
# SEEKING GENE THERAPY CURES

May 2025

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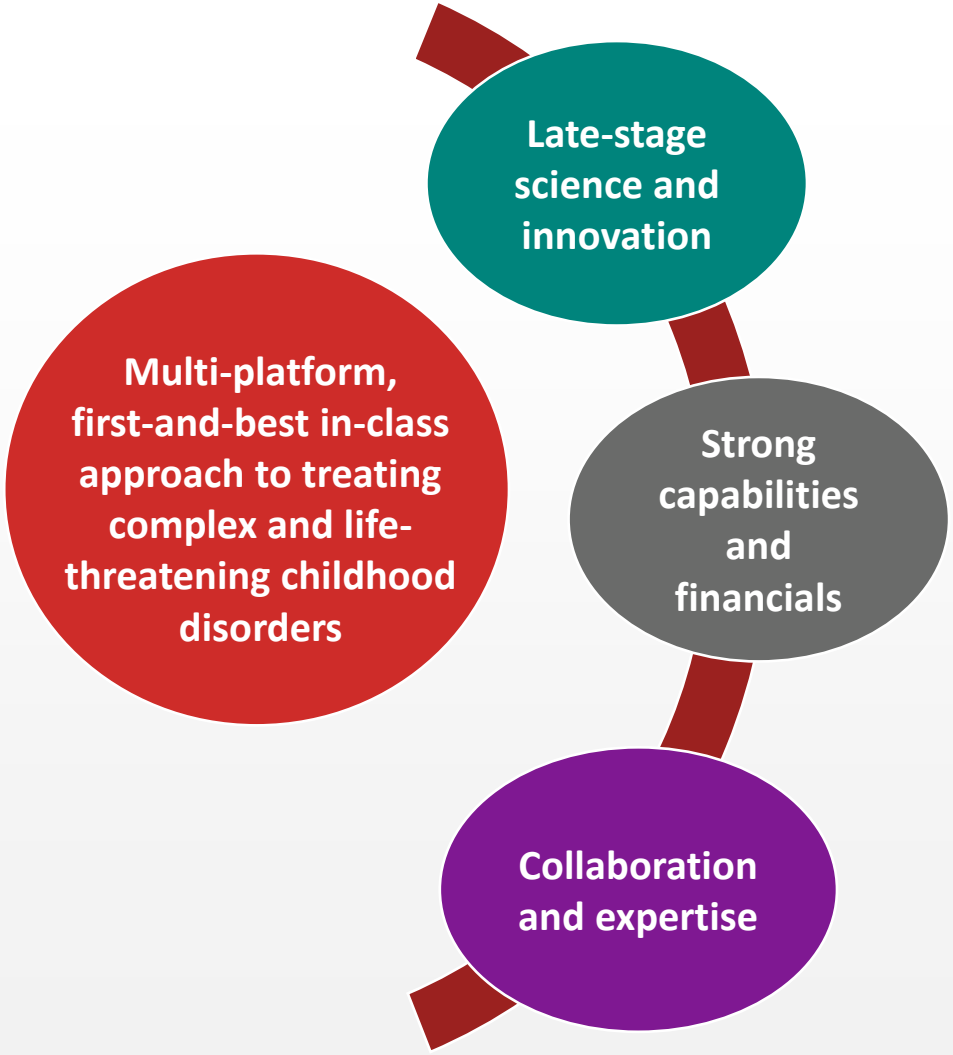
Various statements in this presentation concerning Rocket's future expectations, plans and prospects that involve risks and uncertainties, as well as assumptions that, if they do not materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking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

# **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 Gene Therapy Company




**Promising 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**
First 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

**$318.2M[1]**

in cash and cash equivalents; **sufficient to fund operations into the fourth quarter of 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**

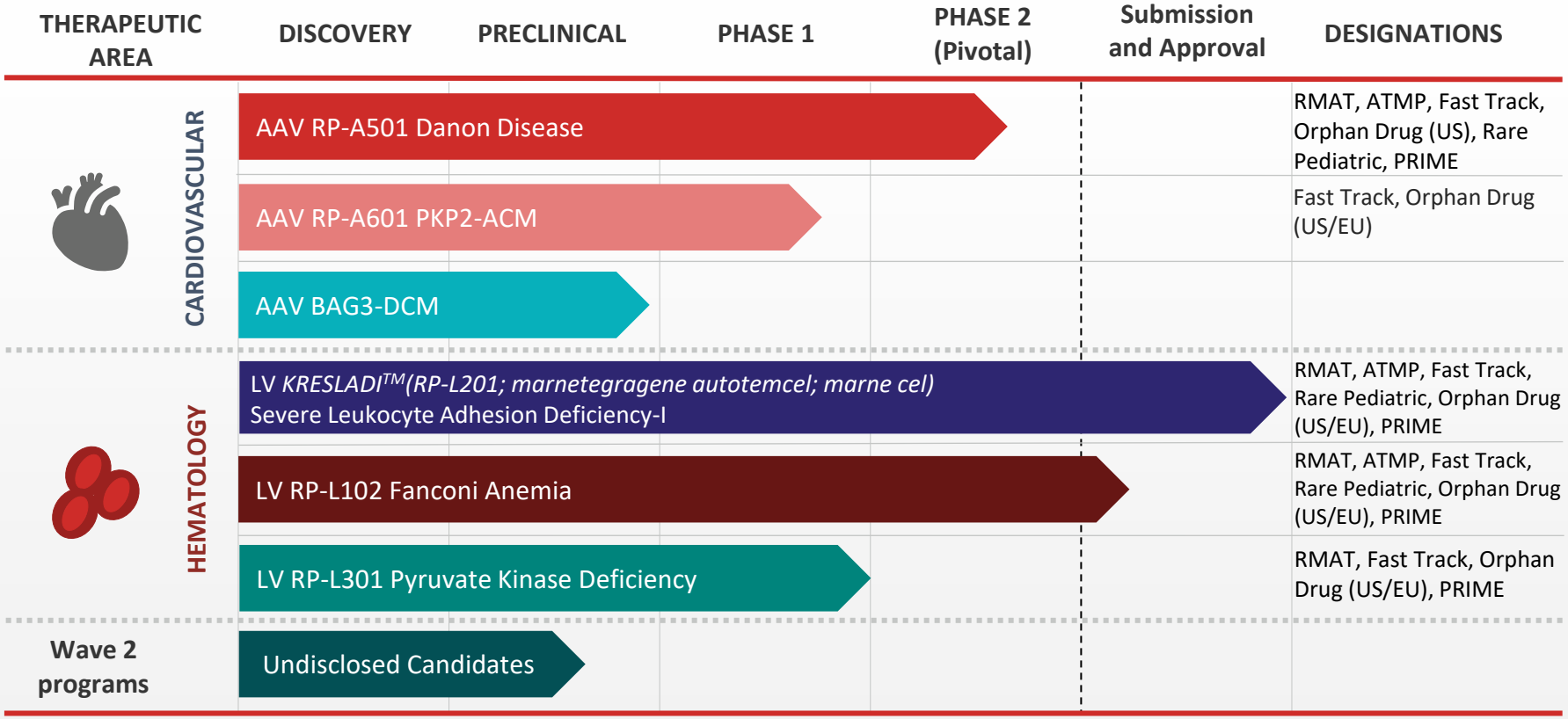
[1]Cash balance as of March 31, 2025.

# Strong Science, Carefully-selected Assets and Smart Execution

## 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; ACM, Arrhythmogenic Cardiomyopathy; ATMP, advanced therapy medicinal product; BAG3, BLC2-associated athanogene 3 DCM, Dilated Cardiomyopathy; LV, lentiviral vector; MOA, mechanism of action; PKP2, plakophilin 2; PRIME, Priority Medicines; RMAT, regenerative medicine advanced therapy. KRESLADI™, formerly RP-L201.

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

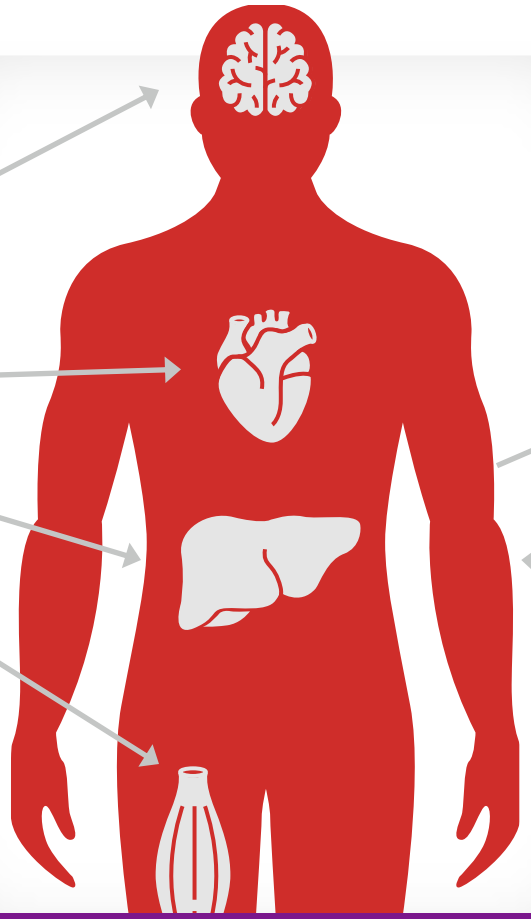
## IN VIVO platform

Laboratory-produced AAV

Therapeutic AAV

Direct intravenous injection

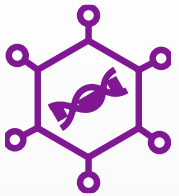
**RP-A501**: Danon Disease
**RP-A601:** PKP2-ACM
**AAV** BAG3-DCM



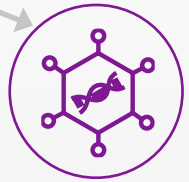
## EX VIVO platform

Remove cells and isolate patient HSCs

Laboratory-produced LV



Therapeutic LV



Gene-modified HSCs

Infusion of 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; ACM, Arrhythmogenic Cardiomyopathy; BAG3: BLC2-associated athanogene 3 HSC, hematopoietic stem cell; LV, lentiviral vector; DCM, Dilated Cardiomyopathy, PKP2, plakophilin 2.

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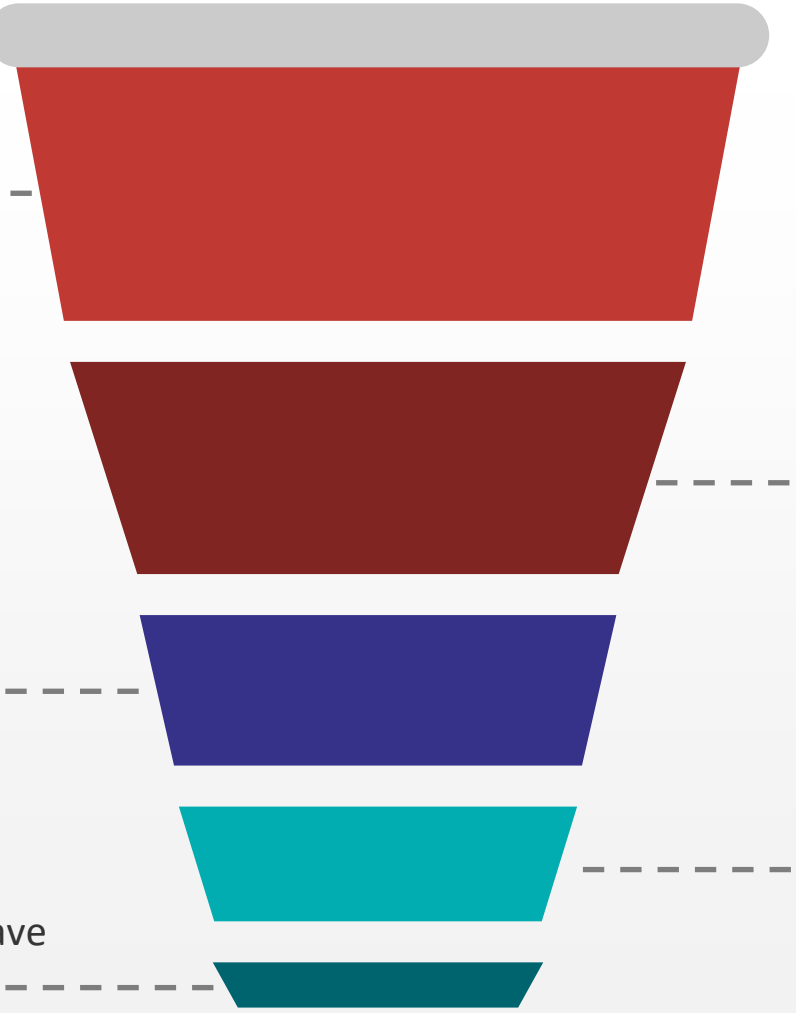
# **Rare Diseases** Are Associated With a Reduced Lifespan[1]

