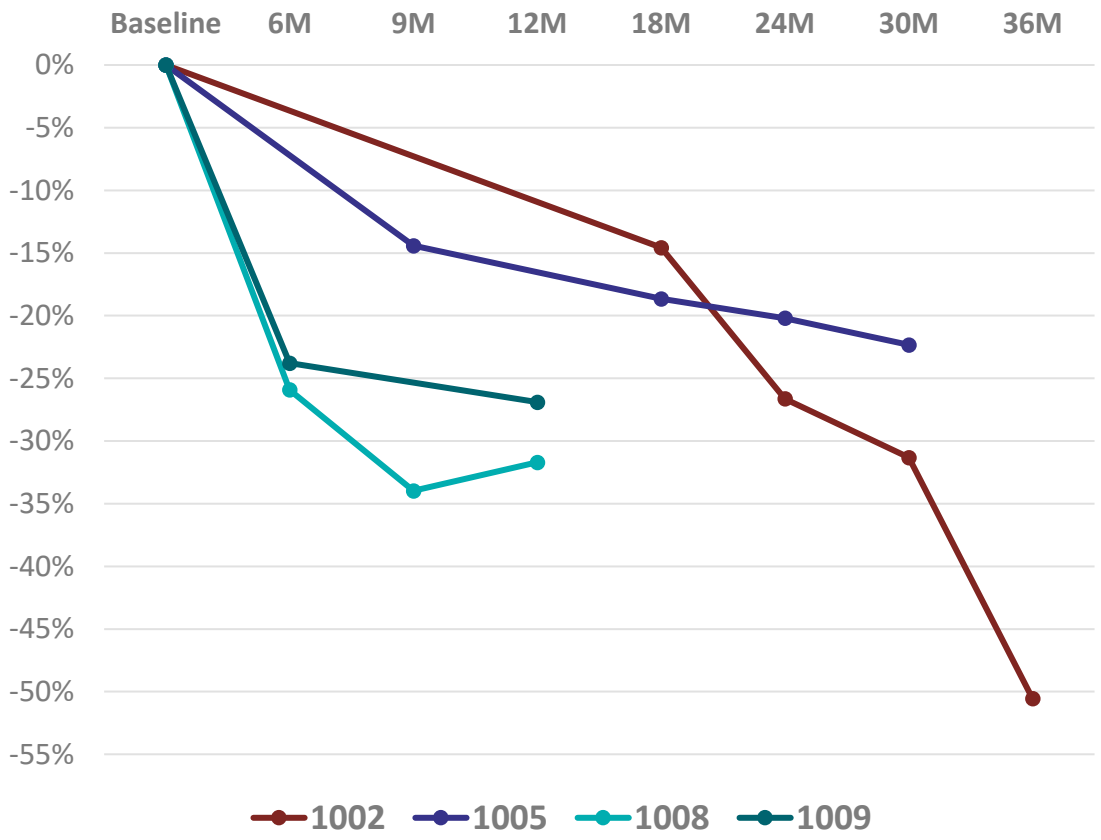
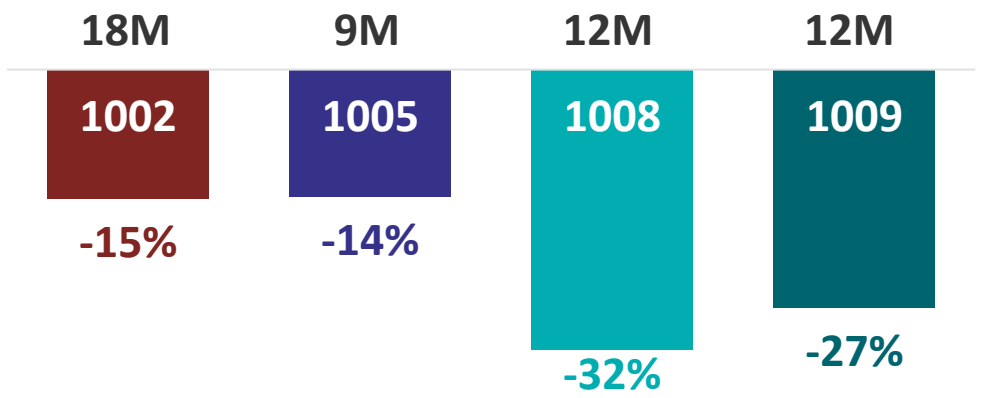
# LV Mass Index in RP-A501 Phase 1 Study

## RP-A501 Phase 1 Low-Dose Cohort: LV Mass Index % Change from Baseline[1]




## RP-A501 Phase 1 Study: LV Mass Index % CFB at ~12M

(9M or 18M where 12M not available)[2]



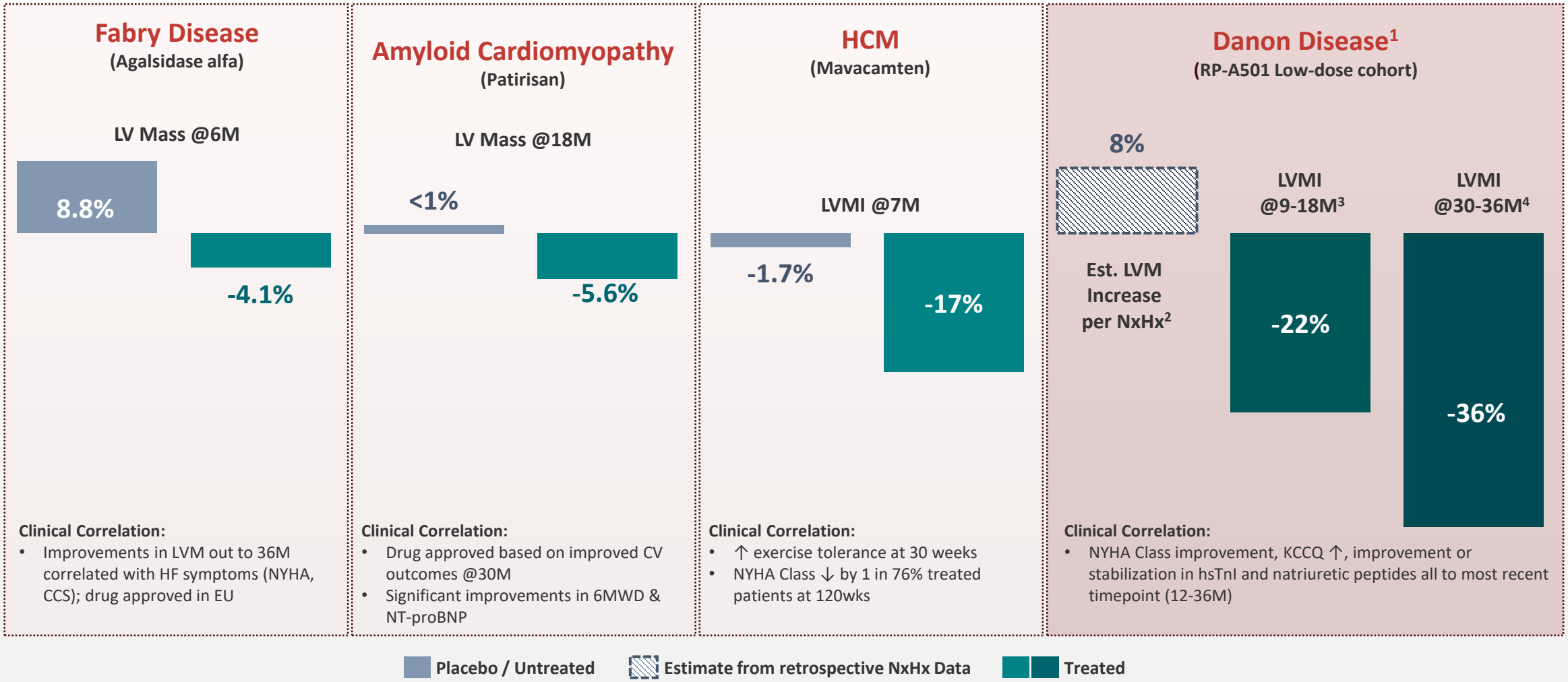

- >20% LVMI decrease observed as early as 6M in pediatric cohort, sustained to 12M timepoint
- Adult patients with appropriate immunomodulation show >10% LVMI decrease around 12M[2] with further decreases out to 30-36M of 22% to 51%



[1] Does not include patient 1001 (unmonitored immunomodulation). [2]12M visit data missing for 1002 and 1005 due to pandemic-related travel issues.

