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

# FORM 8-K

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

Date of Report (Date of earliest event reported): September 9, 2022

# Rocket Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

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

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

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

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

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

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

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

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

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

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

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

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

Emerging growth company ☐

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

**Item 8.01. Other Events.**

On September 9, 2022, Rocket Pharmaceuticals, Inc. (the "Company") updated information reflected in a slide presentation, which is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. Representatives of the Company intend to use the updated presentation in meetings with investors from time to time.

**Item 9.01. Financial Statements and Exhibits.**

**(d) Exhibits.**

| | |
|---|---|
| 99.1 | Investor Presentation of Rocket Pharmaceuticals, Inc. |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document). |

**SIGNATURES**

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

**Rocket Pharmaceuticals, Inc.**

Date: September 9, 2022

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


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SEEKING GENE THERAPY CURES

# DISCLAIMER

Various statements in this release concerning Rocket's future expectations, plans and prospects, including without limitation, Rocket's expectations regarding its guidance for 2022 in light of COVID-19, the safety, effectiveness and timing of product candidates that Rocket may develop, to treat Fanconi Anemia (FA), Leukocyte Adhesion Deficiency-I (LAD-I), Pyruvate Kinase Deficiency (PKD), and Danon Disease, and the safety, effectiveness and timing of related pre-clinical studies and clinical trials and related data readouts, may constitute forward-looking statements for the purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995 and other federal securities laws and are subject to substantial risks, uncertainties and assumptions. You should not place reliance on these forward-looking statements, which often include words such as "believe," "expect," "anticipate," "intend," "plan," "will give," "estimate," "seek," "will," "may," "suggest" or similar terms, variations of such terms or the negative of those terms. Although Rocket believes that the expectations reflected in the forward-looking statements are reasonable, Rocket cannot guarantee such outcomes. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Rocket's ability to monitor the impact of COVID-19 on its business operations and take steps to ensure the safety of patients, families and employees, the interest from patients and families for participation in each of Rocket's ongoing trials, our expectations regarding when clinical trial sites will resume normal business operations, our expectations regarding the delays and impact of COVID-19 on clinical sites, patient enrollment, trial timelines and data readouts, our expectations regarding our drug supply for our ongoing and anticipated trials, actions of regulatory agencies, which may affect the initiation, timing and progress of pre-clinical studies and clinical trials of its product candidates, Rocket's dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the section entitled "Risk Factors" in Rocket's Annual Report on Form 10-K for the year ended December 31, 2021, filed February 28, 2022 with the SEC and subsequent filings with the SEC including our Quarterly Reports on Form 10-Q. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and Rocket undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.



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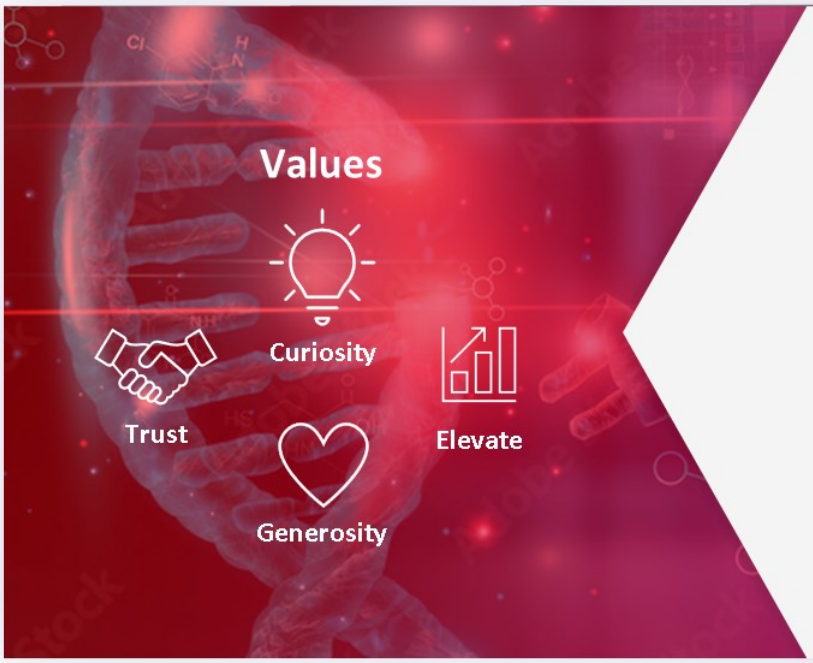
# ABOUT ROCKET PHARMACEUTICALS

"For the first time in history, **we are discussing not just effective treatments but potential cures at the genetic level**, which is the deepest essence of who we are as physical beings."