**400 million**
**people globally are affected by a rare disease**

Children account for **50%** **of rare disease patients**



**80%** **of rare diseases** have monogenic origins

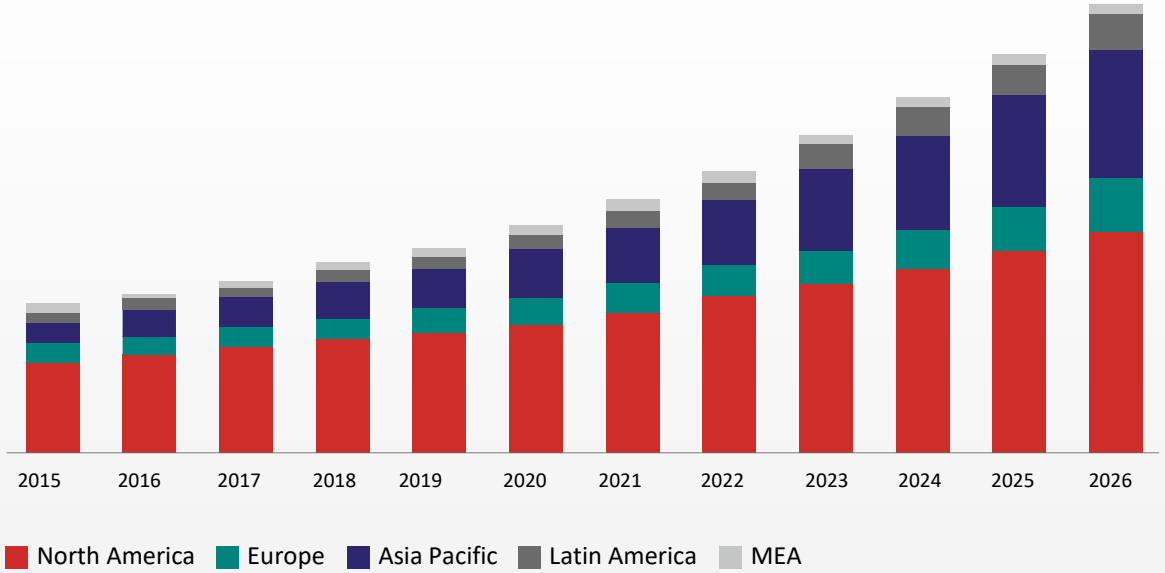
**3 of 10 children** with a rare disease die before their fifth birthday

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

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

# 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.

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]

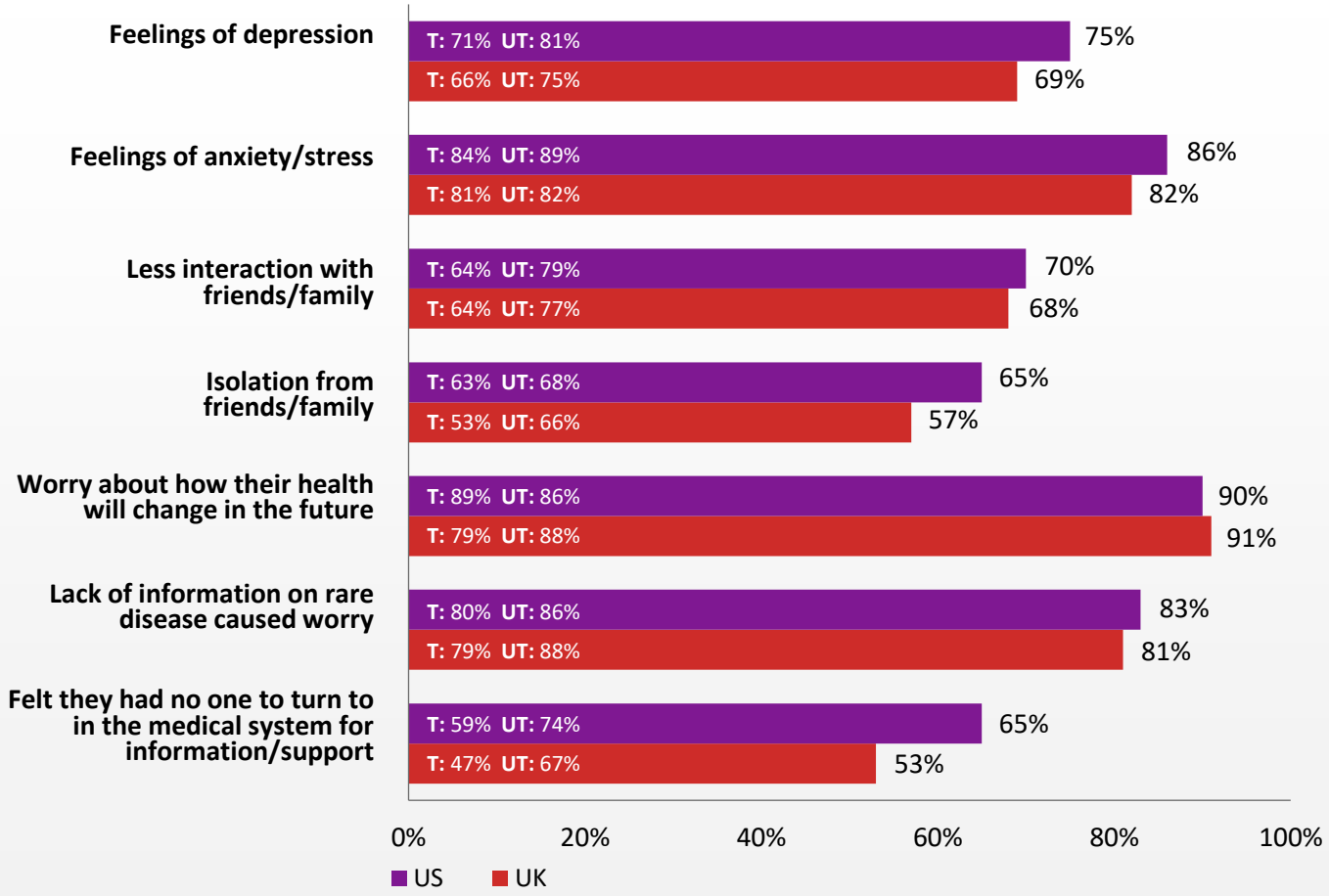
## Economic impact[1]

**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[3]




*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. Global Genes. Accessed April 2022. https://globalgenes.org/wp-content/uploads/2013/04/ShireReport-1.pdf

# Danon Disease: Serious Condition with High Unmet Medical Need

**Market Opportunity[1] – 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
- Limitations:
  - Considerable morbidity and mortality
  - Only ~20% of patients receive HTx[2]
  - 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[2,3]
- Females: Delayed median presentation (~20 years later) due to additional X chromosome, highly morbid and fatal disorder[2,3]

CNS, central nervous system; *LAMP-2B*, lysosome-associated membrane protein 2B; HTx, heart transplant.

1. Rocket Pharmaceuticals data on file
2. Boucek D, Jirikowic J, Taylor M. Natural history of Danon disease. *Genet Med.* 2011;13(6):563-568.
3. Brambatti M, Caspi O, Maolo A, et al. Danon disease: Gender differences in presentation and outcomes. *Int J Cardiol*. 2019;286:92-98.

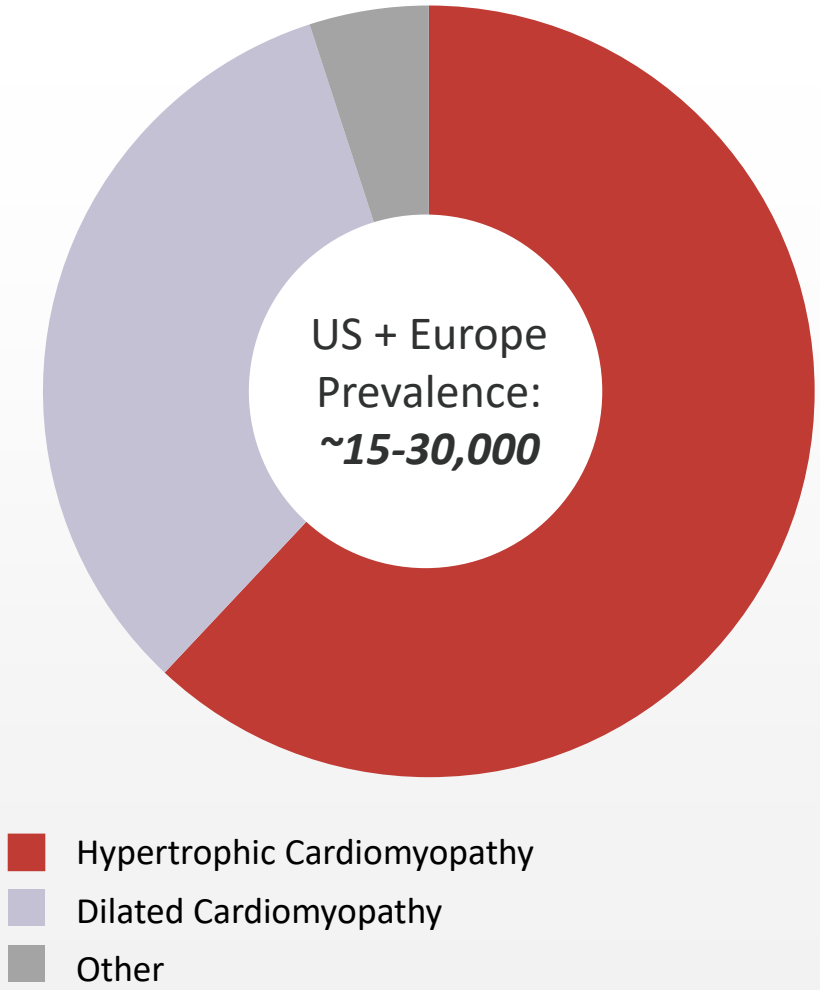
# Danon Disease – Epidemiology and Market Opportunity

## 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

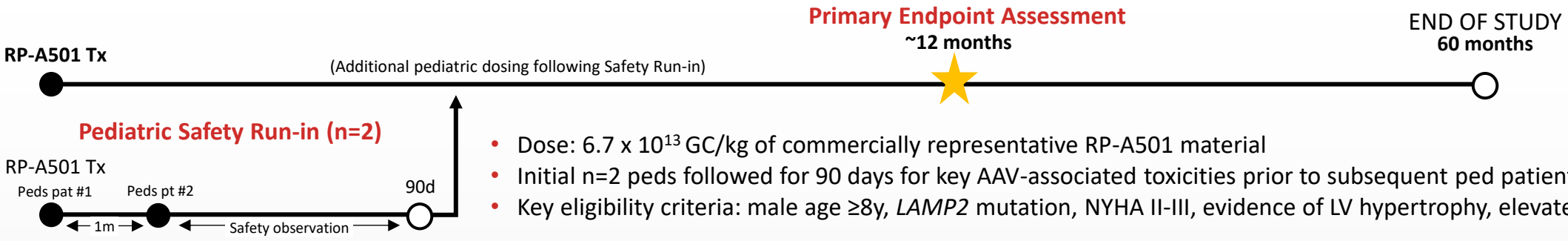



* *J Am Coll Cardiol.* 2015 Mar 31;65(12):1249-1254.
** *Heart*. 2004 Aug;90(8):842-6. *N Engl J Med*. 2005 Jan 27;352(4):362-72. *Genet Med*. 2015 Nov;17(11):880-8. Gene. 2016 Feb 15;577(2):227-35. *J Cardiovasc Transl Res*. 2017 Feb;10(1):35-46
*** *Neurology*. 2002 Jun 25;58(12):1773-8. *Genet Med*. 2011 Jun;13(6):563-8. *Rev Esp Cardiol* (Engl Ed). 2018 Aug 11.

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

*Pivotal, global, single-arm, open label study – Program update expected Mid-year 2025*

## 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 patient 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: ≥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



6MWT, 6-minute walk test; hsTnI, high-sensitivity troponin I; IDSMC, Independent Data Safety and Monitoring Committee; IHC, immunohistochemistry; KCCQ, Kansas City Cardiomyopathy Questionnaire; LAMP2, lysosome-associated membrane protein 2; LV, left ventricular; NYHA, New York Heart Association; PedsQL, Pediatric Quality of Life Inventory; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; QoL, quality of life; Tx, treatment.
ClinicalTrials.gov Identifier NCT06092034.

# Primary Endpoint 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*



LAMP2, lysosome-associated membrane protein 2; LV, left ventricle; MRI, magnetic resonance imaging; QOL, quality of life; WT, wild type .