# LV Mass / LV Mass Index (LVMI) Improves in DD with RP-A501

*LV hypertrophy decreases greater than/comparable to other approved therapies*






*[1] RP-A501 Phase 1 low-dose cohort data; averages do not include 1001 (unmonitored immunomodulation) and 1006, 1007 (high dose patients). [2] Reflects estimated LV Mass increase over 12-18M for DD patients based on retrospective natural history data-set (shown on slide 20). [3] Reflects average of 1002 18M, 1005 9M, 1008 12M, 1009 12M. [4] Reflects average of 1005 30M, 1002 36M*
*Hughes 2008. Heart; Solomon 2019. Circulation; Saberi 2021. Circulation*

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# Insights from Danon Disease Patients Treated on the Phase 1 Trial

He can walk upstairs without being short of breath or having to stop half-way. He doesn't have chest pain or fast heart rates like he used to. Another amazing thing we have seen is about 4 months after his therapy trial he started working and stopped using his motorized scooter altogether. -**Pt 1005**

Prior to therapy, he was afraid of dying and wanted a chance at life……After gene therapy, we see him smile more now, he bought his own place and working a couple of days a week, he has started to open up for meeting more friends in real life and has gotten a whole new peace of mind now …he feels better, and he didn't think that would ever happen –**Pt 1006**

He went to overnight summer camp on his own for the first time and is no longer out of breath walking up stairs. **-Pt 1008**

He walked a 10K with his father following treatment. He is exercise training twice a week for an hour. -**Pt 1009**



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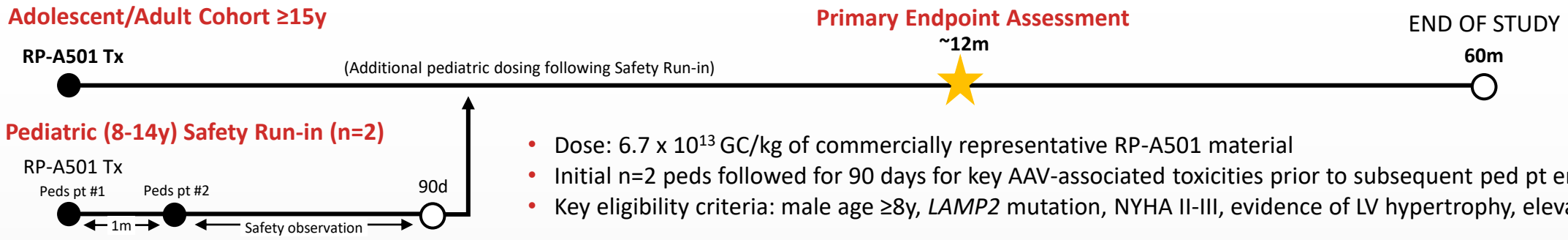
# Phase 2 Trial Design – 12 Patients with 12-month Primary Endpoint Duration

*Pivotal, global, single-arm, open label study with external comparator*

## PIVOTAL PHASE 2 STUDY DESIGN




- Dose: 6.7 x $10^{13}$ GC/kg of commercially representative RP-A501 material
- Initial n=2 peds followed for 90 days for key AAV-associated toxicities prior to subsequent ped pt enrollment
- Key eligibility criteria: male age ≥8y, *LAMP2* mutation, NYHA II-III, evidence of LV hypertrophy, elevated hsTnI

### CO-PRIMARY ENDPOINT (AA)

- LAMP2 protein ≥ Grade 1 (IHC) AND
- Left Ventricular Mass (LV Mass): ≥10% ↓

### SECONDARY & EXPLORATORY ENDPOINTS

- hs-troponin I (key secondary)
- Natriuretic peptides
- QoL instruments (KCCQ, PedsQL, PGI-C, PGI-S)
- NYHA Class
- 6MWT
- Event free survival
- Treatment emergent safety events
- Actigraphy

### RISK MANAGEMENT PLAN, TRIAL OVERSIGHT

- Immunomodulatory regimen of Rituximab, Sirolimus, corticosteroids.
- Clinical monitoring team to closely monitor labs, clinical sequelae for AAV-associated toxicities.
- IDSMC: expertise in adult and pediatric cardiomyopathy, immunology, and biostatistics

## CONCURRENT NATURAL HISTORY STUDY



Tx, treatment; LV, left ventricular; NYHA; IDSMC, Independent Data Safety and Monitoring Committee; hs-troponin I; KCCQ; HF; m, month; y, year; pts, patients

# Primary Endpoint Is Reasonably Likely to Predict Clinical Benefit

*Justification for use of LAMP2 protein expression and LV Mass*

## WT Full Length LAMP2 Protein Expression

- Mutation of *LAMP2* is root cause of Danon disease
- Epidemiologic support: even modest levels of LAMP2 confer a 2-decade survival advantage in female patients
- RP-A501 delivers full coding sequence of WT *LAMP2* gene
- Pre-clinical LAMP2 restoration conferred histologic, functional and survival benefits in LAMP2 knock-out model[1]
- Phase 1: LAMP2 expression associated with decreased vacuolar area, improved myofibrillar disarray, clinical improvement

## Left Ventricular Mass

- Largest known hearts are Danon disease hearts
- Severity of the cardiomyopathy in Danon disease is the major prognostic factor[2]
- Retrospective natural history shows year-over-year increases in LV mass in Danon disease patients
- Phase 1: Consistent and significant reductions in LV mass as early as 6 months by echocardiography and cardiac MRI

### Primary Endpoint Will Be Interpreted in a Clinical Context:

- *All components are measurable and unlikely to improve in the absence of a true treatment effect*
- *Primary endpoint will be assessed in the context of biomarkers, symptoms, QOL, clinical events derived from secondary endpoints and concurrent natural history study*
- *Phase 1 trial: LAMP2 expression and LV Mass improvements seen as early as 6 months in pediatric subjects with updated immunomodulation regimen*



[1] Manso 2020. *Sci Transl Med.;* [2] D'souza 2017. *J Community Hosp Intern Med Perspect*.

# Natural History Studies

### Prospective Natural History Study

9 Males + 1 Female

Initiated in 2019, study complete

### US Retrospective Natural History

51 Males + 67 Females

Initiated in 2006

### EU Retrospective Natural History Study

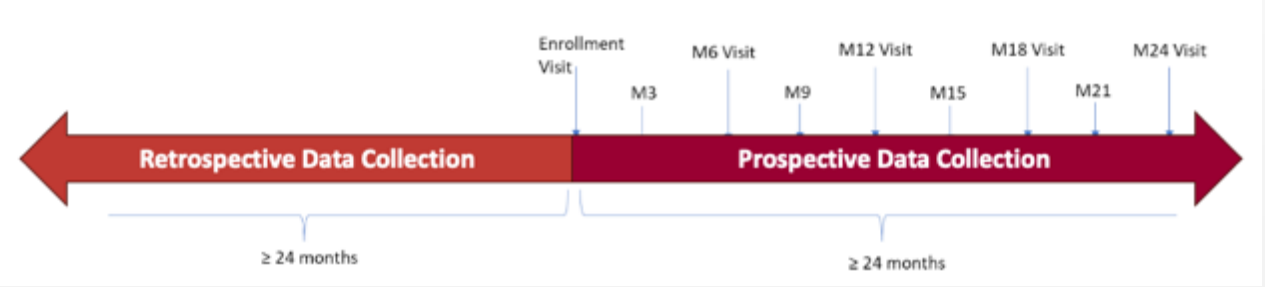
21 Males + 38 Females

Enrollment complete; analysis in Q4 2023

**To be expanded through an additional prospective Rocket-initiated natural history study**

**Key Elements of Study Design:**

- Entry criteria and endpoints similar to Phase 2 trial
- Appropriate matching to ensure robust comparisons
- Retrospective data collection to supplement prospective evaluation to ensure sufficient comparative data






HTx, heart transplant; LVEF, LVEF, left ventricle ejection fraction.

# In-House Manufacturing to Support Danon Pivotal Study and Commercial Production

- **2 Successful Danon AAV cGMP batches produced in Q4 2022**
- **Superior specifications to Phase I material**; allow for full dosing with lower total viral particles, potentially further improving safety profile
  - *Productivity:* ~3X increase in number of patient treatments per batch
  - *Product Quality:* Significant increase in full versus empty viral particles
  - *Product Comparability:* All attributes tested to date are comparable or improved
- **Regulatory progress and production capacity can support pivotal study and commercialization**
  - FDA clearance on continued utilization of HEK-293 cell-based process through commercial
  - FDA alignment on comparability approach
  - Potency assay developed in-house

***Overall, in-house cGMP manufacturing delivers commercial-ready product with higher yield, improved quality, and potential for enhanced safety profile***

# RP-L102 for Fanconi Anemia Complementation Group A (FA-A)

Fanconi Anemia (A, C, and G)

**Market Opportunity – US and EU**
Prevalence of **5,500 to 7,000** individuals
Annual incidence of **200 to 275** individuals

## Disease etiology

- **FA-A is an autosomal recessive disease caused by *FANCA* gene mutations**
- **FA proteins enable DNA repair**
- **FA-A accounts for 60% to 70% of FA cases**

## Therapeutic challenges

**Standard of care**:
- Allogeneic HSCT

**Limitations**:
- Significant toxicities, especially for patients who do not have an HLA-identical sibling donor (~80%)
- 100-day mortality
- GvHD
- Increased long-term cancer risk

## Clinical manifestations

**Disorder of DNA repair characterized by:**
- Progressive BMF; 80% of patients experience BMF within first decade of life
- Predisposition to hematologic malignancies and solid tumors

*Gene therapy approach: Selective advantage of corrected cells allows for **ex-vivo LV therapy without conditioning**; highly favorable benefit risk profile*



BMF, bone marrow failure; FA, Fanconi Anemia; FA-A, FA, group A; FANC, FA complementation group; GvHD, graft-versus-host disease; HLA, human leukocyte antigen; HSCT, hematopoietic stem cell transplantation.
Alter BP, Giri N, Savage SA, et al. Malignancies and survival patterns in the National Cancer Institute inherited bone marrow failure syndromes cohort study. Br J Haematol. 2010;150(2):179-188.