— GAURAV SHAH, MD | CEO

# **Vision:** Seeking Gene Therapy Cures




## Mission

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



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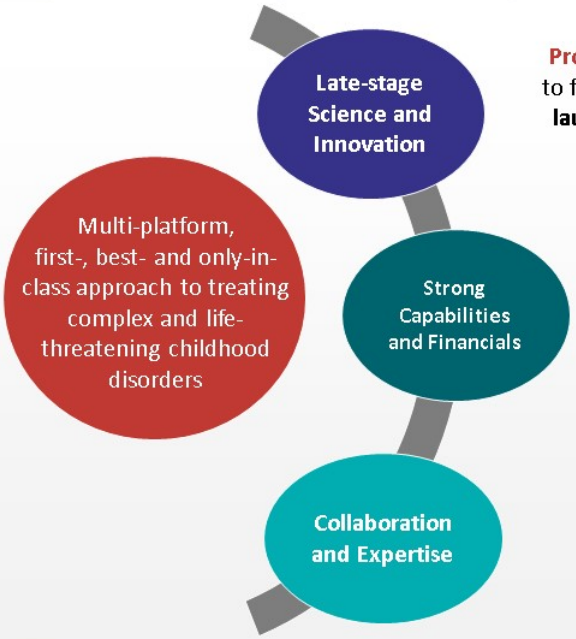
# Generating **Value-based** Gene Therapies




**Promising top-line clinical data** designed to facilitate **US & European registration & 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 ft²**
US-based in-house facility dedicated to AAV cGMP manufacturing

**$321M**
in cash and cash equivalents

Leadership team with proven track record
**20+**
drug approvals and launches

**World-class scientific experts** and partners learning from and collaborating with **patient communities**



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# **Expert** Leadership With Proven Track Record

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

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

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

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

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

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

**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

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

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

**Jessie Yeung, MBA**
Investor Relations & Corporate Finance, VP
15+ years investor relations, corporate finance and capital market experience

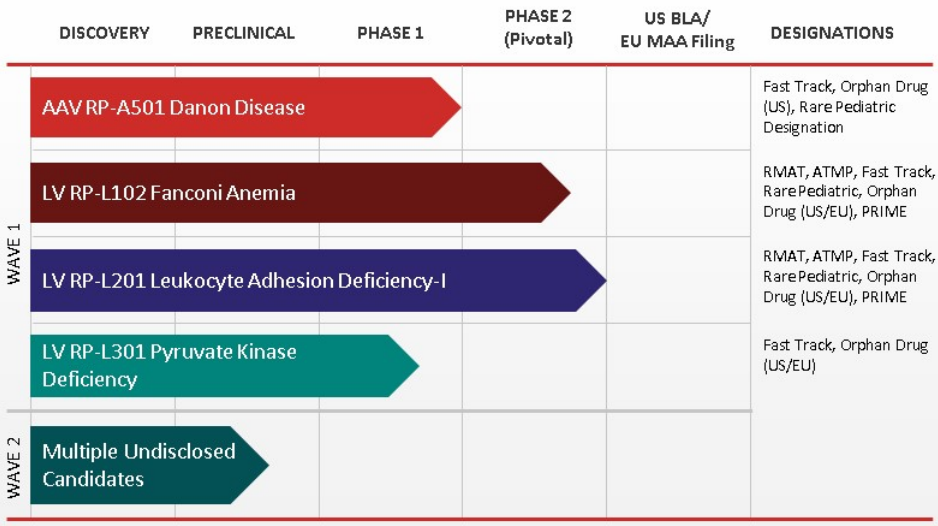
**Peggy Speight**
Head of Quality Assurance, VP
20+ years quality assurance and regulatory compliance expertise gained in pharma and at FDA

# Strong Science, Carefully-selected Assets and Smart Execution:
## Four Programs With Compelling Clinical POC

### Criteria used to select programs

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

### Four programs with compelling clinical proof of concept




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.
Data on file. Rocket Pharmaceuticals. 2022.

# Developing **First-, Best- and Only-in-Class** Therapies for Rare Diseases With Extensive Unmet Needs

## Strong science, carefully-selected assets and smart execution

- Right technology for the target
- Clean MOAs: correct proteins are made in correct cells for disorders caused by single gene mutations
- Well-defined, achievable endpoints
- In-house AAV cGMP manufacturing with capabilities to support commercial products and scaling

## Proven management expertise

- Strong drug development track record, successful BLA filings
- Engagement with health authorities to outline a predictable review pathway
- HEOR work to inform value-based pricing strategy
- Creation of "go-to commercial" infrastructure

## Near term inflection points drive value

**2022**

**Q2**

- ✓ Achieve in-house AAV (cGMP) readiness
- ✓ **LAD-I**: Pivotal Phase 2 data
- ✓ **FA**: Phase 2 primary endpoint readout