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

# RP-A501 Phase I Study: Sustained LAMP2 Expression in Cardiomyocytes

*Durable myocardial LAMP2 protein expression seen in all patients*

## Myocardial LAMP2 Protein Expression

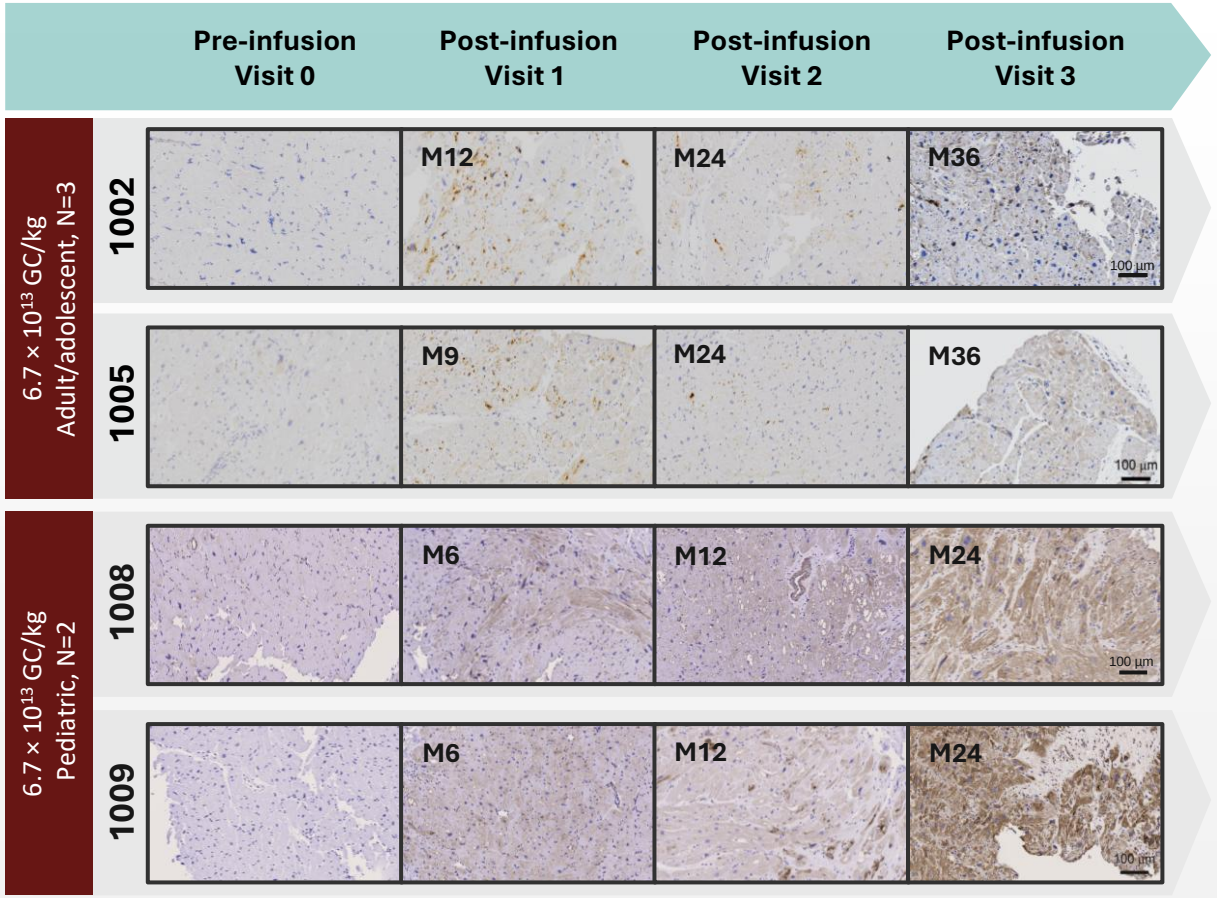
| Cohort | Patient | BL | M6 | M12 | M18 | M24 | M30 | M36 | M60 |
|---|---|---|---|---|---|---|---|---|---|
| 6.7 × $10^{13}$ GC/kg Adult/adolescent | 1001 | 0 | ++ | + | NP | NP | 0* | 0* | +++‡ |
| | 1002 | 0 | NP | +++ | ++ | ++ | ++ | ++ | |
| | 1005 | 0 | NP | ++† | NP | + | + | + | |
| 1.1 × $10^{14}$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

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

**Legend: IHC Staining Grade¶ (% Positive Cardiomyocytes)**

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

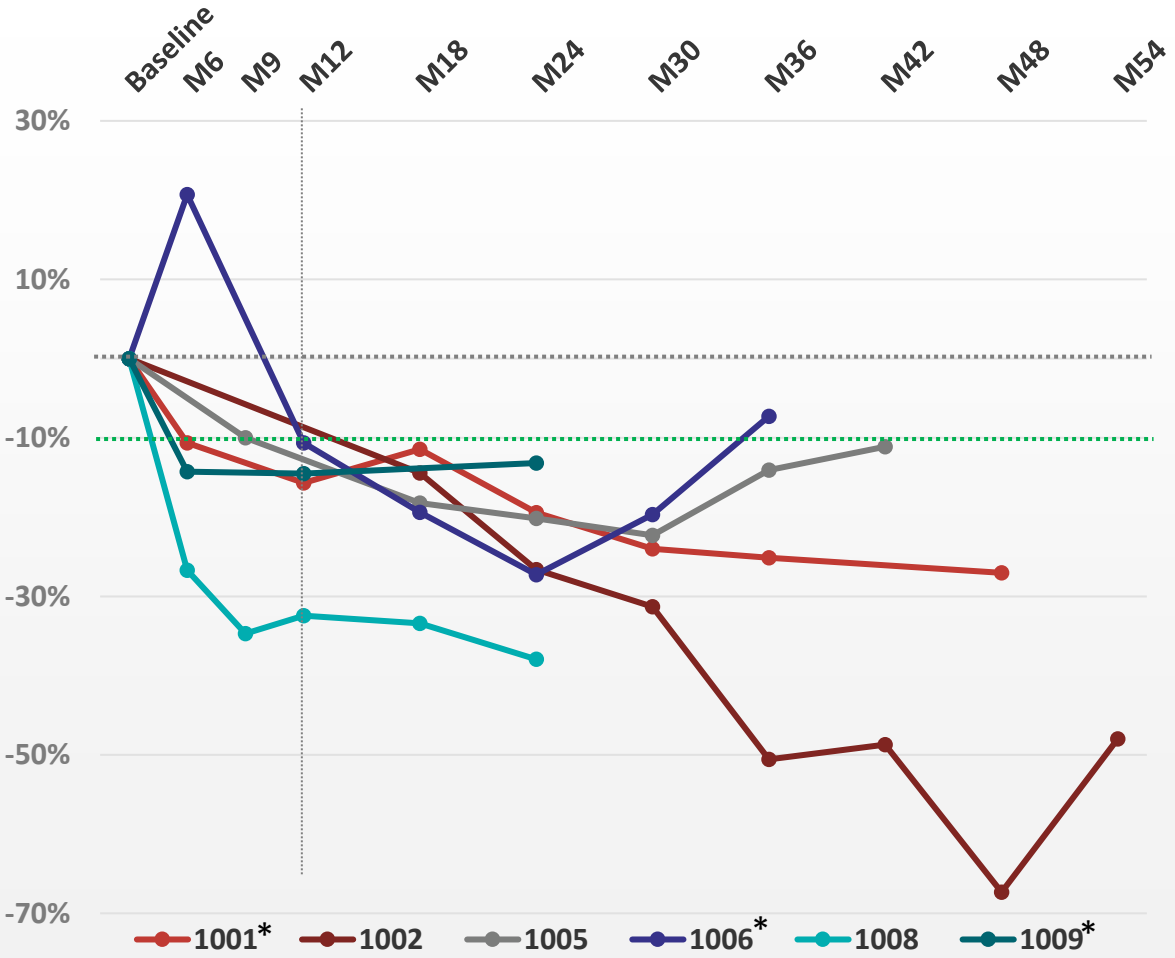
## Representative LAMP2 IHC Images



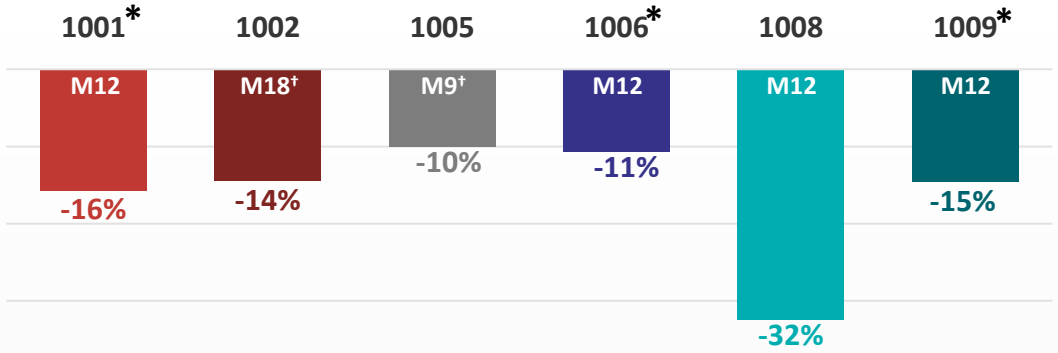

Data up to month 36 timepoint adapted from Greenberg B., et al. *N Engl J Med.* 2025;392(10):972-983; Month 60 data for patient 1001 referenced from Data on file. Rocket Pharmaceuticals, Inc.
**Note:** Patient 1007 had LV systolic dysfunction (LVEF <40%) at enrollment and had progressive heart failure requiring transplantation 5m following RP-A501 treatment; this patient is currently stable 3 years post-transplant.
*Patient 1001 demonstrated Grade 0 LAMP2 protein IHC staining at the 30- and 36- month assessments, however, patient 1001's LAMP2B vector RNA and DNA (VCN) levels have persisted through 36 months of follow-up.
¶Grading of LAMP2 protein expression by IHC was done by a board-certified pathologist in a blinded fashion. The semi-quantitative grading reflects the extent of LAMP2 protein expressing cardiomyocytes in the entirety of biopsy sample according to the scale: Grade 0, negative staining; Grade 1 = < 25%; Grade 2 = 26%-50%; Grade 3 = 51%-74%; Grade 4 = >75%.
IHC=immunohistochemistry; LAMP2=lysosome-associated membrane protein 2; M=month(s); VCN=vector copy number.

# RP-A501 Phase 1 Study: Sustained Improvements in LV Mass Index

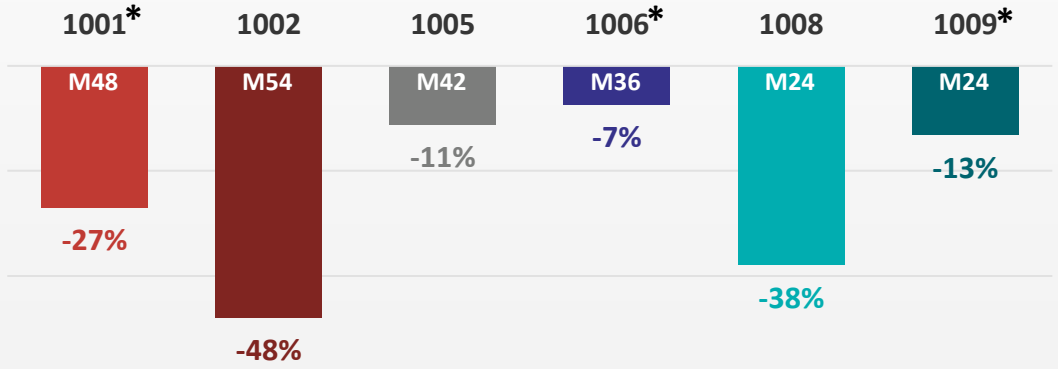
## LVMI % Change from Baseline




## LVMI % Change: Baseline to 12m†




## LVMI % Change: Baseline to Most Recent Visit*




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



Data published in Greenberg B., et al. *N Engl J Med.* 2025;392(10):972-983 [supplementary appendix]; Data cut-off: April 19, 2024.
* Where possible, cardiac MRI assessments shown (patients 1001, 1006, and 1009); otherwise, echocardiogram data presented. All assessments were conducted by a single reviewer blinded to both patient and timepoint, except for Patient 1001 cardiac MRI data, which includes reads from multiple reviewers (note, these data not included in *NEJM* publication). Patient 1001 most recent visit with MRI assessment was at 48m
† Utilized 9m or 18 m data when 12m assessment was not done.
LVMI, left ventricular mass index; MRI, magnetic resonance imaging; m, month(s).