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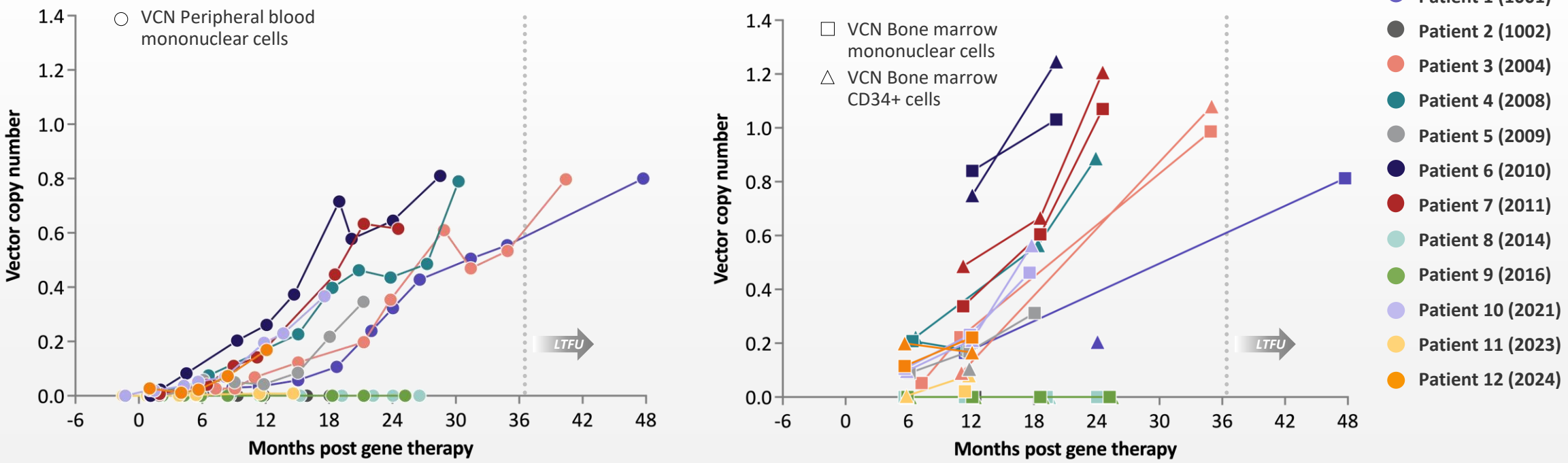
# Progressively Increasing and Sustained Genetic Correction in 8 of 12 Patients ≥1 Year Post–RP-L102 in Pivotal Phase 2 Trial

## Progressive increases in PB and BM gene marking in 8 patients






BM, bone marrow; CD34, cluster of differentiation 34; PB, peripheral blood; PBMC, PB mononuclear cells; VCN, vector copy number.
BM VCN not available at some stipulated time points due to insufficient sample to perform assay.
Data cut-off: April 17, 2023; Preliminary interim results are presented from the ongoing clinical studies.

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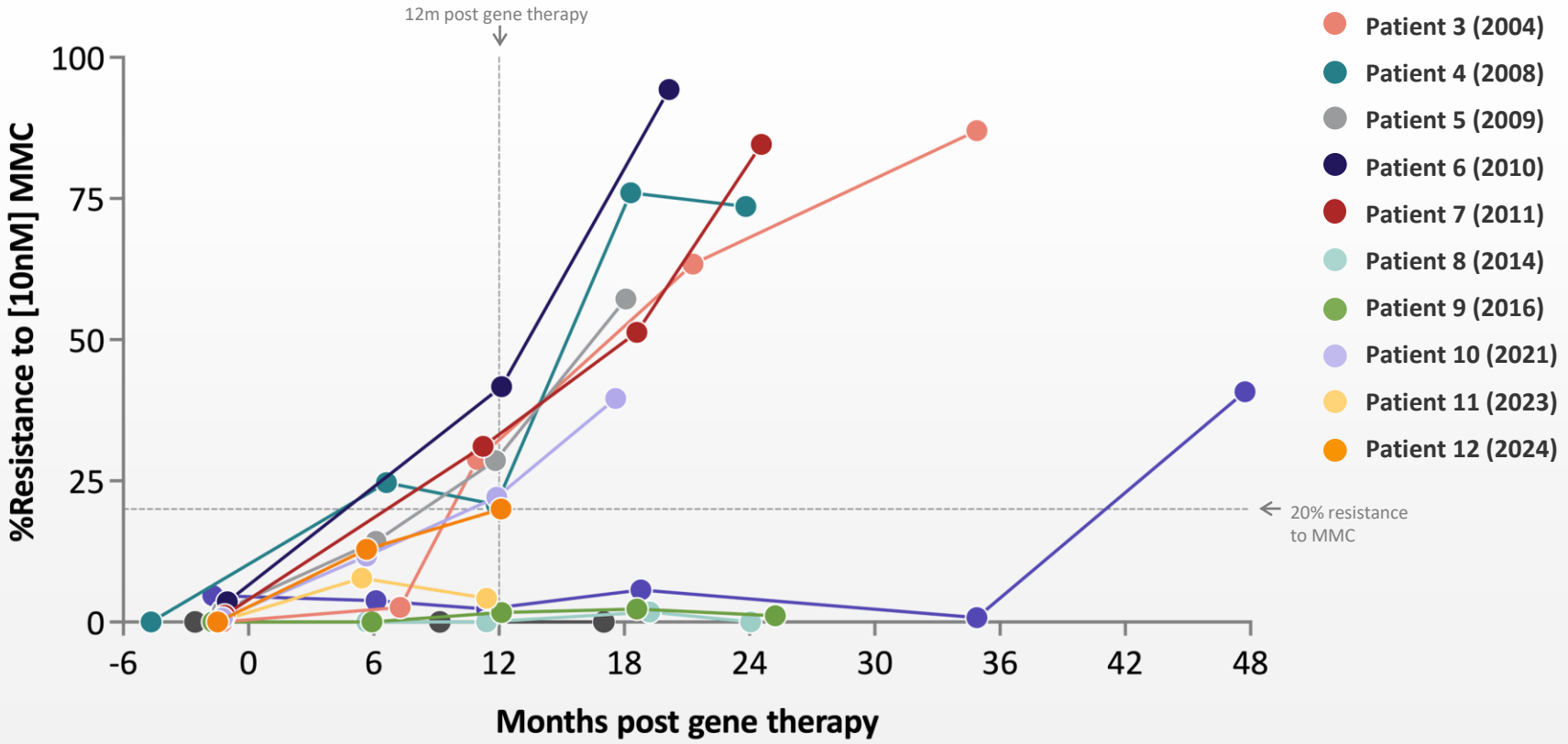
# Increasing Phenotypic Correction (MMC-resistance) over 1 to 3 Years Post RP-L102 in Pivotal Phase 2 Trial

## BM MMC-resistance ≥20% at 12m in 7 of 12 patients
## Sustained BM CFC MMC resistance confirmed in 6 patients *




**7 of 12 patients had MMC resistance of ≥20% at 12 months**

**For 6 patients, increased BM CFC MMC resistance (40% to 94%) was observed 18 to 24 months post RP-L102** *(confirmatory assessment pending for pt 2024)*



BM, bone marrow; CFC, colony-forming cells; MMC, mitomycin-C.
*One additional patient (Patient 1: 1001) was noted to have BM MMC resistance of 49% at ~40 months post–RP-L102 infusion (Unscheduled visit, not shown) and ~41% at 48 months post–RP-L102 infusion.
Data cut-off: April 17, 2023; Preliminary interim results are presented from the ongoing clinical studies.

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# Development Plan

## Moving toward BLA/MAA submission

### INITIAL EFFICACY AND HIGHLY FAVORABLE SAFETY PROFILE

- Initial comprehensive efficacy in 7/12 evaluable patients (≥12-month follow-up)
- No cytotoxic conditioning, only 1 transient RP-L102 related SAE (Grade 2)

### TOP-LINE DATA READOUT ACHIEVED

- Rejection of null hypothesis with minimum of 5 patients with increased MMC resistance >10% at 2 timepoints between 12 and 36 months

### NEXT STEPS

- **Anticipated simultaneous BLA/MAA filings in 1H 2024**

**Additional life-cycle management activities:**

- Expansion to FANC C and G
- Exploration of non-genotoxic conditioning and HSC expansion

**REGULATORY DESIGNATIONS:**

- RMAT, PRIME
- Orphan Drug designation in the US/EU
- Rare Pediatric Disease designation (eligible for PRV)
- Fast Track (US), ATMP



ATMP, advanced therapy medicinal product; BLA, Biologics License Application; CMC, chemistry, manufacturing, and controls; FANC, Fanconi Anemia complementation group; FDA, Food and Drug Administration; HSC, hematopoietic stem cell; MAA, Market Authorization Application; MMC, mitomycin-C; PRIME, PRIority MEdicines; PRV, priority review voucher; RMAT, Regenerative Medicine Advanced Therapy; SAE, severe adverse event.
Data on file. Rocket Pharmaceuticals. 2023.

# RP-L201 for LAD-I: *ITGB2* Gene Mutation

**Market Opportunity – US and EU**
Prevalence of **800 to 1,000** individuals
Annual incidence of **50 to 75** individuals

## Disease etiology

- ***ITGB2* gene mutations (21q22.3), encoding the beta-2-integrin, CD18; essential for leukocyte adhesion to endothelium**
- **CD18 absent or reduced on neutrophils**

## Therapeutic challenges

**Standard of care**:
- Allogeneic HSCT

**Limitations**:
- Donor availability
- Infections
- Frequent GvHD
- Graft failure

## Clinical manifestations

**Patients suffer from recurrent infections; fatal in majority**
- Severe LAD-I: Death prior to age 2 in 60% to 75% of patients, infrequent survival >5 years in absence of allogeneic HSCT
- Moderate LAD-I: Death prior to age 40 in >50% of patients, extensive morbidity with recurrent infections and inflammatory lesions



CD18, cluster of differentiation 18; GvHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplant; *ITGB2*, integrin subunit beta 2; LAD-I, leukocyte adhesion deficiency-I.
Almarza NE, Kasbekar S, Thrasher AJ, et al. Leukocyte adhesion deficiency-I: A comprehensive review of all published cases. J Allergy Clin Immunol Pract. 2018;6(4):1418-1420.e10.