**Q3**

- **Danon**: Phase 1 pediatric cohort data

**Q4**

- **Danon**: Initiate Phase 2 pivotal trial activities
- **FA**: Potential guidance on BLA filing timeline
- **PKD**: Phase 1 data

**2023**

- **LAD-I, FA**: BLA/MAA filings
- **PKD**: Initiate Phase 2 pivotal trial activities
- Wave 2 pipeline enters clinic



AAV, adeno-associated virus; BLA, Biologics License Application; cGMP, current Good Manufacturing Processes; FA, Fanconi Anemia; H1, first half of the year; HEOR, health, economics and outcomes research; LAD-I, Leukocyte Adhesion Deficiency-I; MOA, mechanism of action; PKD, Pyruvate Kinase Deficiency; Q2, second quarter of the year; Q3, third quarter of the year; Q4, fourth quarter of the year.
Data on file. Rocket Pharmaceuticals. 2022.

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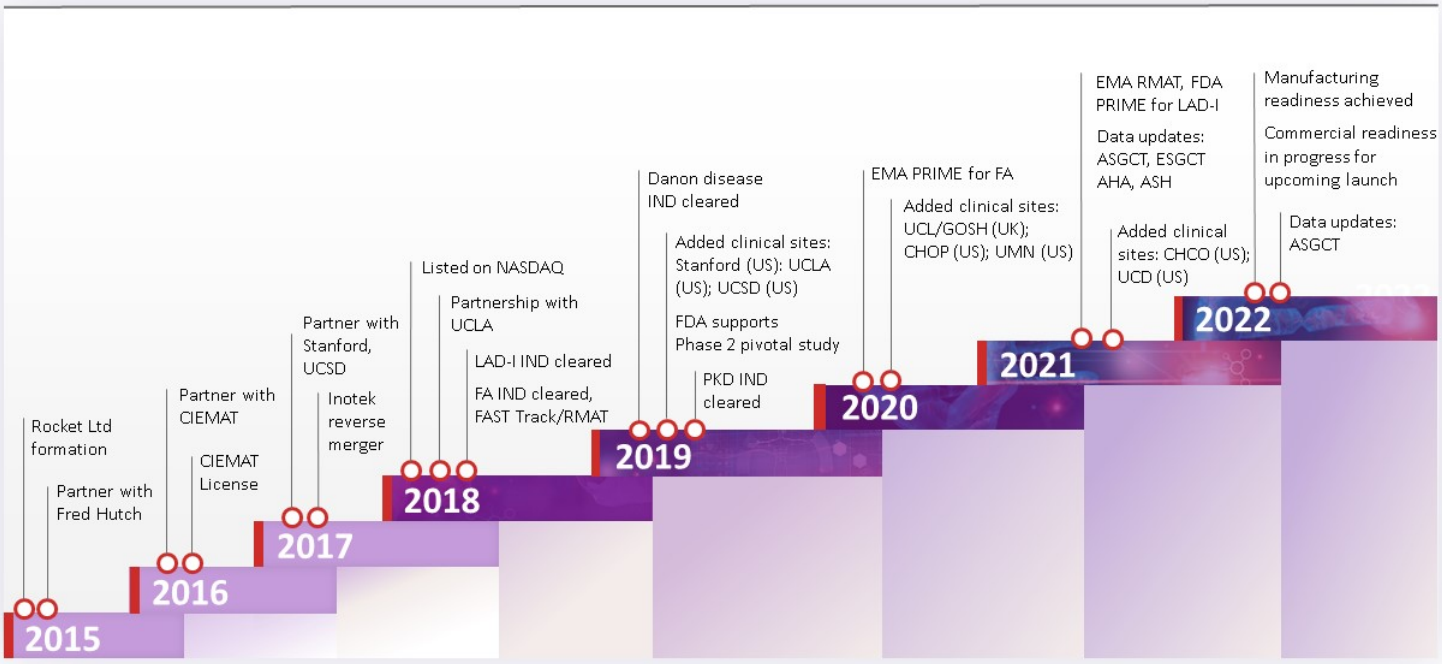
# **Strategically Building** a Leading Gene Therapy Company






ASGCT, American Society of Gene & Cell Therapy; ASH, American Society of Hematology; CHCO, Children's Hospital of Colorado; CHOP, Children's Hospital of Philadelphia; CIEMAT, Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas; EMA, European Medicines Agency; ESGCT, European Society for Gene and Cell Therapy; FA, Fanconi Anemia; FDA, Food and Drug Administration; IND, Investigational New Drug; LAD-I, Leukocyte Adhesion Deficiency-I; PKD, Pyruvate Kinase Deficiency; PRIME, PRIority MEdicines; RMAT, Regenerative Medicine Advanced Therapy; UCLA, University of California, Los Angeles; UCSD, University of California San Diego; UCD, University of Colorado, Denver; UMN, University of Minnesota. Data on file. Rocket Pharmaceuticals. 2022.