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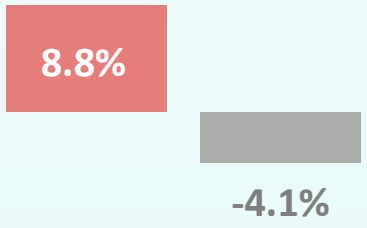
# LV Mass / LV Mass Index (LVMI) Improvements with Low Dose RP-A501 Comparable to Other Recently Approved Therapies for Cardiomyopathy

## Fabry Disease
(Agalsidase alfa)

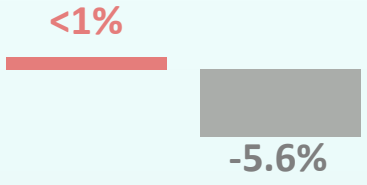
LV Mass @6M




**Clinical Correlation:**
- Improvements in LVM out to 36M correlated with HF symptoms (NYHA, CCS); drug approved in EU

## Amyloid Cardiomyopathy
(Patirisan)

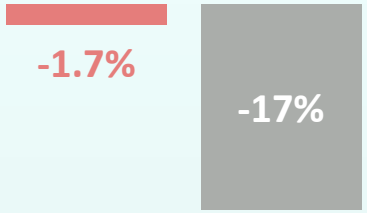
LV Mass @18M




**Clinical Correlation:**
- Drug approved based on improved CV outcomes @30M
- Significant improvements in 6MWD & NT-proBNP

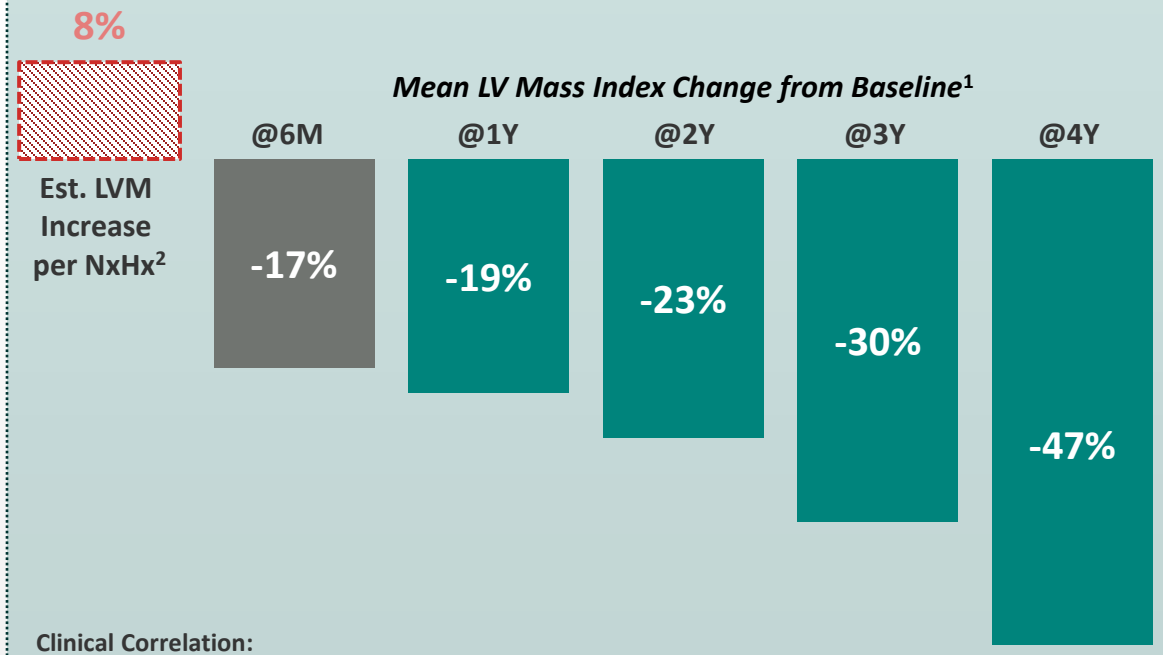
## HCM
(Mavacamten)

LVMI @7M




**Clinical Correlation:**
- ↑ exercise tolerance at 30wks
- NYHA Class ↓ by 1 in 76% treated patients at 120wks

## Danon Disease
(RP-A501 Phase 1 Study – Low Dose Adult and Pediatric Cohorts)




**Clinical Correlation:**
- NYHA Class improvement, KCCQ ↑, improvement or stabilization in hsTnI and natriuretic peptides all to most recent timepoint (24-56M)

Placebo / Untreated | Estimate from retrospective NxHx Data | Treated

[1] Data Cutoff April 9, 2024; Mean change from baseline includes only patients treated with Low Dose ($6.7x10^{13}$ GC/kg) and calculated as follows: M6 = 1001,1008,1009 (no 6M data for 1002,1005); 1Y = 1001,1008,1009 12M data and 1002,1005 18M data (no data from 1002,1005 12M visits); 2Y = 1001,1002,1005,1008,1009 24M data; 3Y = 1001,1002,1005 36M data, 4Y = 1001,1002 48M data. * Where possible, cardiac MRI assessments shown (patients 1001, 1006, and 1009); otherwise, echocardiogram data used.. All assessments were conducted by a single reviewer blinded to both patient and timepoint, except for Patient 1001 cardiac MRI data, which includes reads from multiple reviewers.
[2] Reflects estimated LV Mass increase over 12-18M for DD patients based on retrospective natural history data-set.
Data for comparable therapies from the following publications: Hughes 2008. *Heart*; Solomon 2019. *Circulation*; Saberi 2021. *Circulation*



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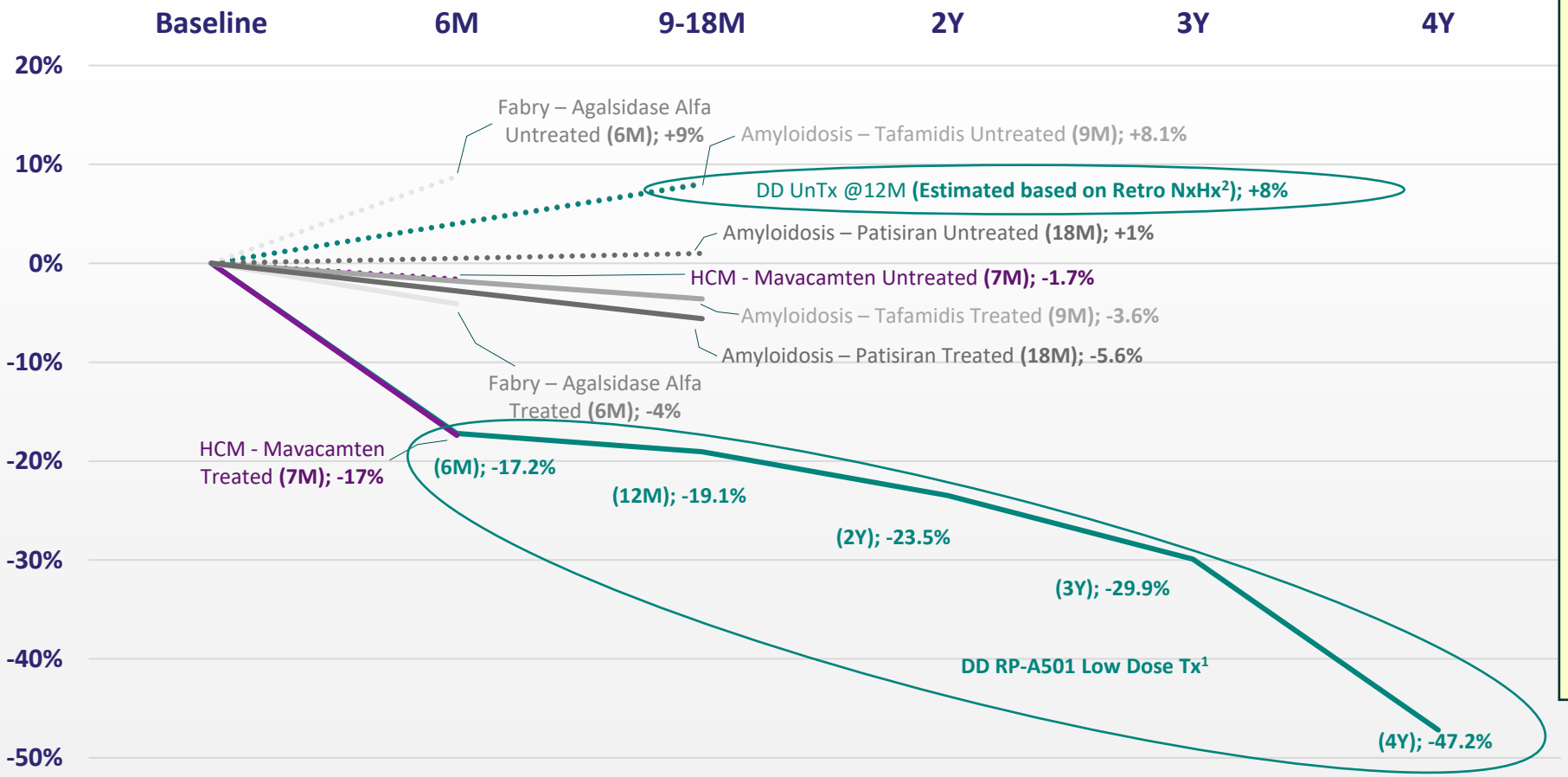
# LV Mass / LV Mass Index (LVMI) Improvements with Low Dose RP-A501 Comparable to Other Recently Approved Therapies for Cardiomyopathy

## LV Mass / LVMI Change from Baseline in Treated vs Untreated Patients: RP-A501 Low-Dose Adult and Pediatric Patients[1] and Recently Approved CV Therapies




- Data from Phase 1 study shows RP-A501 is potentially transformative for cardiac structure improvements and remodeling
- On par with recently approved therapies in other CV indications at similar timepoints (across different disease etiologies and drug MOA's)
- Sustained improvements seen with longer follow-up

[1] Data Cutoff April 9, 2024; Mean change from baseline includes only patients treated with Low Dose (6.7x10^13 GC/kg) and calculated as follows: M6 = 1001,1008,1009 (no 6M data for 1002,1005); 1Y = 1001, 1008,1009 12M data and 1002,1005 18M data (no data from 1002,1005 12M visits); 2Y = 1001,1002,1005,1008,1009 24M data; 3Y = 1001,1002,1005 36M data, 4Y = 1001,1002 48M data. * Where possible, cardiac MRI assessments shown (patients 1001, 1006, and 1009); otherwise, echocardiogram data used.. All assessments were conducted by a single reviewer blinded to both patient and timepoint, except for Patient 1001 cardiac MRI data, which includes reads from multiple reviewers.

[2] Reflects estimated LV Mass increase over 12-18M for DD patients based on retrospective natural history data-set.

Data for comparable therapies from the following publications: Hughes 2008. *Heart*; Rettl 2022. *EHJ CV Imaging*; Solomon 2019. *Circulation*; Saberi 2021. *Circulation*



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# RP-A501 Phase I Study: Benefit Observed Across All Key Parameters

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

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

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

Improved Stabilized Worsened



Data published and used with permission from Greenberg B., et al. *N Engl J Med.* 2025;392(10):972-983; Data cut-off: April 19, 2024.
BL=Baseline; BNP=Brain Natriuretic Peptide; cTnI=cardiac troponin I; ICD=Implantable Cardioverter Defibrillator; IVSd=Intraventricular Septum in diastole; KCCQ=Kansas City Cardiomyopathy Questionnaire; NT-Pro-BNP=N-terminal pro–B-type natriuretic peptide; NYHA=New York Heart Association; LV=Left Ventricle; LVEF=Left Ventricular Ejection Fraction; LVMI=Left Ventricular Mass Index, LVPWd=Left Ventricular Posterior Wall in diastole, RV=(Most) Recent Visit.