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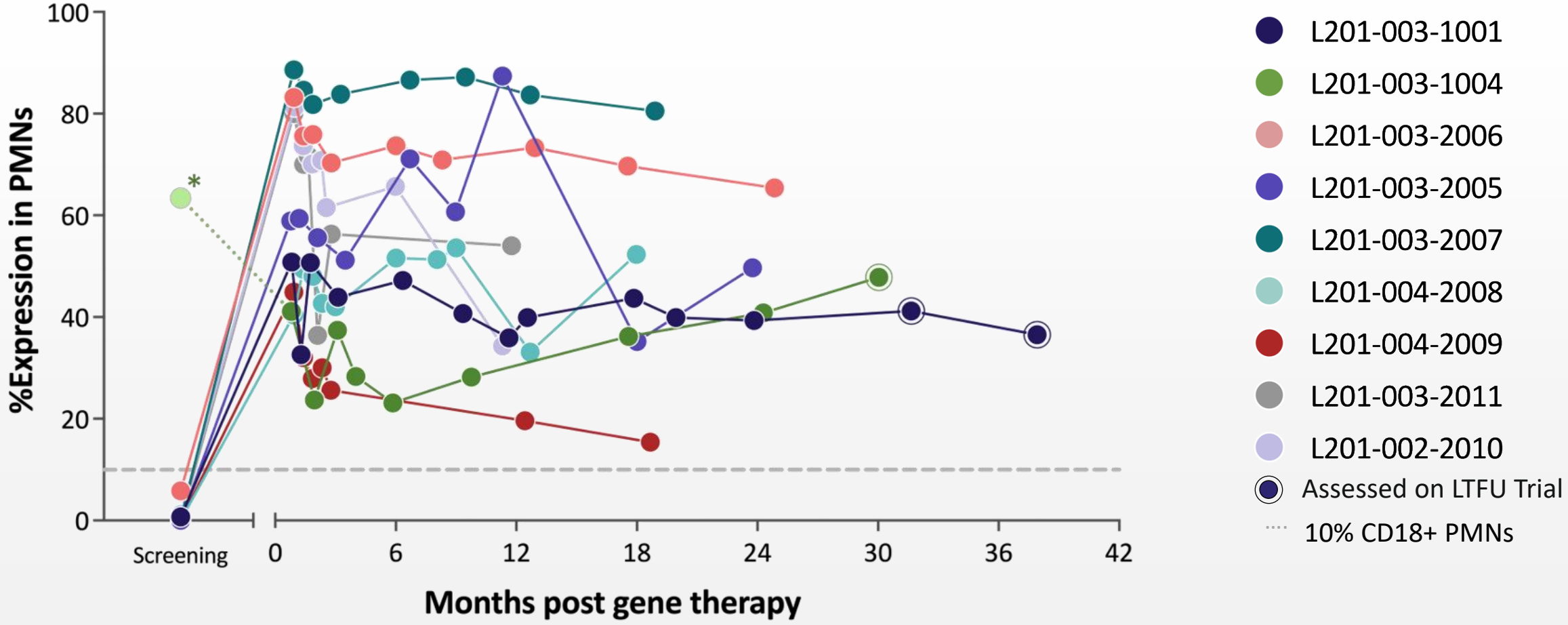
# CD18 Expression in PB Polymorphonuclear Cells (PMNs) in Pivotal Phase 1/2 Trial

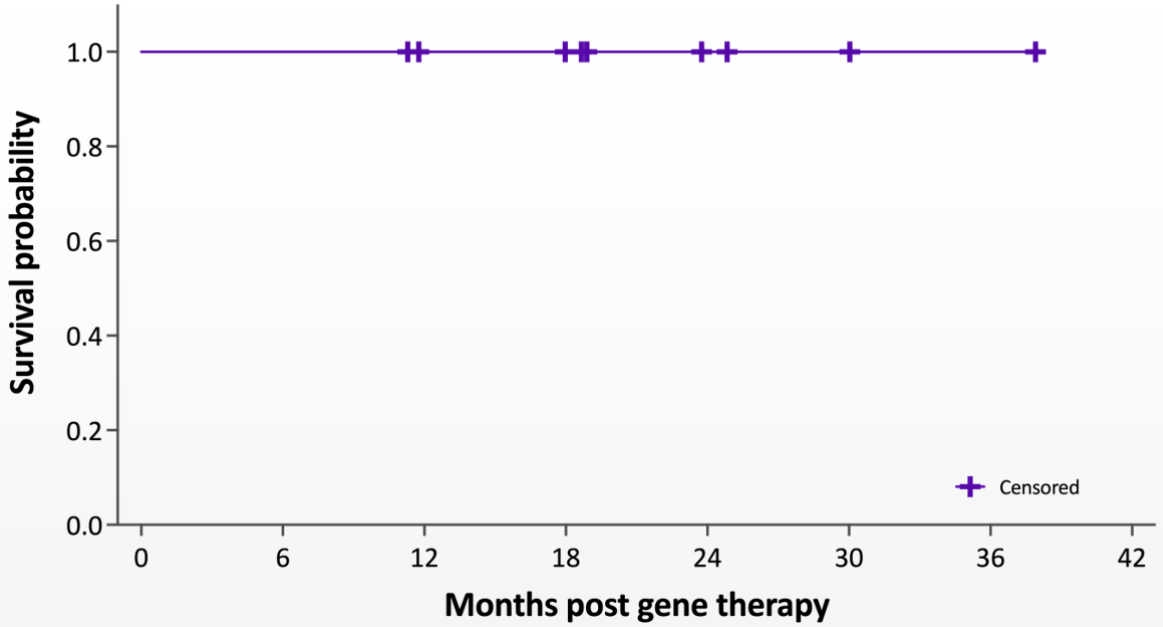
## Sustained >10% PMN CD18 expression after 1 year of gene-corrected cell infusion across the entire cohort



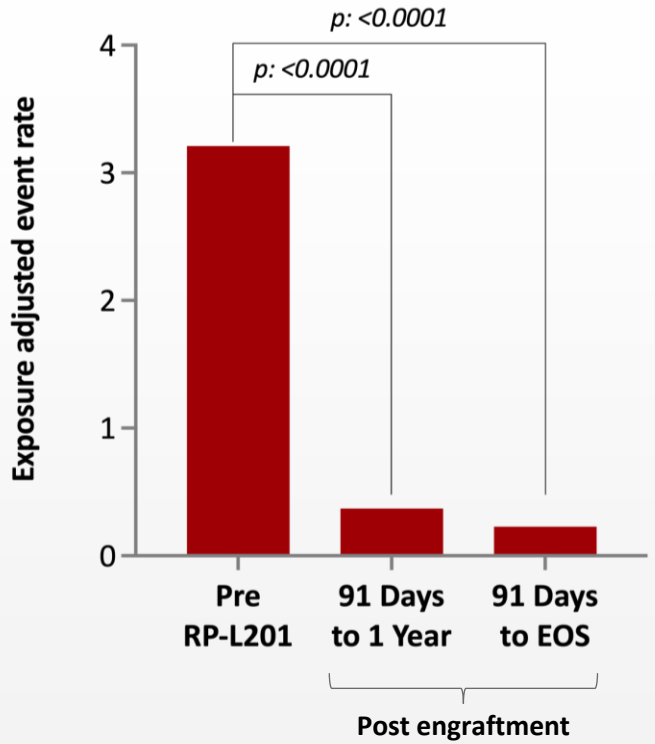

*Dim/weak CD18 expression reported at baseline for Subject L201-003-1004 in ~63% of cells in conjunction with <2% CD11a/CD11b expression, likely indicating abnormal/unstable protein.
LAD-I, Leukocyte Adhesion Deficiency-I; PB, peripheral blood; PMN, polymorphonuclear neutrophil.
Data on file. Rocket Pharmaceuticals. 2023. Data Cut-Off: November 2, 2022; Preliminary interim results are presented from the ongoing clinical study.

# Significant Reduction in Hospitalizations and 100% HSCT-free Survival in Pivotal Phase 1/2 Trial

## 100% HSCT-free survival Kaplan–Meier estimate




## Significant reduction in incidence of hospitalizations^




## Survival without allogeneic HSCT*

### Primary outcomes

- ≥1-year post–RP-L201 infusion AND
- ≥2 years of age for subjects enrolled < 1 year of age

*All patients have been able to stop prophylactic antibiotics*



EOS, end of study; HSCT, hematopoietic stem cell transplantation; LAD-I, leukocyte adhesion deficiency-I.
Data cut-off: November 2, 2022,*, March 9, 2022^
Data on file. Rocket Pharmaceuticals. 2023.