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# Strong, Strategic Approach to **Gene Therapy Manufacturing**

## In-house capabilities

**AAV cGMP**
manufacturing with capabilities to support commercial products and scaling

**Process Development, Analytics and QC testing**

Streamlined manufacturing capabilities to allow for
**cost-effective commercialization**

**~100,000 ft²**
facility in Cranbury, NJ



AAV, adeno-associated virus; cGMP, current Good Manufacturing Processes.
Data on file. Rocket Pharmaceuticals. 2022.

# World-class **Scientific Experts** and Partners

Ciemat

UCL

UCLA

FRED HUTCH

Children's Hospital of Philadelphia

IIS FJD INSTITUTO DE INVESTIGACIÓN SANITARIA FUNDACIÓN JIMÉNEZ DÍAZ

NHS Great Ormond Street Hospital for Children NHS Foundation Trust

REGENXBIO

University of Colorado

Penn

Stanford Medicine

Hospital Infantil Universitario Niño Jesús

UC San Diego

University of Minnesota

Fundación Jiménez Díaz

CIRM CALIFORNIA STEM CELL AGENCY

ciber



Data on file. Rocket Pharmaceuticals. 2022.

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# UNMET NEEDS AND MARKET

"Caring for someone with Danon, while you, yourself have Danon is very hard. Most days we are at clinic appointments or having a procedure done to check on our hearts. The other times we are at home dealing with chest pain, rapid heart rates, muscle pains and learning issues in school. With each new day we have a renewed hope that with time and clinical trials we will be able to someday cure this rare and deadly disease."

— DANON DISEASE PATIENT AND MOTHER OF TWO BOYS LIVING WITH DANON

"We never went through the bone marrow transplant route and only had to deal with cancer and the complications associated with chemotherapy and radiation therapies. We lost two children…to this awful condition. May future research yield positive outcomes."

— FATHER OF TWO CHILDREN WITH FANCONI ANEMIA

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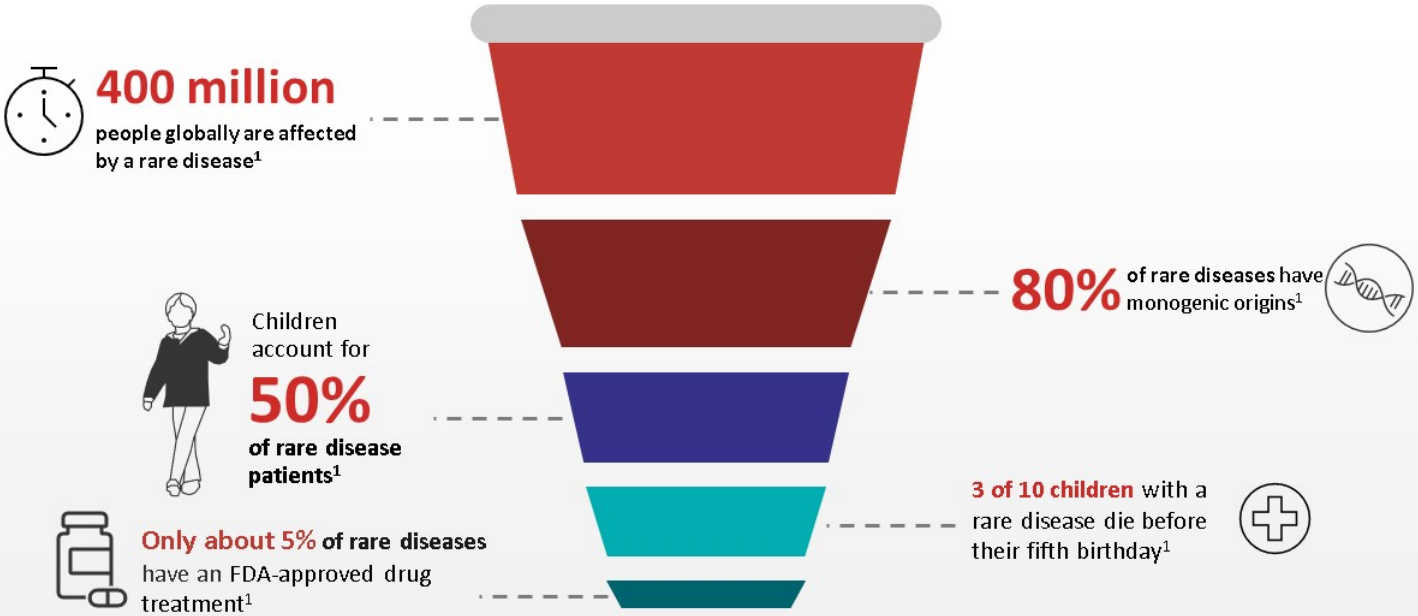
# Rare Diseases Are Associated With a Reduced Lifespan[1]