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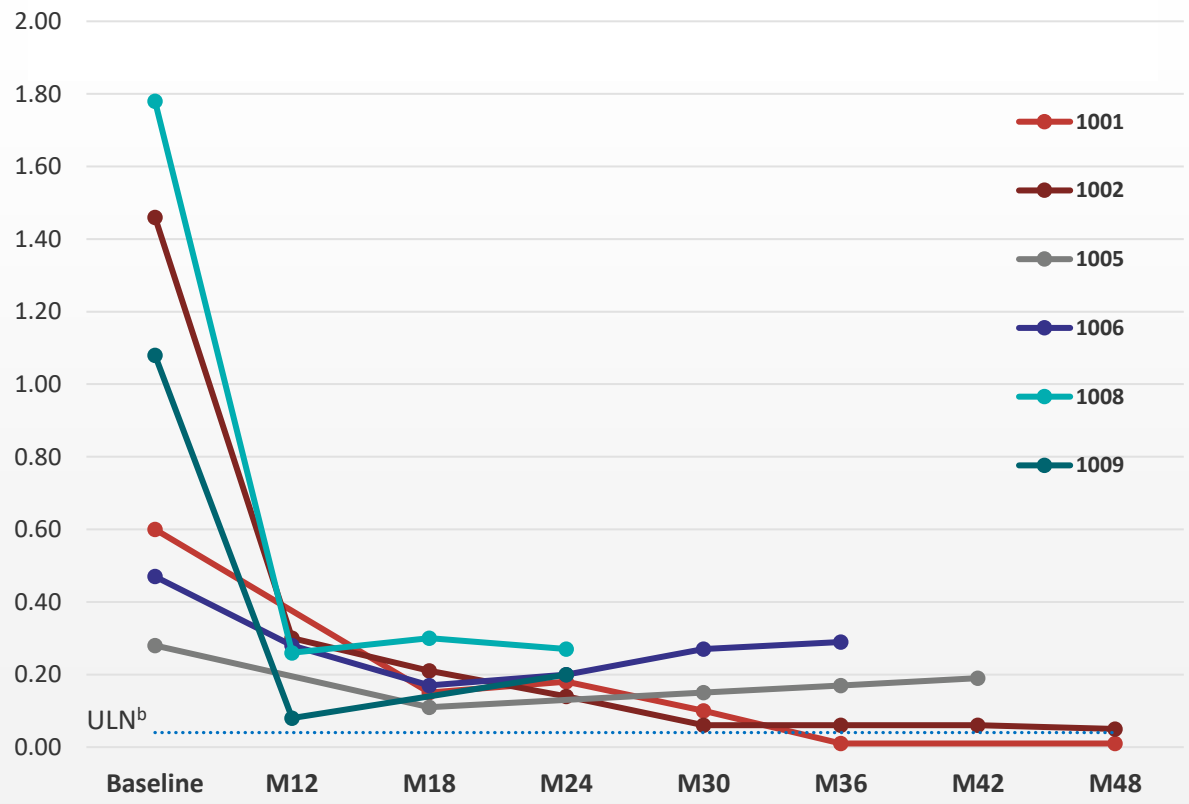
# RP-A501 Phase 1 Study: Reduction in Troponins and HF Symptoms

*Troponin Levels a Key Secondary Endpoint That Correlates with Reductions in Measures of Cardiac Injury and HF Symptoms*

### *Sustained Reduction in Cardiac Troponin-I Levels[a] after Treatment with RP-A501*




### *Corresponding Improvement in NYHA class and KCCQ-OS after Treatment with RP-A501*

| Patient ID | NYHA Class Baseline | NYHA Class* Most Recent Follow-up | Δ KCCQ-12 OS, BL → RV | Time of Follow-up |
|---|---|---|---|---|
| 1001 | II | I | +52 | 4.5 yrs |
| 1002 | II | I | +27 | 4.5 yrs |
| 1005 | II | I | +7 | 3.5 yrs |
| 1006 | II | I | +9 | 3 yrs |
| 1008 | II | I | +27 | 2 yrs |
| 1009 | II | I | +30 | 2 yrs |

- **Troponins significantly elevated in all subjects at baseline; marked decreases and/or stabilization sustained 2-4.5 years post treatment.**
- **Associated with clinical improvement to NYHA Class I in all patients (Class I = no clinical symptoms of HF)**
- **Patient reported outcomes (KCCQ) further support reduction in HF symptoms and improved quality of life out to 4.5 yrs**

Data published in Greenberg B., et al. *N Engl J Med.* 2025;392(10):972-983 [supplementary appendix]; Data cut-off: April 19, 2024

[a]Visits not conducted, and results pending or unavailable at various timepoints; data shown are cTnI levels performed on high-sensitivity and older assays. Values from both assays are expressed in nanograms per milliliter for consistency. B Representative Troponin Upper Limit of Normal: 0.04 ng/mL.

cTnI, cardiac troponin I; HF, heart failure; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire – Overall Score; M, month(s); NYHA, New York Heart Association; ULN, upper limit of normal.



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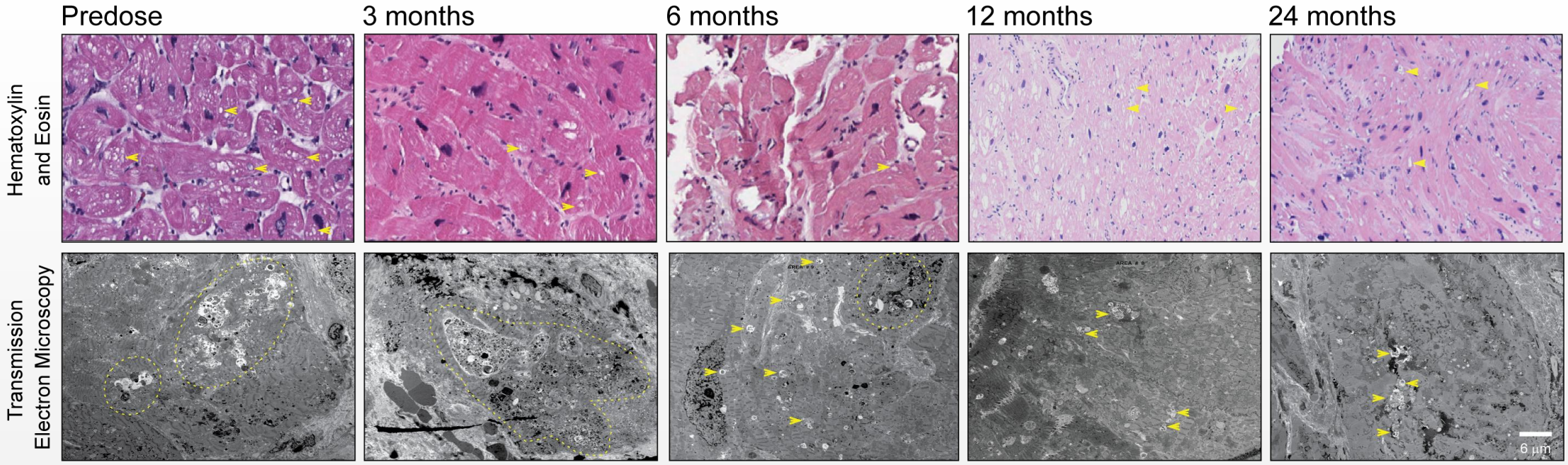
# RP-A501 Phase I Study: Decreased Cardiomyocyte Vacuolization

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

## Representative Images from the Endomyocardial Biopsy of Patient 1008




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



Data published in Greenberg B., et al. *N Engl J Med.* 2025;392(10):972-983 [supplementary appendix]; Data cut-off: April 19, 2024

# 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. **(Patient 1005)**

Prior to therapy, he would say "my wish is not to die young." After gene therapy, we see him smile more because he was able to hold down a steady part-time job and can live independently in an apartment of his own. He is living a life he didn't think would be possible. **(Patient 1006)**

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

He is now able to exercise on a more regular basis. After treatment, he was able to participate in an organized walk with his father completing most of the 10K course. **(Patient 1009)**

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

- **Multiple Successful Danon AAV cGMP batches produced since 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***

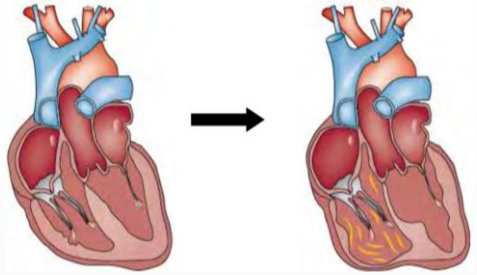


AAV; adeno-associated virus; cGMP, current good manufacturing practice; FDA, Food and Drug Administration.

# PKP2-Arrhythmogenic Cardiomyopathy (ACM)*:

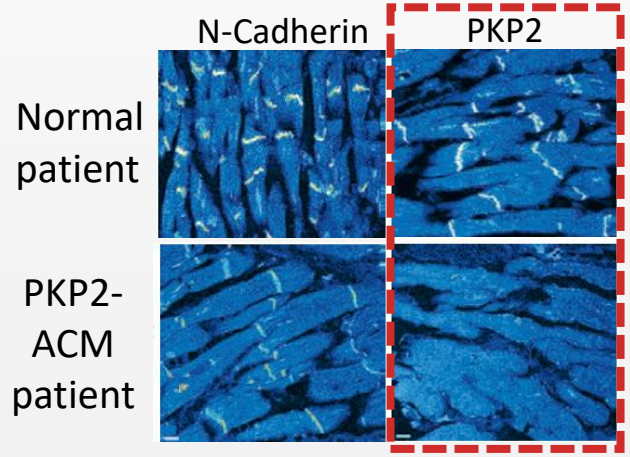
## *A high-risk disease with no curative options*

### 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

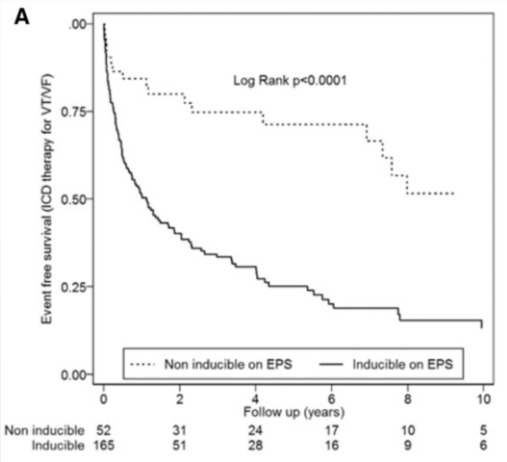
### Therapeutic Challenges

- 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 patients [5]
- For patients 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]

### 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*

*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". ECG, electrocardiogram; EPS, electrophysiologic study; ICD, implantable cardioverter defibrillator; LBBB, left bundle branch block; LV, left ventricle; PKP2; plakophilin 2; RV, right ventricular; RVEF, right ventricular ejection fraction; SD, standard deviation; SVA, sustained ventricular arrhythmia; TWI, T-wave inversion; VT, ventricular tachycardia.

Biopsy figure adapted from: Asimaki et al. NEJM, 2009; Table adapted from Dalal et al. Circulation 2006; 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**[1,2]

**PKP2 variants**

**32.9%**

2,572 ACM patients assessed from 13 publications an aggregated mean of **32.9% had *PKP2* mutations**[3]

**ACM-PKP2 US & EU Prevalence**

**~50,000**

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

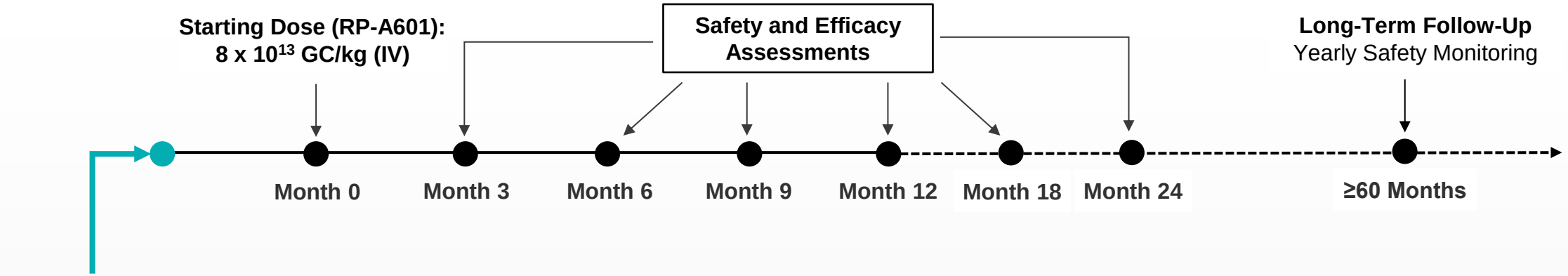


1. Peters S, Trümmel M, Meyners W. Prevalence of right ventricular dysplasia-cardiomyopathy in a non-referral hospital. Int J Cardiol. 2004;97(3):499-501.
2. McKenna WJ, Judge DP. Epidemiology of the inherited cardiomyopathies. Nat Rev Cardiol. 2021;18(1):22-36. 3.Rocket Pharmaceuticals data on file.