# Development Plan

## Moving toward product filing

### ENROLLMENT AND INITIAL EFFICACY

- Enrollment completed; 9/9 patients treated
- Efficacy observed in 9/9 patients with 12 to 36 months follow-up
- Efficacy is comprehensive, across all efficacy parameters including CD18 expression and survival

### TOP-LINE DATA READOUT Q2 2022

- Survival for 9/9 patients, ≥2 years age and ≥1 year post-treatment
- No graft failure, GvHD
- No RP-L201 related SAEs

### NEXT STEPS

- **PDUFA Date: March 31, 2024**

**Life-cycle management**

- Potential label expansion to include moderate LAD-I population

**REGULATORY DESIGNATIONS:**

- RMAT, PRIME
- Orphan Drug designation in the US/EU
- Rare Pediatric Disease designation (eligible for PRV)
- Fast Track (US), ATMP



ATMP, advanced therapy medicinal product; BLA, Biologics License Application; GvHD, graft-versus-host disease; LAD-I, leukocyte adhesion deficiency-I; MAA, Market Authorization Application; PRIME, Priority Medicines; PRV, priority review voucher; RMAT, Regenerative Medicine Advanced Therapy; SAE, severe adverse event.
Data cut-off: November 22, 2022.
Data on file. Rocket Pharmaceuticals. 2023.

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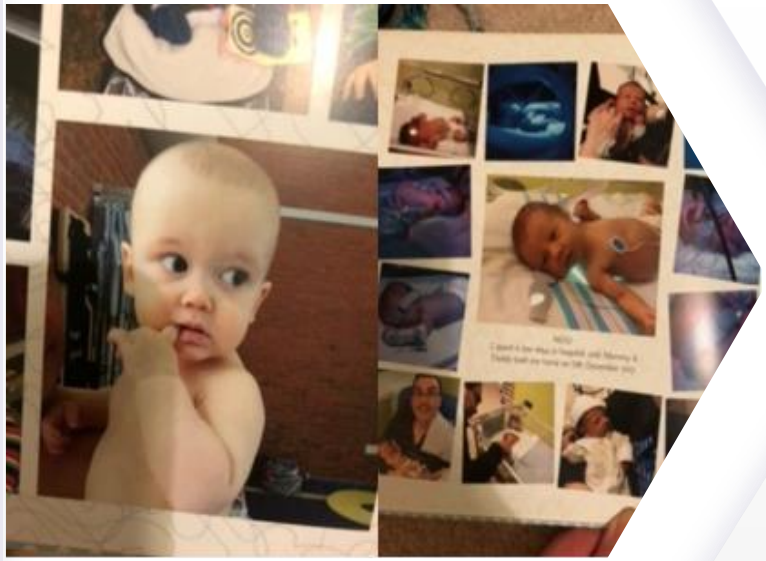
# RP-L301 for PKD: ***PKLR*** Gene Mutation



**Market Opportunity – US and EU**
Prevalence of **4,000 to 8,000** individuals
Annual incidence of **75 to 125** individuals

## Disease etiology

- Autosomal recessive inheritance
- Pyruvate kinase deficient RBCs cannot synthesize ATP, resulting in hemolytic anemia

## Therapeutic challenges

- Standard of care: Chronic blood transfusions and splenectomy
- Limitations:
  - Iron overload
  - Extensive end-organ damage
  - Splenectomy confers lifelong infection and thrombotic risk

## Clinical manifestations

- Lifelong chronic hemolysis
- Other clinical manifestations:
  - Anemia
  - Jaundice
  - Iron overload



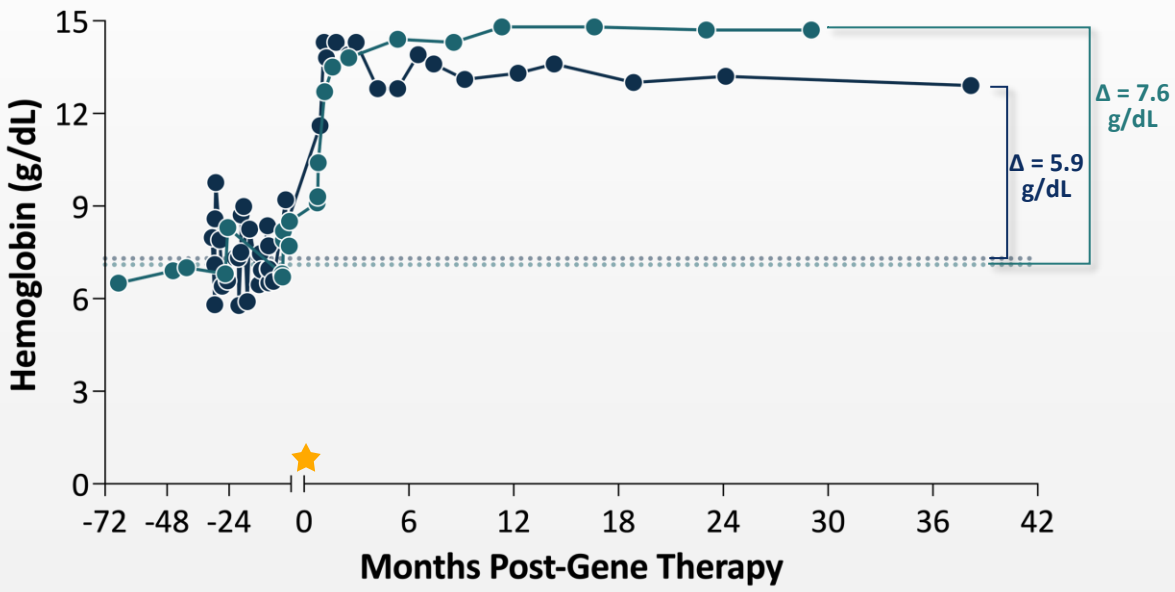
ATP, adenosine triphosphate; PKD, pyruvate kinase deficiency; PKLR, pyruvate kinase L/R; RBC, red blood cell.

Zanella A, Fermo E, Bianchi P, Valentini G. Red cell pyruvate kinase deficiency: molecular and clinical aspects. Br J Haematol. 2005;130(1):11-25.

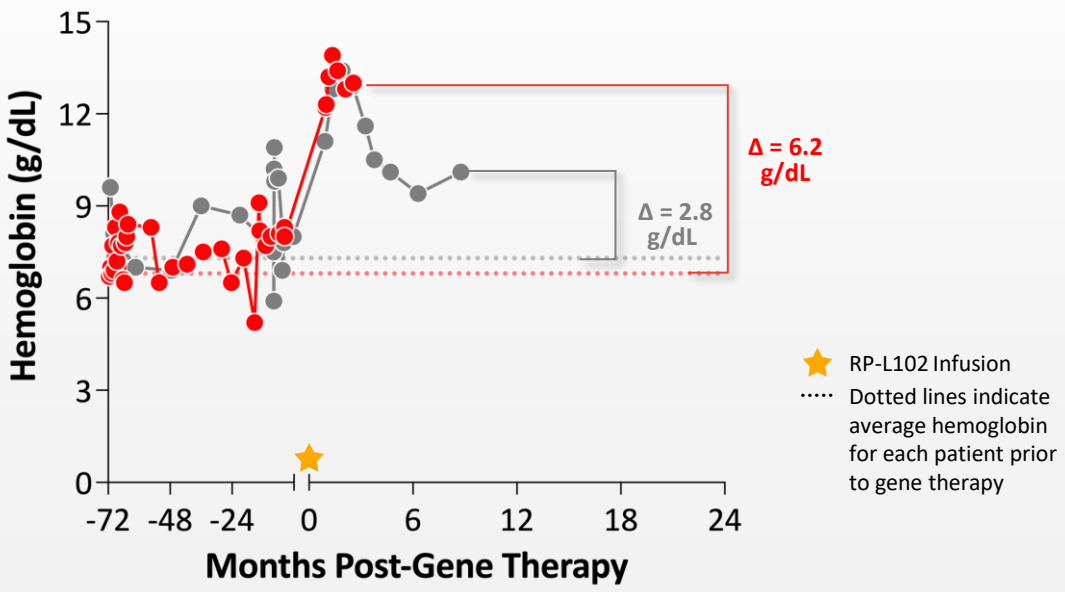
# Preliminary Phase 1 Efficacy Results: Adult and Pediatric Patients

**Sustained & meaningful hemoglobin improvements from severe (<8 g/dL) baselines**
**No RBC transfusions required following neutrophil engraftment**
**Comprehensive improvement across hemolysis markers (LDH, bilirubin); PB VCNs up to 2.0**

## ADULT COHORT




## PEDIATRIC COHORT






LDH, lactate dehydrogenase; PB, peripheral blood; VCN, vector copy number.
Data cut-off: November 28 2023; preliminary interim results are presented from the ongoing clinical study.
Data on file. Rocket Pharmaceuticals. 2023.

# Development Plan

## Alignment reached with FDA on pivotal Phase 2 study design

### PLAN FOR PHASE 2 AND LAUNCH

**High level pivotal Phase 2 Trial Design**

- Single-arm, 10 patient study
- Primary endpoint of ≥1.5-point Hgb improvement at 12 months
- Supports accelerated approval

**Well-delineated natural history in recent PKD NHS publications**

### REGULATORY DESIGNATIONS

Fast Track, RMAT, Orphan Drug (US/EU), PRIME, Rare Pediatric Disease (eligible for PRV)

### NEXT STEPS

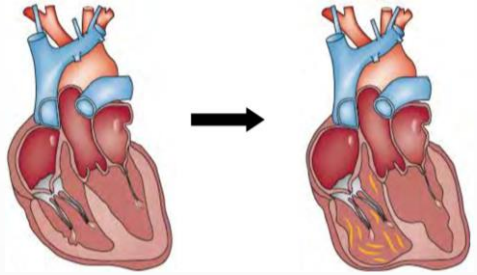
- **Initiation of Pivotal Phase 2 Study**



FDA, Food and Drug Administration; NHS, National Health Service; PKD, pyruvate kinase deficiency; RMAT, Regenerative Medicine Advanced, PRIME, Priority Medicines, PRV, priority review voucher.
Data on file. Rocket Pharmaceuticals. 2023.