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

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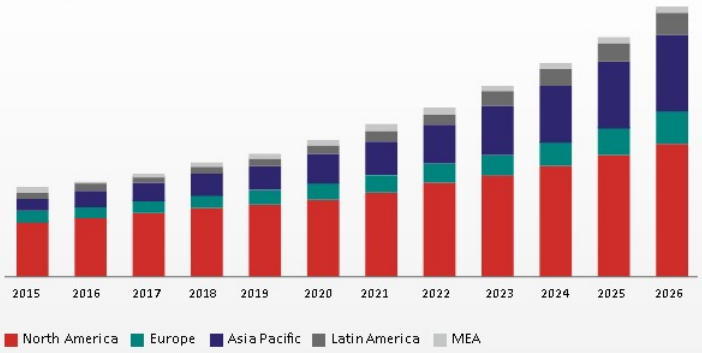
# Market for Rare Disease Treatment Is **Rising**

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




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

Biologics Non-biologics

- 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



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

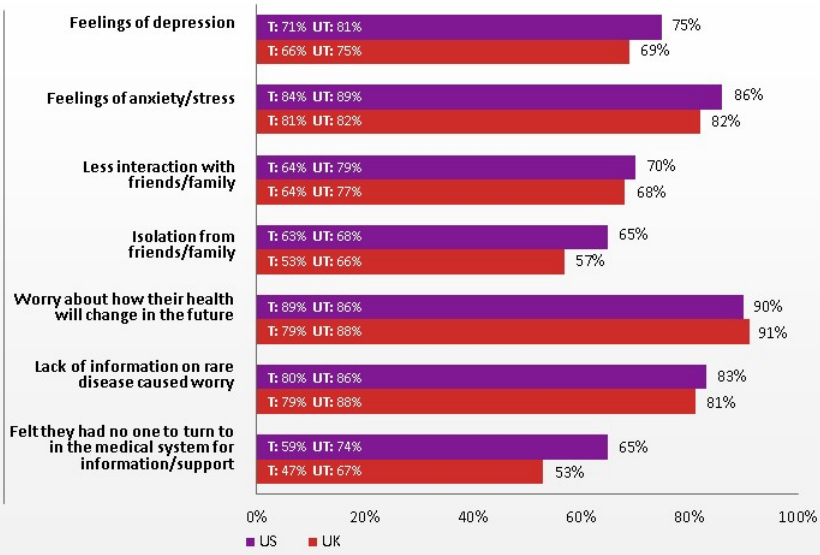
## Economic impact[1]

**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** range between **$600K** and **$1.5M** respectively, plus **$50k** to **150K** annually in associated costs[3]

## 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 2. Every Life Foundation for Rare Diseases. Accessed April 2022. https://everylifefoundation.org/wp-content/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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# PIONEERING GENE THERAPY CLINICAL PROGRAMS

"Due to the high unmet need, there is significant interest within the FA community from both patients and health care providers for an alternative low-toxicity therapy to address and, more specifically, prevent BMF. Overall, the investigational gene therapy – administered with a preventative intent and requiring no cytotoxic conditioning therapy – represents a compelling potential option for FA patients, even though this approach requires a more protracted time interval (i.e., 1-3 years) for recognition of phenotypic, genetic, and hematologic correction, relative to allogeneic HSCT."

— PRINCIPAL INVESTIGATOR OF ROCKET'S FA PROGRAM

"During the kids' entire childhood they had multiple infections – 'you name it they had it' – and were admitted to the hospital several times due to these infections. Since treatment, the kids are back in day care and have scraped their knees – but unlike their experience before gene therapy, this has not resulted in infections. This therapy "saved their lives" and without it don't know whether or not the kids would be alive at present. The therapy gave hope and hope that it will be available for other kids with severe LAD-I."

— FATHER OF THREE CHILDREN WITH SEVERE LAD-I

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

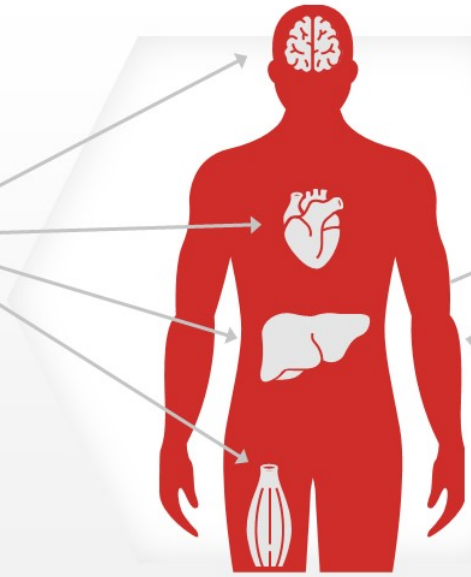
## IN VIVO platform

Laboratory-produced AAV

Therapeutic AAV

Direct intravenous injection

**RP-A501:** Danon Disease



## 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



AAV, Adeno-Associated Virus; LV, Lentiviral Vector.
Data on file. Rocket Pharmaceuticals. 2022.