# Phase 1 Trial Design of RP-A601 in Adult Patients with PKP2-ACM

*First-in-human, multi-center, open-label, dose escalation trial– Initial data expected May 2025*

## PIVOTAL PHASE 2 STUDY DESIGN




### INCLUSION CRITERIA

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

### EXCLUSION CRITERIA

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

### PRIMARY ENDPOINT: SAFETY

- Incidence of TEAEs and SAEs
- Identification of dose limiting toxicities

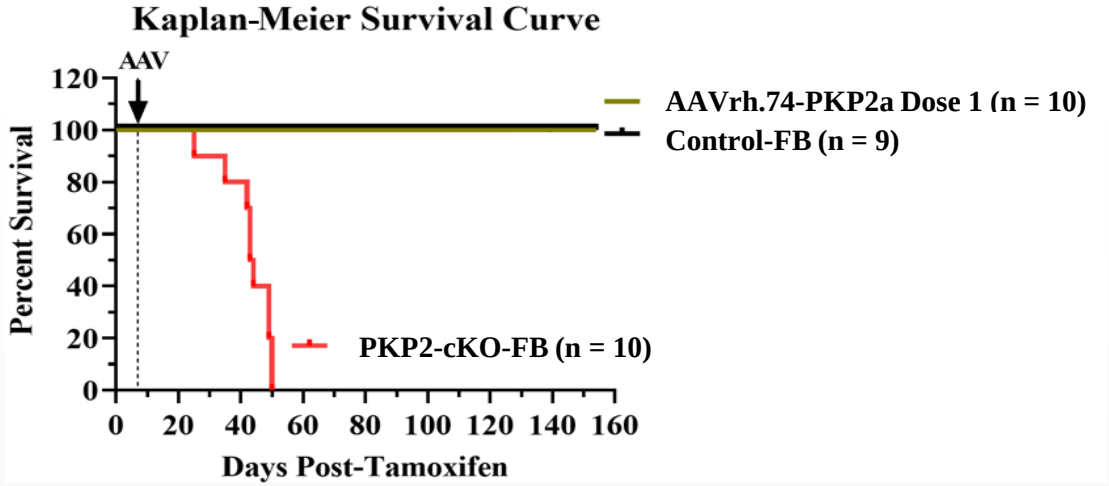
### SECONDARY & EXPLORATORY ENDPOINTS: EFFICACY

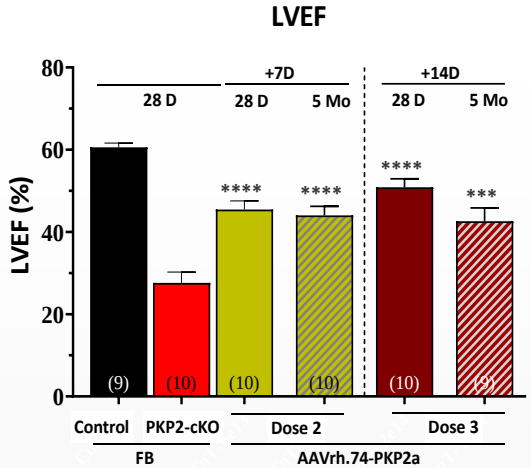
- Change in PKP2 protein expression
- Change in frequency of clinical markers of life-threatening ventricular arrhythmias
- Cardiac biomarkers

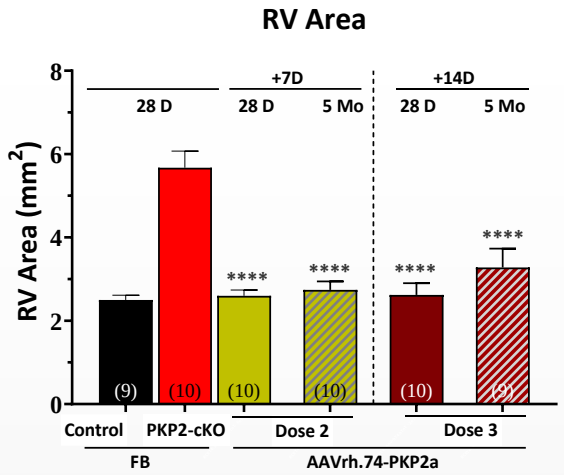
Natural history studies planned to provide context for the Phase 1 trial and additional information on disease progression

ACM, arrhythmogenic cardiomyopathy; GC, genome copies; ICD, implantable cardioverter-defibrillator; IV, intravenous; SAE, serious adverse event; TEAE, treatment emergent event.
Phase 1 Trial of RP-A601 in Adult Patients with PKP20ACM (NCT05885412)
PKP2-ACM Natural History Study (NCT06644742)

# Increased Survival & Preserved Cardiac Function in the PKP2-cKO Model Treated with AAVrh.74-PKP2

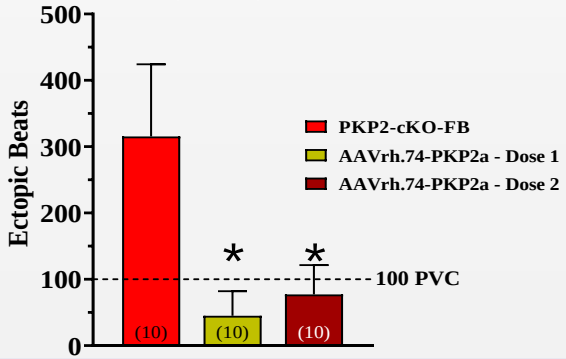


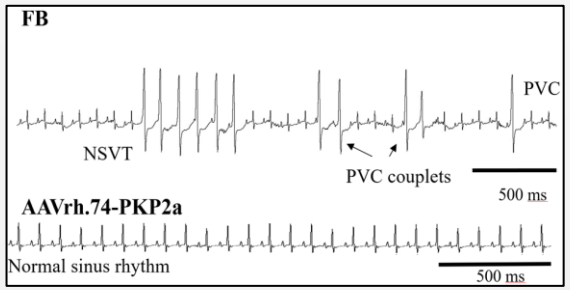




- AAVrh.74-PKP2 delivered ***7 days post-TAM***:
  - **100% survival to 5 months,** compared to 100% mortality by day ~50 in PKP2-cKO control animals
  - **Preserved Ejection Fraction and Right Ventricular Area** at 28 Days, sustained to 5 months
- AAVrh.74-PKP2 delivered ***14 days post-TAM:***
  - 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

AAV, adeno-associated virus; AAV.rh74; Recombinant AAV serotype 74; ACM, Arrhythmogenic Cardiomyopathy; cKO, conditional knockout; LVEF, left ventricular ejection fraction; PVCs, premature ventricular contractions; RV, right ventricle; TAM, tamoxofin.

# 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[1-3]; 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:**

- **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)



AAV, adeno-associated virus; AAV.rh74, Recombinant AAV serotype 74; ACM, Arrhythmogenic Cardiomyopathy; cKO, conditional knockout; DMD, Duchenne muscular dystrophy; LGMD2E, limb-girdle muscular dystrophy 2E; IV, intravenous; PKP2; plakophilin. 2.

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. 3. van Opbergen et al., Circ Genom Precis Med, 2024; Feb;17(1):e004305. DOI: 10.1161/CIRCGEN.123.004305.

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# BAG3 Regulates Critical Functions in Cardiomyocytes

## Cardiac contractility

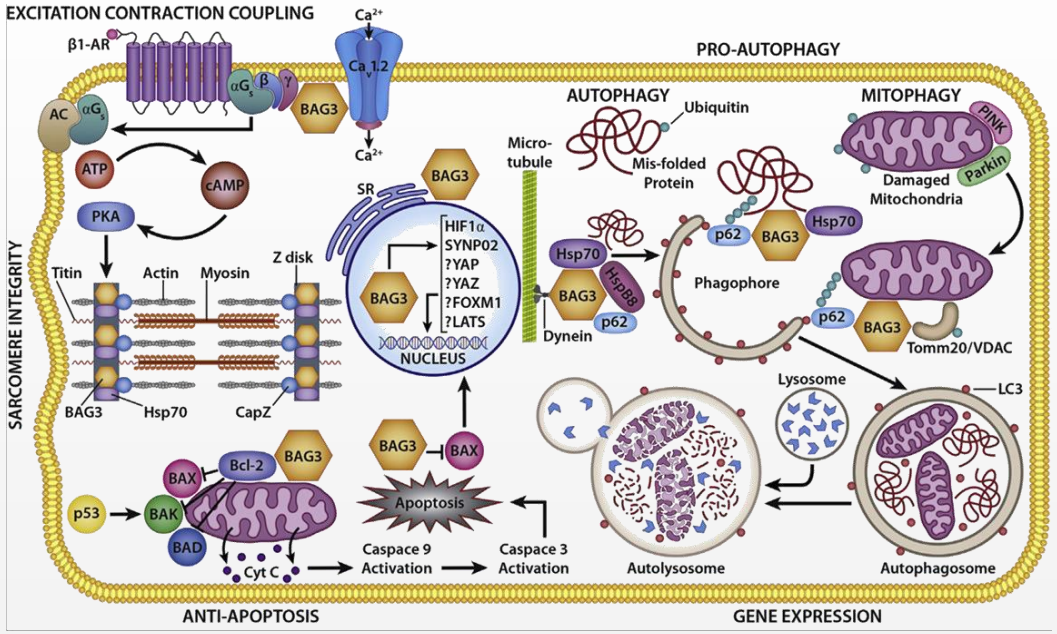
1

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

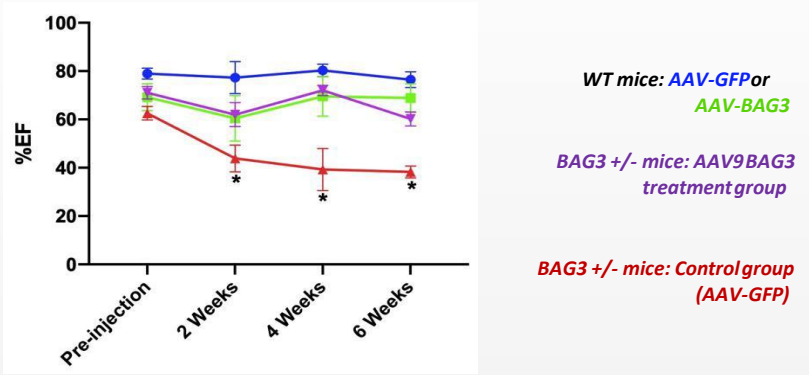
## BAG3-DCM Represents a Significant Market with Unmet Need

- 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[1,2]
- Scientific societies have endorsed clinical genetic testing for DCM patients and families[3,4]
- Prevalence of BAG3 DCM in US is estimated to be as high as 30,000 patients[5,6] 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**




- **Evaluating optimal development pathway**
- **IND submission expected mid-year 2025**



AAV, adeno-associated virus; BAG3, BCL2-associated athanogene 3; DCM, dilated cardiomyopathy; EF, ejection fraction; GFP, green fluorescent protein; IND, investigational new drug; WT, wild type.

1. Hershberger et al., Nat Rev Cardiol, 2013; 2. Petretta et al., Am J Cardiol, 2011; 3. Ackerman et al., Heart Rhythm, 2011; 4. Wilde et al, Europace, 2022; 5.Dominguez et al, JACC, 2018; 6. Martin et al., Circulation, 2024. 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.

# RP-L102 for Fanconi Anemia Complementation Group A

Fanconi Anemia (A, C, and G)

**Market Opportunity[1] – 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[2]

**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[3]
- Predisposition to hematologic malignancies and solid tumors

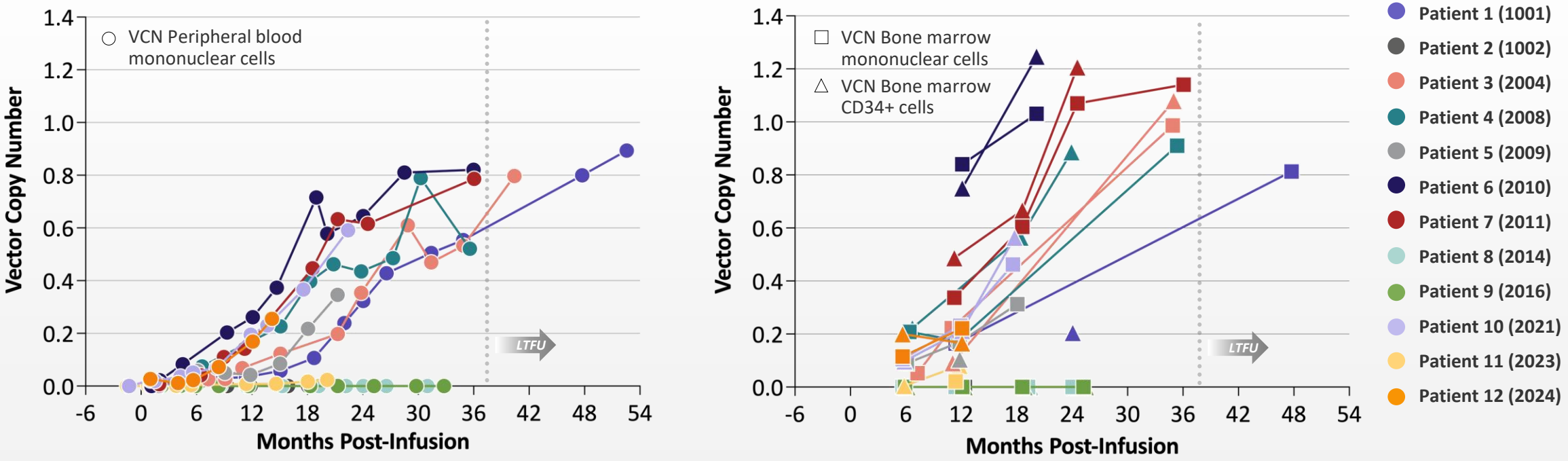
*Gene therapy approach: Selective advantage of corrected cells allows for **ex-vivo LV therapy without conditioning**; highly favorable benefit risk profile*

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.