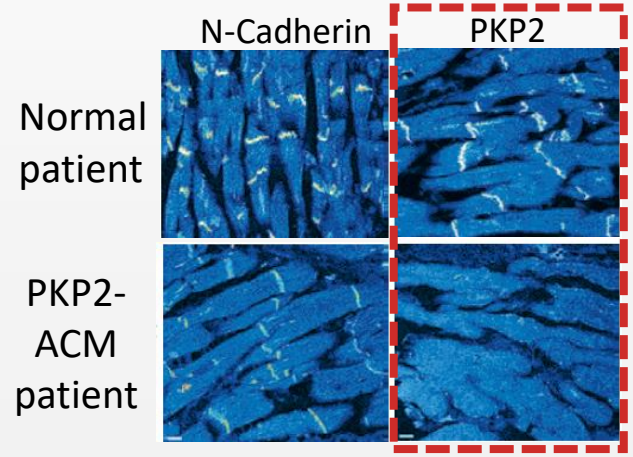
# PKP2-Arrhythmogenic Cardiomyopathy (ACM)*:
## A high-risk disease with no curative options

### Advanced ACM Heart with fibrofatty replacement in right ventricle



Electrical manifestations can precede structural abnormalities

### ACM: Diminished Myocardial PKP2




### Disease Etiology

- Autosomal dominant mutations in *PKP2* gene, which encodes for Plakophilin-2, a component of the desmosome localized to cardiac intercalated discs

### Therapeutic Challenges

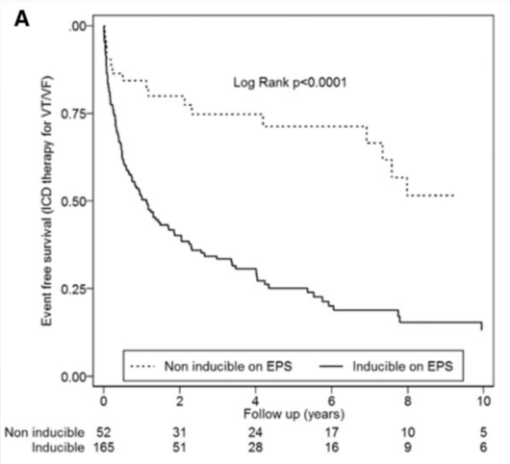
- Current standard of care includes beta-blockers, anti-arrhythmic agents, and ablation
- Available treatments do not modify disease progression; no curative therapeutic options

### Clinical Manifestations

- Mean age at presentation: 35y (±18) [1]
- 5-10% annual risk of sustained ventricular arrhythmias (VA), with higher risk in patients who present with symptoms of disease (index patients)[2-3]
- In one study, >70% risk of VAs in index patients (median follow up, 7 years) [4]
- ICD placement in >80% of index pts [5]
- For pts with ICDs:
  - 45-75% will have ICD firing (shock) over 3-5 years
  - ≥50% 2 year incidence of firing in subgroups:
    - male; • EPS-induced VT; • history of VT;
    - ≥3 ECG leads with TWI; • >1000 PVC/24h [5-6]

**Estimated Prevalence (US+EU): ~50,000**

### Kaplan-Meier Incidence of ICD Firing




**Event free survival in ACM patients who underwent EP study prior to placement of an ICD**

- *~70% of patients who were inducible on EP study had an ICD firing at 2 years*

Biopsy figure adapted from: Asimaki et al. NEJM, 2009; Table adapted from Dalal et al. Circulation 2006. SOC: standard of care; CM: cardiomyopathy; HF: heart failure: HTx: heart transplantation; RV: Right ventricular; SD: Standard Deviation; VT: ventricular tachycardia; LBBB: left bundle branch block; ICD: implantable cardioverter defibrillator; RVEF: right ventricular ejection fraction; LV: left ventricle; SVA: sustained ventricular arrhythmia.

*This cardiomyopathy initially manifests in the right ventricular free wall, so the disease was termed arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/ARVC). However, since left dominant and biventricular forms have also been observed, this has led more recently to the use of the term "ACM". 1. Bhonsale. EHJ 2015; 36: 847-55. 2. Towbin JA. Heart Rhythm 2019;16(11). 3. Cadrin-Tourigny J. Eur Heart J 2022;43. 4. Groenweg. Circ Cardiovasc Genet 2015; 8: 437-46. 5. Calkins. Circ 2017; 136: 2068-82. 6. Orgeron. J Am Heart Assoc 2017: e006242.



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# PKP2-ACM Prevalence in the US and EU

**ACM prevalence**

**1:1000 to 1:5000**

Peters 2004, McKenna 2021

**PKP2 variants**

**32.9%**

2,572 ACM patients assessed from 13 publications an aggregated mean of **32.9% had *PKP2* mutations**[1]

**ACM-PKP2 US & EU Prevalence**

**~50,000**

Utilizing the conservative ACM prevalence (1:5000) and the 32.9% PKP2 mutation frequency in ACM



Peters S, Trümmel M, Meyners W. Prevalence of right ventricular dysplasia-cardiomyopathy in a non-referral hospital. Int J Cardiol. 2004;97(3):499-501.
McKenna WJ, Judge DP. Epidemiology of the inherited cardiomyopathies. Nat Rev Cardiol. 2021;18(1):22-36.
[1] Data on file

# Proof of Concept in Translationally Relevant Animal Model

## Completed RCKT Studies with *Cardiomyocyte-specific PKP2 Knockout Mouse Model of ACM*

- Initial POC evaluated 4 AAV Vectors: Cardiac Functional & Structural Analyses
- Dose-related effects evaluated with 2 AAV vectors: Cardiac Functional & Structural Analyses
- Evaluated Survival, Functional, and Anatomic Benefit in 'Arrest Progression' Models
  - Including delivery of AAV *+7 or +14 Days after* induction of PKP2 knockout and subsequent disease onset

### Analyses Include:

- Survival
- Echocardiography and ECG
- PKP2 expression (IF and WB)
- Cardiac pathology & fibrosis
- Vector DNA, transgene mRNA
- General safety including pathology

### Academic Partner:

NYU Grossman School of Medicine

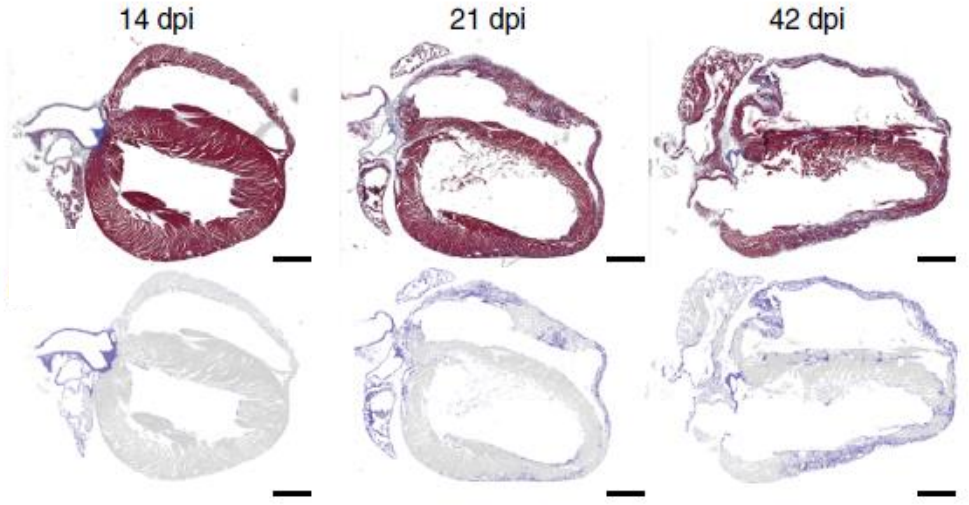
**Mario Delmar, MD, PhD**
Patricia and Robert Martinsen Professor of Cardiology,
Department of Medicine; Division of Cardiology,
NYU Grossman School of Medicine

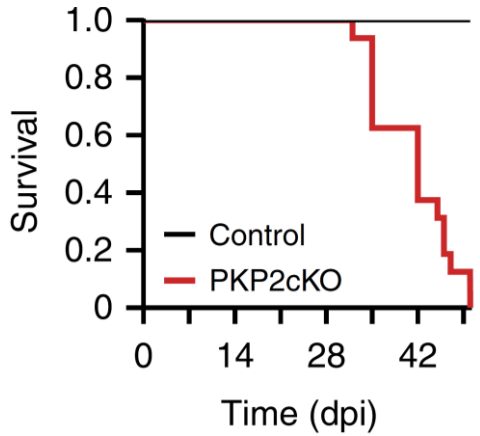
**Marina Cerrone, MD**
Research Associate Professor,
Co-Director, Inherited Arrhythmia Clinic,
Department of Medicine; Division of Cardiology,
NYU Grossman School of Medicine

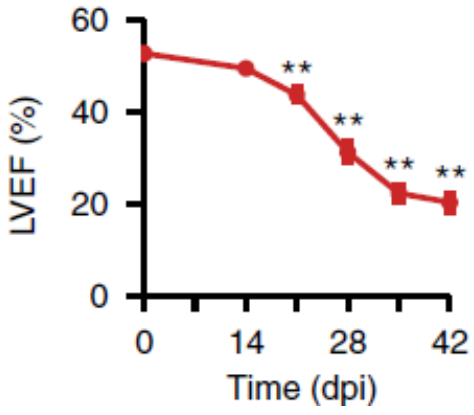
***Ongoing sponsored research. No future royalty obligations***