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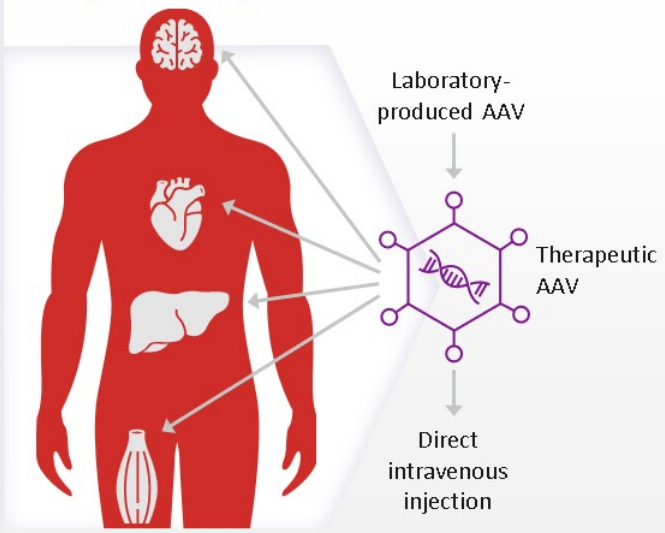
# **In Vivo Platform**: Adeno-associated Virus (AAV)

**IN VIVO (inside the body)**
**AAV gene therapy**




**DANON DISEASE**

*Multi-system disorder with severe cardiomyopathy*

- Transduction of non-dividing, terminally differentiated cardiomyocytes
- AAV9 serotype has been shown to have a particular propensity for cardiomyocytes
- rAAV9-vector DNA expresses *LAMP2B* gene
- Long-term durable expression anticipated because cardiomyocytes have minimal cell turnover

**IDEAL FOR**

AAV platform ideal for disorders that affect the heart, liver, eye or central nervous system

**GOAL**

Express an adequate quantity of normal protein to normalize cardiomyocyte structure and function



*Different AAV serotypes differ in their tropism, or the types of cells they infect, making AAV a very useful system for preferentially transducing specific cell types.
AAV, Adeno-Associated Virus; LAMP2B, Lysosome-Associated Membrane Protein 2B; rAAV9 , Recombinant Adeno-Associated Virus Serotype 9
Data on file. Rocket Pharmaceuticals. 2022.

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# RP-A501 for Danon Disease: *LAMP2B* Gene Mutation

## Disease etiology

- **LAMP2 mutation**
- **Autosomal dominant, monogenic X-linked disease**

## Therapeutic challenges

- **Standard of care:**
  - Heart transplant
- **Limitations:**
  - Considerable morbidity and mortality
  - Not curative
  - Available to ~20% of patients

## Cellular pathology

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

## Clinical manifestations

- **Severe cardiomyopathy**
  - Mortality secondary to heart failure or arrhythmia
  - Males: Aggressive disease course, median overall survival: 19 years
  - Females: Delayed presentation (~20 years) due to additional X chromosome; highly morbid & fatal disorder
- **Other clinical manifestations**
  - Skeletal myopathy
  - CNS manifestations
  - Ophthalmologic manifestations

**Market Opportunity – US and EU**

Prevalence of **15,000 to 30,000** individuals

Annual Incidence of **800 to 1,200** individuals



CNS, central nervous system; LAMP2B, lysosome-associated membrane protein 2B; MOA, mechanism of action.

Boucek D et al. *Genet Med.* 2011;13(6):563-568.

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# **First** AAV Program in History to Address Monogenic Cardiomyopathy

## Description

Recombinant AAV9 containing the human *LAMP2B* transgene

## Clinical study

N=7 (Phase 1)

**Primary endpoints:**

- Safety
- Cardiomyocyte transduction, LAMP2B protein expression, histologic normalization
- Clinical stabilization or improvement

**Selected secondary endpoints:**

- Sustained stabilization or improvement in CV pathophysiology
- Sustained stabilization or improvement in echocardiographic, serologic and other clinical parameters of heart failure
- Overall survival

## Key efficacy data

Efficacy in low-dose adult cohort:

- Robust LAMP2B cardiac expression
- Decreased BNP
- Improved ventricular wall thickness
- Improved NYHA class
- Stable or improved cardiac function