1. Rocket Pharmaceuticals data on file; 2. Mehta PA, et al. Radiation-free, alternative-donor HCT for Fanconi Anemia patients: results from a prospective multi-institutional study. Blood. 2017;129(16):2308-2315; Fink O, et al. Two decades of stem cell transplantation in patients with Fanconi Anemia: Analysis of factors affecting transplant outcomes. Clin Transplant. 2023;37(1):e14835; 3. Sebert M, et al. Clonal hematopoiesis driven by chromosome 1q/MDM4 trisomy defines a canonical route toward leukemia in Fanconi Anemia. Cell Stem Cell. 2023;30(2):153-170; Kutler DI, et al. A 20-year perspective on the International Fanconi Anemia Registry (IFAR). Blood. 2003;101(4):1249-1256.

# 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; PB, peripheral blood; PBMC, peripheral blood mononuclear cells; VCN, vector copy number.
Data cut-off: September 11, 2023; Preliminary interim results are presented from the ongoing clinical studies.

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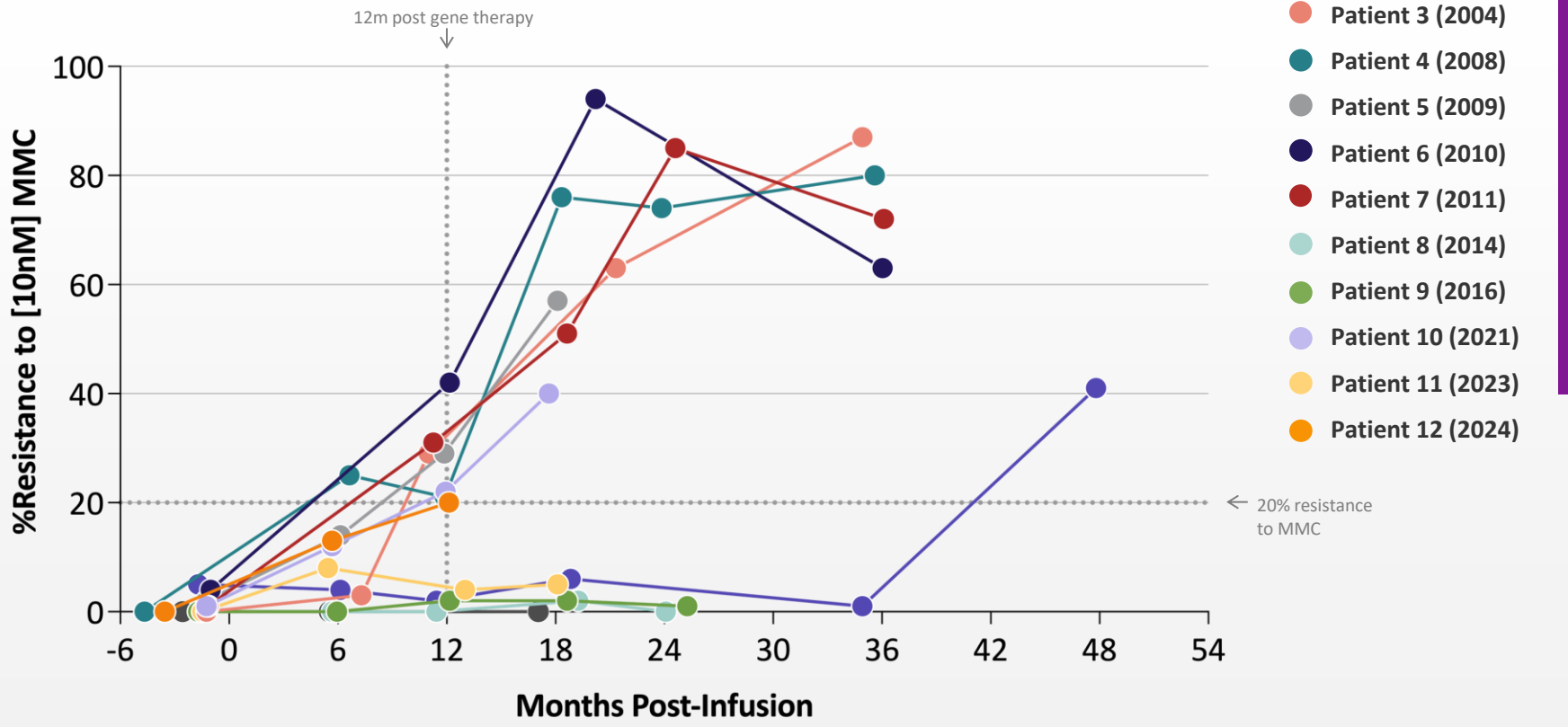
# Increasing Phenotypic Correction over 1 to 3 Years Post RP-L102 in Pivotal Phase 2 Trial

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




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

**For 6 patients, increased MMC-resistance in BM CFU (40% to 94%) was observed 18 to 24 months post RP-L102**

*(confirmatory assessment pending for patient 12)*



BM, bone marrow; CFU, colony-forming units; 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: September 11, 2023; Preliminary interim results are presented from the ongoing clinical studies.

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# Development Plan

## Regulatory Progression Ongoing

### INITIAL EFFICACY AND HIGHLY FAVORABLE SAFETY PROFILE

- 7 of 11 patients evaluable for efficacy are clinical therapeutic successes based on ≥ 18 months of data.*
- No cytotoxic conditioning, only 1 transient RP-L102 related SAE (Grade 2)

### TOP-LINE DATA READOUT ACHIEVED

- Met clinical criterion of at least 5 patients achieving primary composite endpoint, including BM MMC resistance at least 20% at 12 months and confirmed at 18- or 21-months post-infusion.*

### NEXT STEPS

- **MAA submission accepted – under review**
- **Initiated Rolling BLA with the FDA and submission of the final module is anticipated in late 2025/early 2026**

**Additional life-cycle management activities:**

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

**REGULATORY DESIGNATIONS:**

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



ATMP, advanced therapy medicinal product; BLA, Biologics License Application; BM, bone marrow; 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. SAE observed in Rocket-sponsored study.

* Data cut-off: September 11, 2023.

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

**Market Opportunity[1] – 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

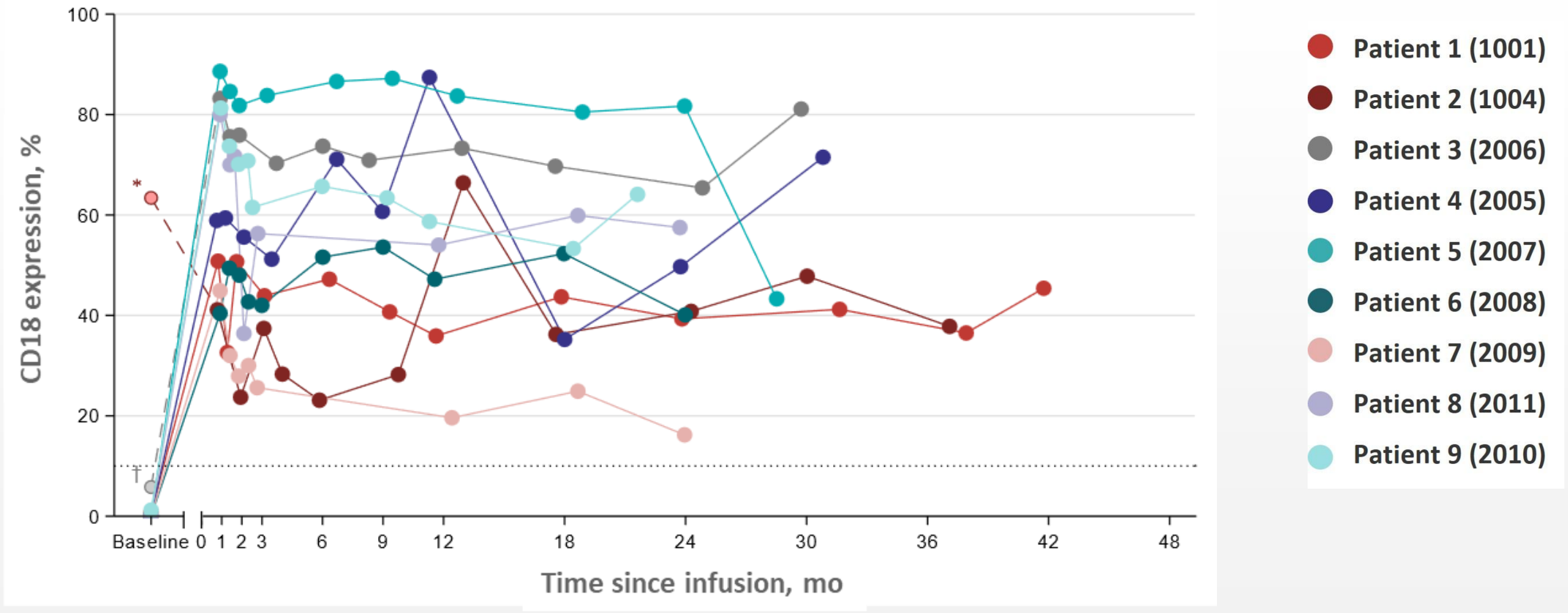
**Patients suffer from recurrent infections; fatal in majority[2]**
- Severe LAD-I: Death prior to age 2 in 60% to 75% of patients, infrequent survival >5 years in absence of allogeneic HSCT
- Moderate LAD-I: Death prior to age 40 in >50% of patients, extensive morbidity with recurrent infections and 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.
1. Rocket Pharmaceuticals data on file; 2. Almarza NE, Kasbekar S, Thrasher AJ, et al.: A comprehensive review of all published cases; 3. J Allergy Clin Immunol Pract. 2018;6(4):1418-1420.e10.

# CD18 Expression in PB Polymorphonuclear Cells in Pivotal Trial

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




Neutrophil CD18 expression is reported utilizing CD18 monoclonal antibody (clone 6.7).
*Baseline dim or weak CD18 neutrophil expression in Patient 2 in 63.4% of cells with CD11a or CD11b neutrophil expression of less than 2% most likely indicates abnormal or unstable protein.
†Baseline CD18 neutrophil expression in Patient 3 in 5.8% of cells with CD11a or CD11b neutrophil expression of less than 2% most likely indicates abnormal or unstable protein.
PB, peripheral blood; PMN, polymorphonuclear neutrophil.
Data cutoff July 24, 2023; results are presented from the on-going clinical trial and interim data from long term follow-up study.
Pt 5 (2007) VCN at 30m timepoint remained stable relative to prior months, consistent with aberrant (artifactually low) CD18 result.
Images used with permission from Booth C, et al. *N Engl J Med.* 2025;392(17):1698-1709.



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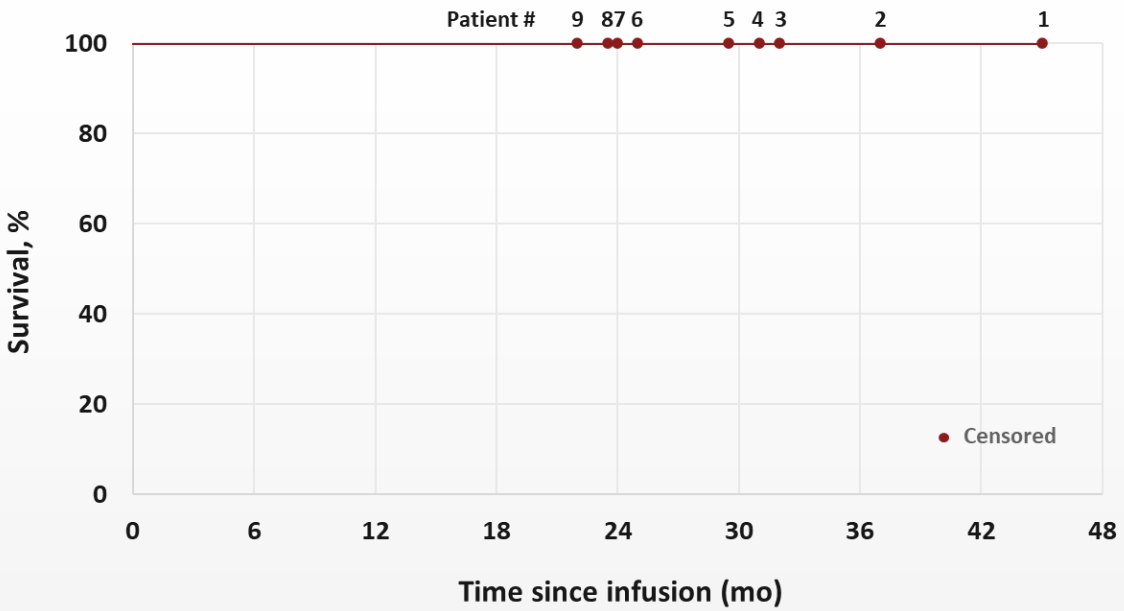
# Reduction in Hospitalizations and 100% HSCT-free Survival in Pivotal Trial

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




## Meaningful reduction in infection-related hospitalizations following immune reconstitution

***Predefined serious infections: annualized event rate†**

| Pre-infusion | >90 d post-engraftment to EoS | Annualized decrease of | |
|---|---|---|---|
| 3.50 | 0.53 | **2.97** (95% CI, -3.72, -2.22) | **85%** reduction |

**Infection-related hospitalizations: annualized event rate**

| Pre-infusion | >90 d post-engraftment to EoS | Annualized decrease of | |
|---|---|---|---|
| 2.07 | 0.53 | **1.54** (95% CI, -2.16, -0.92) | **74%** reduction |

**Prolonged infection-related hospitalizations: annualized event rate**

| Pre-infusion | >90 d post-engraftment to EoS | Annualized decrease of | |
|---|---|---|---|
| 1.46 | 0.26 | **1.20** (95% CI, -1.69, -0.70) | **82%** reduction |

## Survival without allogeneic HSCT

### Primary outcomes

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

- ***Infections that developed beyond 90 days post-infusion were consistent with typical childhood infections*** *frequently observed in immunocompetent (healthy) children*
- ***All patients have been able to stop prophylactic antibiotics*** *(when permitted by institutional policy)*

* Predefined serious infections were those infections requiring hospitalization or parenteral (intravenous) antimicrobials.
† Annualized event rate is calculated as the Total Number of Events / Total Time in each Time Period. Results are adjusted event rate per year. Pre-infusion includes all lifelong medical history prior to RP-L201 infusion. p-values from Poisson regression with event and time period in the model with an offset of log exposure.
CI, confidence interval; d, day; EoS, end of study; HSCT, hematopoietic stem cell transplantation; mo, month.
Data cutoff July 24, 2023; results are presented from the on-going clinical trial and interim data from long term follow-up study.
Adapted from Booth C, et al. *N Engl J Med.* 2025;392(17):1698-1709.