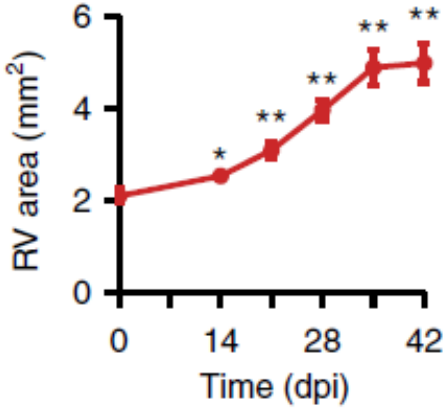
# Tamoxifen-induced ACM in the PKP2-cKO Mouse Model

- The PKP2-cKO mouse model recapitulates ACM following induction of PKP2 KO by tamoxifen (TAM) injection
- Progression of cardiomyopathy evidenced by Masson's trichrome staining of heart sections in PKP2-cKO mice from 14 to 42 days post-TAM (dpi)
- 100% mortality by day ~50 following TAM injection
- Left ventricular ejection fraction (LVEF) diminishes significantly across time
- Right ventricular (RV) enlargement occurs across time
- Premature Ventricular Contractions (PVCs) are a clinical hallmark of ACM and emerge in the animal model because of Pkp2 loss






Cerrone M, Montnach J, Lin X, et al. Plakophilin-2 is required for transcription of genes that control calcium cycling and cardiac rhythm. Nat Commun. 2017;8(1):106. Published 2017 Jul 24.
ISO, isoproterenol; cKO: conditional knockout

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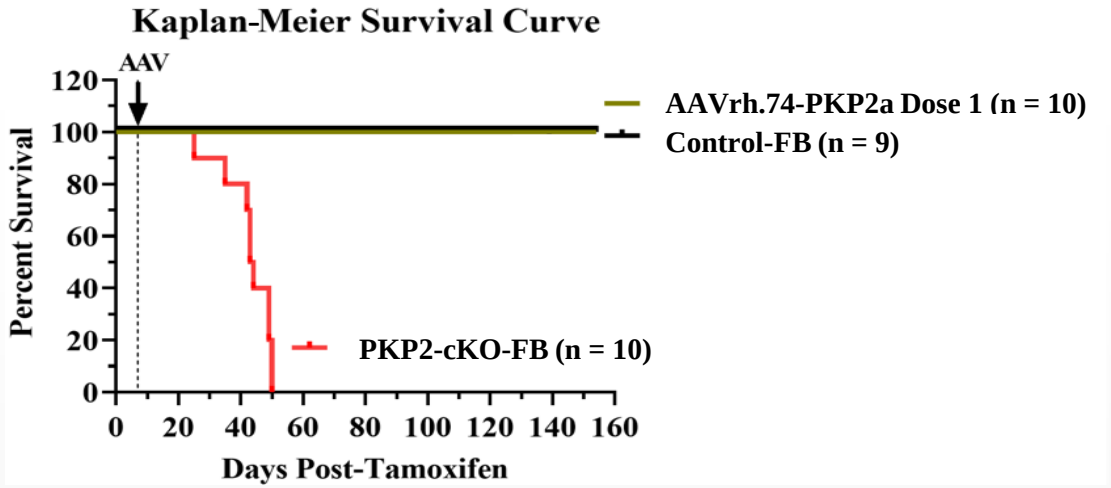
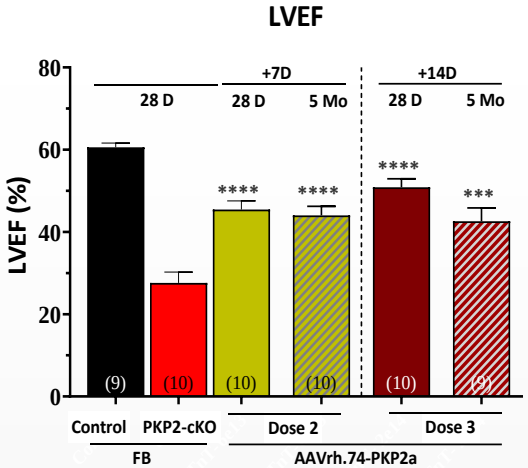
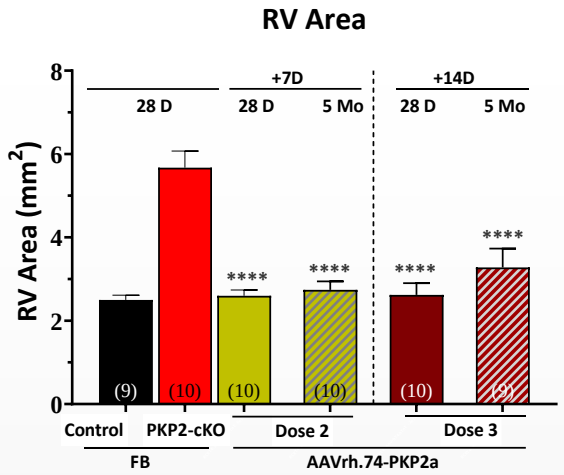
# Increased Survival & Preserved Cardiac Function in the PKP2-cKO Model

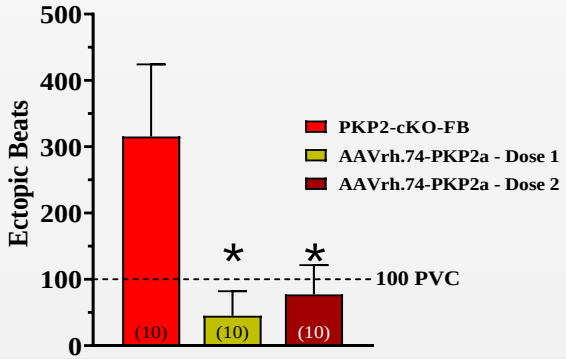


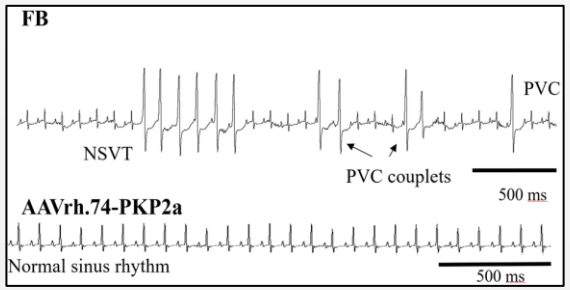




- AAVrh.74-PKP2 delivered ***7 days post-TAM***:
  - **100% survival to 5 months,** compared to 100% mortality by day ~50 in PKP2-cKO control animals
  - **Preserved Ejection Fraction and Right Ventricular Area** at 28 Days, sustained to 5 months
- AAVrh.74-PKP2 delivered ***14 days post-TAM:***
  - Mitigated isoproterenol-induced PVCs and arrhythmia, disease-related characteristics of ACM
  - Robust benefit on survival, cardiac function & structure to 5 months[1]

**ISO-Induced Arrhythmia**
**AAV+14D Post-TAM; ECG at 21D post-TAM**




*p <0.05 vs PKP2-cKO FB
ISO = isoproterenol; TAM = tamoxifen; ECG = Electrocardiography



[1]Data not illustrated in Figures

# Optimal Gene Therapy for PKP2-ACM, Expected to be First-and Best-In-Class

**cDNA/isoform:**

- **PKP2a:** full wild type coding sequence of therapeutic gene, protein loss drives ACM

**AAV Serotype:**

- ***AAV.rh74* serotype associated with favorable safety profile in DMD/LGMD2E[1-2]; potential for safe administration at optimal doses for adult ACM patients**

**Cardiac-Specific Promoter:**

- Effectively drives expression of therapeutic transgene in cardiomyocytes; minimizes off-target effects

**Route of Administration:**

- **Intravenous (IV)** Pharmacology studies demonstrate efficient cardiac transduction with IV administration

**Robust Proof of Concept in Disease Relevant Animal Model:**

- **NYU Cardiac-specific cKO-PKP2 mouse** (biologically relevant translational model)



[1]Rodino-Klapac et. al. Safety, β-Sarcoglycan Expression, and Functional Outcomes From Systemic Gene Transfer of rAAVrh74.MHCK7.hSGCB in LGMD2E/R4. Presented at the Muscular Dystrophy Association (MDA) Conference. Nashville, TN, March 13–16, 2022.
[2]Mendell et. al. A Phase 2 clinical trial evaluating the safety and efficacy of delandistrogene moxeparvovec (SRP-9001) in patients with Duchenne muscular dystrophy. Presented at the 2022 Muscular Dystrophy Association (MDA) Conference Nashville, TN, March 13–16, 2022.