## Safety

- Manageable safety profile
- Enhanced immunomodulatory regimen for pediatric cohort associated with:
  - Limited side effects
  - Mitigation of AEs observed in low- and high-dose adult cohorts

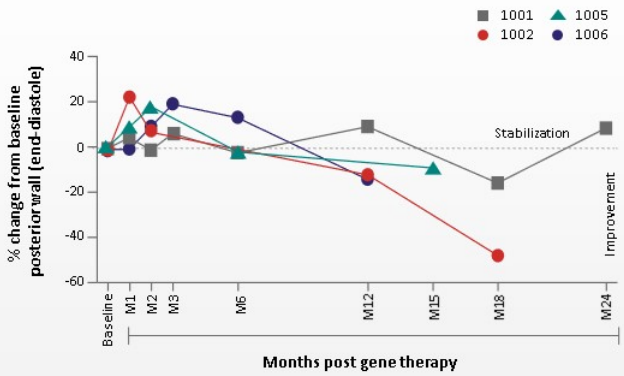


6MWT, 6-minute walk test; AVV, adeno-associated virus; BNP, B-type natriuretic peptide; CV, cardiovascular; LAMP2B, lysosome-associated membrane protein 2B; NYHA, New York Heart Association.
Data on file. Rocket Pharmaceuticals. 2022.

# Reduction in Heart Wall Thickness Indicates Cardiac Remodeling

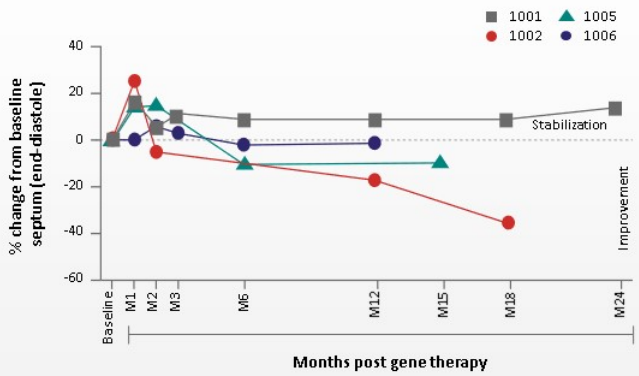
## Treated patients show stabilization or improvement in LV wall and septal wall thickness compared to untreated† males with Danon disease

Posterior wall thickness in RP-A501–treated patients*




**Danon Disease Natural History:** LV posterior wall thickens by 0.74 ± 0.12 mm/year in untreated Danon males

Septal thickness in RP-A501–treated patients*




**Danon Disease Natural History:** septal wall thickens by 0.92 ± 0.15 mm/year in untreated Danon males*

*All echocardiographic parameters from local laboratory assessment; posterior wall: LVPWd, Septal wall: IVS. †Unpublished data from International Danon Disease Registry (not pictured on current slide).
IVS, interventricular septum; LV; left ventricular; LVPWd, left ventricular posterior wall end diastole.
Data on file. Rocket Pharmaceuticals. 2022.



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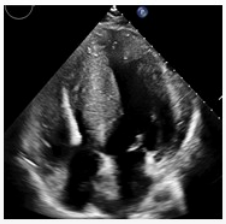
# **Reduction in Heart Wall Thickness** Indicates Cardiac Remodeling

**Baseline**


**Month 15**



**Representative images from patient 1005**



All echocardiographic parameters are from local laboratory assessment by a single reader.

# Improved Cardiac Function Across Dose Levels

## Stabilization or improvement of cardiac biomarkers and functional status is seen across treatment cohorts

| Cohort | Patient ID | Age at enrollment (years) | Variable | Baseline | Most recent follow-up | Time of follow-up (months) |
|---|---|---|---|---|---|---|
| Adult – Low dose | 1001* | 17.5 | NYHA class | II | II | 24 |
| | | | BNP (pg/mL) | 70 | 30 | |
| | | | 6MWT (meters) | 443 | 467 | |
| | 1002 | 20.4 | NYHA class | II | I | 18 |
| | | | BNP (pg/mL) | 942 | 200 | |
| | | | 6MWT (meters) | 405 | 410 | |
| | 1005 | 18.3 | NYHA class | II | I | 15 |
| | | | BNP (pg/mL) | 176 | 44 | |
| | | | 6MWT (meters) | 427 | 435 | |
| Adult – High dose** | 1006 | 21.1 | NYHA class | II | I | 12 |
| | | | BNP (pg/mL) | 123 | 41 | |
| | | | 6MWT (meters) | 436 | 492 | |



*Corticosteroid compliance not closely monitored in initial patient.
6MWT, 6-minute walk test; BNP, brain natriuretic peptide; NYHA, New York Heart Association.
Data on file. Rocket Pharmaceuticals. 2022.