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# Development Plan

## FDA Review Ongoing

### 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

- **Submission of complete BLA to resolve CRL anticipated in 2025**
- **Establish therapy as a safe and effective treatment option for LAD-I patients**
- **Create a commercial infrastructure that can be leveraged for future programs and franchises**

**Life-cycle management**

- Potential label expansion to include moderate LAD-I population

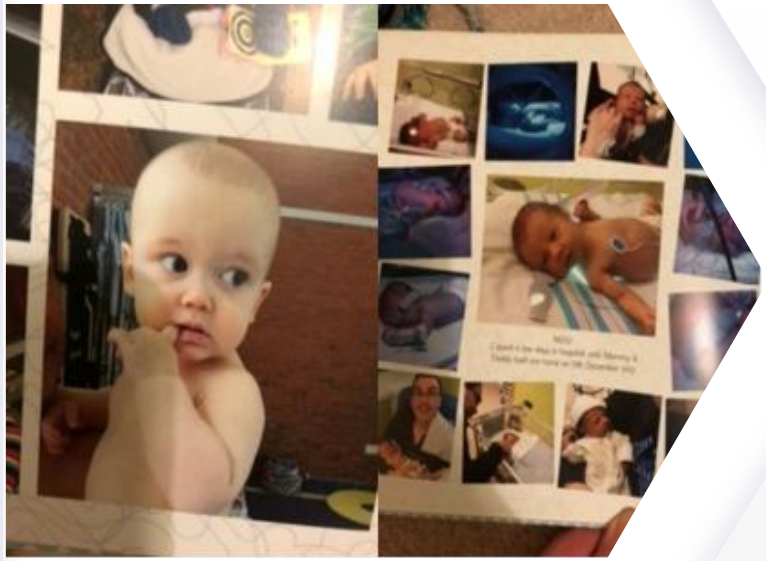
**REGULATORY DESIGNATIONS:**

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



ATMP, Advance Therapy Medicinal Products; CRL, Complete Response Letter; FDA, Food and Drug Administration; GvHD, graft versus host disease; NHS, National Health Service; PKD, pyruvate kinase deficiency; PRIME, Priority Medicines; PRV, priority review voucher; RMAT, Regenerative Medicine Advanced Therapy; SAEs, serious adverse events.

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



**Market Opportunity[1] – US and EU**

Prevalence of **4,000 to 8,000** individuals

Annual incidence of **75 to 125** individuals

## Disease etiology[2]

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

## Therapeutic challenges[3]

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

## Clinical manifestations[4]

- 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.

1. Rocket Pharmaceuticals data on file; 2. Tanaka K, et al. Pyruvate kinase (PK) deficiency hereditary nonspherocytic hemolytic anemia. Blood. 1962;19(3):267-295; 3. Zanella A, et al. Iron status in red cell pyruvate kinase deficiency: study of Italian cases. British Journal of Haematology. 1993;83(3):485-490; Zanella A, et al. Molecular characterization of thePK-LR gene in sixteen pyruvate kinase-deficient patients. Br J Haematol. 2001;113(1):43-48; Marshall SR, et al. The dangers of iron overload in pyruvate kinase deficiency. Br J Haematol. 2003;120(6):1090-1091; 4. Zanella A, et al. E. Pyruvate kinase deficiency. Haematologica. 2007;92(6):721-723; Grace RF, et al. Erythrocyte pyruvate kinase deficiency: 2015 status report. American J Hematol. 2015;90(9):825-830; Canu G, et al. Red blood cell PK deficiency: an update of PK-LR gene mutation database. Blood Cells, Molecules, and Diseases. 2016;57:100-109.



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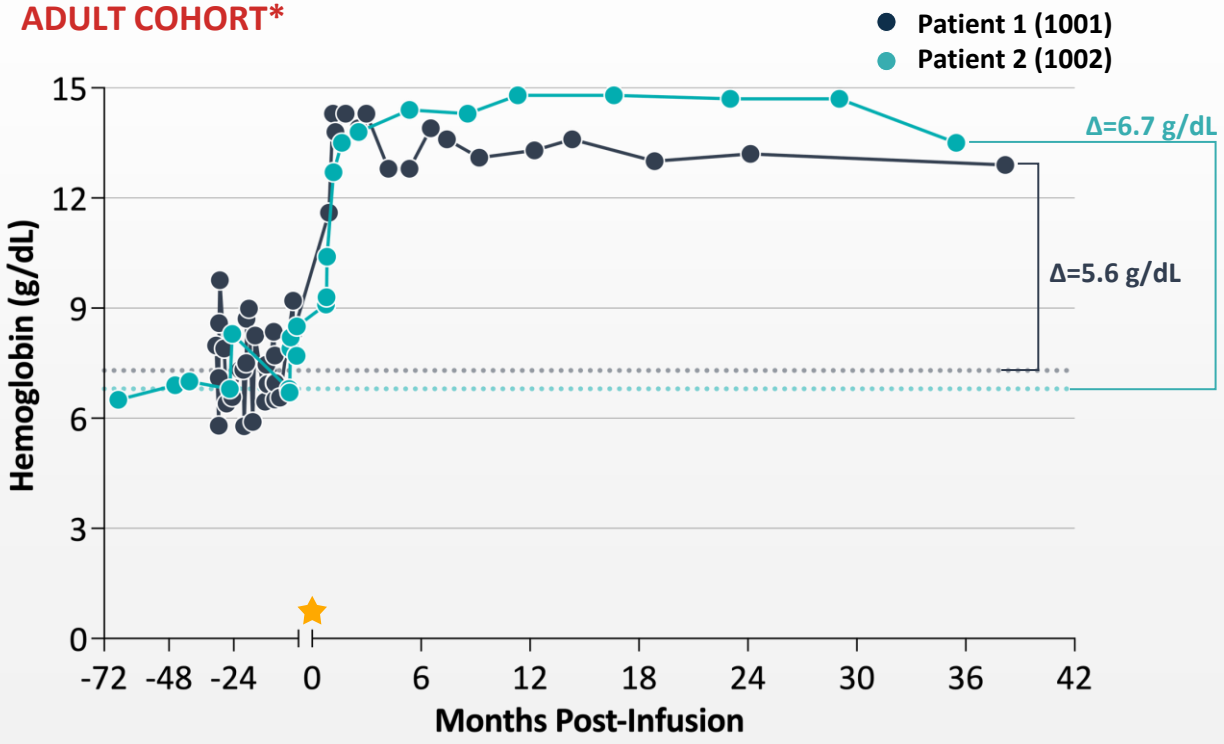
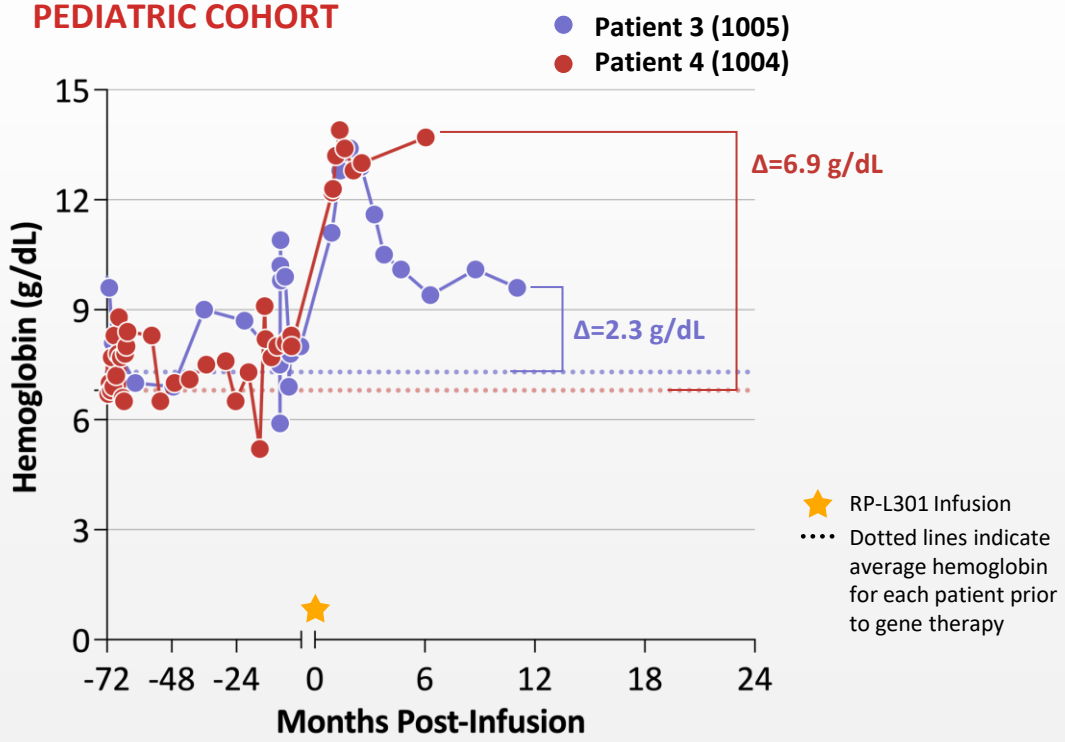
# Preliminary Phase 1 Efficacy Results: Adult and Pediatric Patients

- Sustained & meaningful hemoglobin improvement from severe (<8 g/dL) baseline
- No RBC transfusions required following neutrophil engraftment
- Concurrent improvement across hemolysis biochemical markers

## ADULT COHORT*




## PEDIATRIC COHORT




The average baseline Hb is determined by Hb values from 2y prior to enrollment to immediately prior to stem cell mobilization, excluding those impacted by RBC tx. Post-transfusion Hb values within 61d of a prior RBC tx were excluded unless the reported Hbb value was a pre-tx assessment for a subsequent RBC tx within 3 days of the prior RBC tx date.
RBC, red blood cell. *Adult patient 2 underwent therapeutic phlebotomy 27 months through 36 months after gene therapy.
Data cut-off: February 5, 2024; preliminary interim results are presented from the ongoing clinical study.

# 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**



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

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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, hemetology 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; CV, cardiovascular; MOA, mechanism of action; R&D, research and development.

# 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 · Brigham and Women's Hospital Founding Member, Mass General Brigham · Lilly

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

Pfizer · AstraZeneca · Roche · Bristol Myers Squibb · NOVARTIS

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

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

**Aaron Ondrey**
Chief Financial Officer
20+ years of experience in commercial finance, strategic planning, and M&A across multiple therapeutic areas

MIRATI THERAPEUTICS · ALEXION AstraZeneca Rare Disease · REGENERON SCIENCE TO MEDICINE

**Sarbani Chaudhuri**
Chief Commercial & Medical Affairs Officer
20+ years of experience driving commercial growth for rare cardiac and hematology launches

Johnson&Johnson · AstraZeneca · Pfizer · NOVARTIS

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

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**Gayatri R. Rao, M.D., J.D.**
Chief Regulatory Officer & SVP, Clinical Safety
7-year former Director of FDA's Office of Orphan Products Development

U.S. FOOD & DRUG ADMINISTRATION · SIDLEY

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

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

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

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# THANK YOU!

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