# Clinical Development Plan

## Phase 1 Dose Escalation Study

### Completed or Ongoing Activities

- ✓ **Phase 1 Study Initiated**
- ✓ **Orphan Disease Designation**
- ✓ GMP drug product manufacturing completed
- ✓ Pharmacology and GLP toxicology studies
- ✓ Potency assay
- ✓ Clinical protocol developed, vetted by Scientific Advisory Board and informed by patient insights
- ✓ Launching multi-center, clinical trial

### High Level Phase 1 Trial Design

- Study design:
  - FIH, multi-center, dose escalation study to assess safety and preliminary efficacy
  - Starting dose of $8 \times 10^{13}$ GC/kg
  - Target population: Adult PKP2-ACM patients with ICDs and high risk for arrhythmias
- Primary endpoint:
  - Safety events
- Secondary and exploratory endpoints:
  - PKP2 tissue protein expression
  - Clinical markers of life-threatening ventricular arrhythmias
  - Cardiac biomarkers

### Natural History

- Natural history studies are planned to provide context for the Phase 1 trial and additional information on the progression of PKP2-ACM



FDA, Food and Drug Administration; 1H, first half of the year. FIH, first in human; ICD, implantable cardioverter defibrillators

# BAG3 Regulates Critical Functions in Cardiomyocytes

## Cardiac contractility

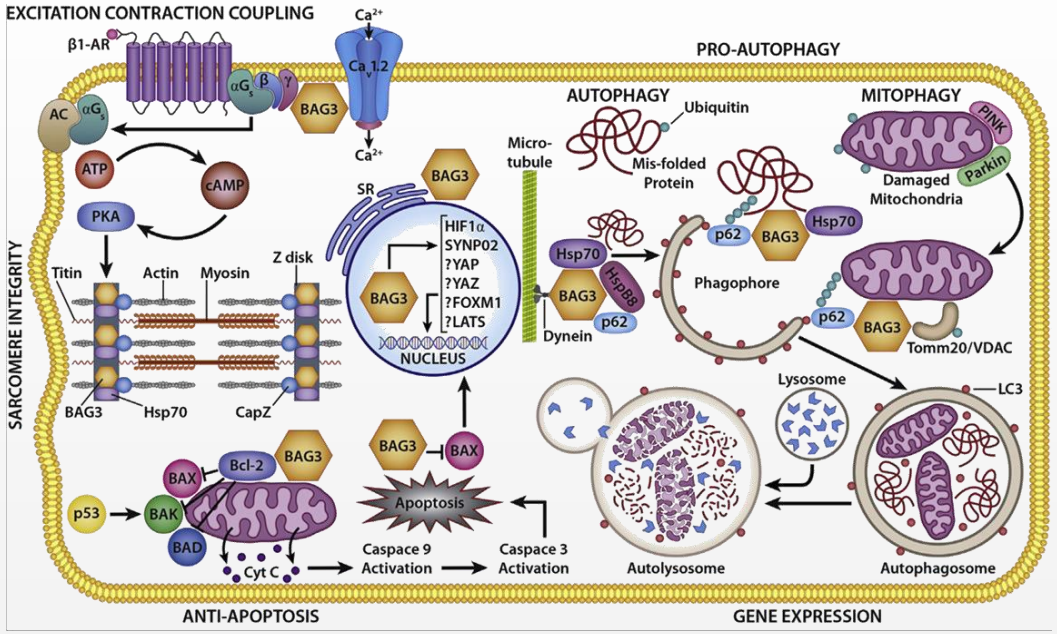
1

Enhances contractility by linking the β-adrenergic receptor and L-type $Ca^{2+}$ channel

## Structural support

2

Provides support for the sarcomere by linking actin myofibrils with the Z-disc




3

## Protein quality control

Facilitates autophagy as a co-chaperone with heat shock proteins, recycling misfolded proteins

4

## Anti-apoptosis

Inhibits apoptosis (programmed cell death) through binding of BCL2

**We believe that a gene therapy approach is best positioned to restore the broad biological functions of BAG3 in the heart**



BAG3, BLC2-associated athanogene 3; BCL2, B-cell lymphoma 2.

Knezevic T, Myers VD, Su F, et al. Adeno-associated Virus Serotype 9 - Driven Expression of BAG3 Improves Left Ventricular Function in Murine Hearts with Left Ventricular Dysfunction Secondary to a Myocardial Infarction. JACC Basic Transl Sci. 2016;1(7):647-656.

Myers VD, Gerhard GS, McNamara DM, et al. Association of Variants in BAG3 With Cardiomyopathy Outcomes in African American Individuals JAMA Cardiol. 2018;3(10):929-938.

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# BAG3-DCM Opportunity and Next Steps

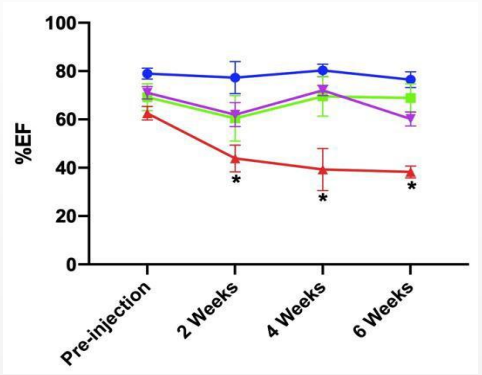
## BAG3-DCM Represents a Significant Market with Unmet Need

- Dilated cardiomyopathy (DCM) is the most common form of cardiomyopathy
- 20% to 50% of DCM patients have familial DCM; up to 40% of whom have an identifiable genetic cause(1)
- Scientific societies recently endorsed clinical genetic testing for DCM patients and families(2,3)
- Prevalence of BAG3 DCM in US is estimated to be as high as 30,000 patients(4) and is expected to grow with increasing genetic testing and disease awareness

## Initial Proof-of-Concept for AAV9-BAG3 Supports Further Development

- Initial proof of concept for AAV9-BAG3 demonstrated in BAG3-knockout mouse model

**Ejection fraction in WT and BAG3 +/- mice treated at age 6 to 8 weeks with AAV9-GFP or AAV9-BAG3**




*WT mice: AAV-GFP or AAV-BAG3*

*BAG3 +/- mice: AAV9 BAG3 treatment group*

*BAG3 +/- mice: Control group (AAV-GFP)*

- Evaluating optimal development pathway
- IND planned for 2024



AAV, adeno-associated virus; BAG3, BCL2-associated athanogene 3; DCM, dilated cardiomyopathy; EF, ejection fraction; GFP, green fluorescent protein; H1, first half of the year; IND, investigational new drug; WT, wild type. Haploinsufficiency data published in Myers VD et. al., *J Cell Physiol.* 2018; AAV-BAG3 administration adapted from data published in Myers VD et. Al., *JAMA Cardiol.* 2018; and unpublished data from the Feldman lab.

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# Cranbury R&D and Manufacturing Facility Overview

- Total Lab Space: ~30,000 sq. ft. for process development, analytical development, MS&T and QC
- Manufacturing capability from small-scale to toxicology-scale material
- Streamlined tech transfer timeline for pipeline assets from plasmid selection to IND in <15 months
- Manufacturing expansion to add media and buffer production capability
- Incorporating fully automated in-house vial filler suite
- Anticipated 2X capacity increase

***Enables rapid, robust and cost-efficient internal development capability for new and existing programs in addition to full-scale commercial manufacturing***

**~100,000 ft$^2$**

**facility in Cranbury, NJ**



MS&T, manufacturing, science and technology. QC, quality control. R&D, research and development. IND, Investigational new drug.

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# **Future Therapies:** Wave 2 (AAV)


## Focused R&D Strategy for Sustainable Innovation

**First-, best- and/or only-in-class**

**On-target MOA; clear endpoints**

**Sizeable market to maximize patient impact**

**3 therapeutic areas (CV, heme and undisclosed)**

**We continue to build our pipeline based on our core R&D strategy, identifying the "most impactful" indications for the most efficient development path.**



AAV, adeno-associated virus; MOA, mechanism of action; R&D, research and development.
Data on file. Rocket Pharmaceuticals. 2023.

# Expert Leadership With Proven Track Record

**Gaurav Shah, M.D.**
Chief Executive Officer
Spearheaded Kymriah (CART-19) development at Novartis towards approval

NOVARTIS · Memorial Sloan Kettering Cancer Center · Lilly · Brigham and Women's Hospital, Founding Member, Mass General Brigham

**Mark White, MB.ChB.**
Chief Medical Officer, SVP
Mark is a passionate and seasoned drug developer with more than 25 years of industry experience

AstraZeneca · MedImmune

**Carlos Martin, BA, MBA**
Chief Commercial Officer, SVP
15+ years global & local leadership, commercial strategy and new product launches

NOVARTIS · MERCK · Lilly

**Raj Prabhakar, MBA**
Chief Business Officer, SVP
~20 years cell, gene and biotech business development

caladrius BIOSCIENCES · PCT · Celsion Corporation · Osiris THERAPEUTICS, INC

**Isabel Carmona, J.D.**
Chief Human Resources Officer, SVP
Seasoned leader in human resources, legal and compliance across life sciences, financial services and IT

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**Kinnari Patel, Pharm.D., MBA**
President and Chief Operating Officer
Led Opdivo and six rare disease indication approvals

Pfizer · AstraZeneca · Roche · Bristol Myers Squibb · NOVARTIS

**Jonathan Schwartz, M.D.**
Chief Gene Therapy Officer, SVP
Led multiple biologics approvals

NewYork-Presbyterian Weill Cornell Medical Center · Mount Sinai · ImClone Systems · Lilly

**Gayatri R. Rao, M.D., J.D.**
Chief Development Officer of LV, SVP
7-Year former Director of FDA's Office of Orphan Products Development

FDA U.S. FOOD & DRUG ADMINISTRATION · SIDLEY

**Martin Wilson, J.D.**
General Counsel & Chief Compliance Officer, SVP
~20 years legal, compliance and executive experience and accomplishment in life sciences

endo · Teligent · PAR PHARMACEUTICAL · ...ichnos...

**Mayo Pujols**
Chief Technical Officer, EVP
~30 years technical operations and GMP manufacturing expertise

Celgene · Andelyn BIOSCIENCES · NOVARTIS · MERCK



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# THANK YOU!

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