**Patient 1007 underwent heart transplant at 5 months for progressive Danon Disease, thus no subsequent data reported

# Improved Protein Expression Across Dose Levels

## Endomyocardial LAMP2B protein expression is seen across dose levels

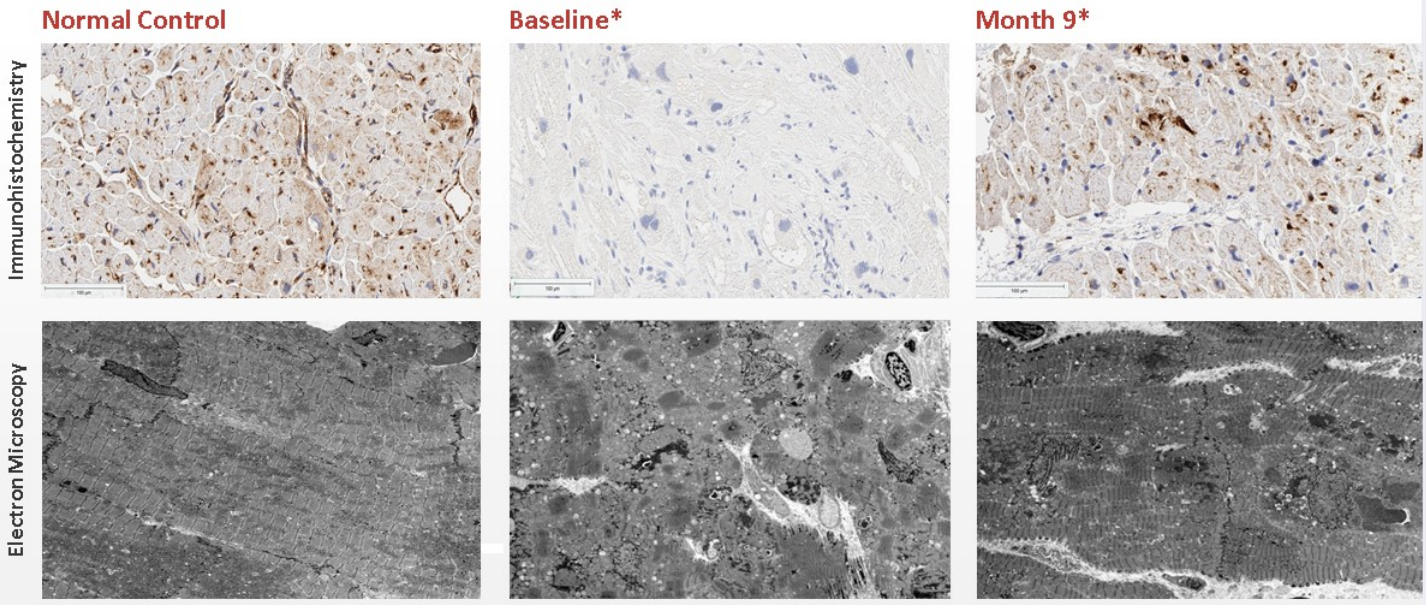
| Cohort | Patient ID | LAMP2B protein expression (by IHC)* Month 12 | LAMP2B protein expression (by Western Blot) Month 5-18 |
|---|---|---|---|
| Adult – Low dose | 1001† | 2.5% (previously <15%)[a] | 17.9%[d] |
| | 1002 | 67.8% | 21.2%[e] |
| | 1005 | 92.4%[b] | 61.1%[f] |
| Adult – High dose | 1006 | 100% | 18.2%[d] |
| | 1007 | 100%[c] | RV: 45.1%[g]<br>LV: 44.0%[g] |

[a]Previously disclosed as a range due to high variance, now clarified.
[b]Month 9 data.
[c]Explant sample at Month 5.
[d]Month 6 data; inadequate sample at Month 12.
[e]Month 18 data; inadequate sample at Month 12.
[f]Month 9 data.
[g]Explanted heart; Month 5 data.



*Endomyocardial biopsies stained for LAMP2 compared to normal control samples. Percent area of cell staining was quantitated using software in a blinded fashion from 2 to 14 sections.
†Patient 1001 was only locally monitored for compliance for two weeks; longer compliance monitoring initiated after 1001 Qualitative assessment reported for samples with high variance.
IHC, immunohistochemistry; LAMP2, Lysosomal Associated Membrane Protein 2; LAMP2B, lysosome-associated membrane protein 2B; LV, left ventricle; RV, right ventricle.
Data on file. Rocket Pharmaceuticals. 2022.

## **Robust LAMP2 Cardiac Protein Expression** by Immunohistochemistry
## **Vacuole Reduction** and **Restored Myofibrillar Structure** by Electron Microscopy






* Representative images from patient 1005: endomyocardial biopsy

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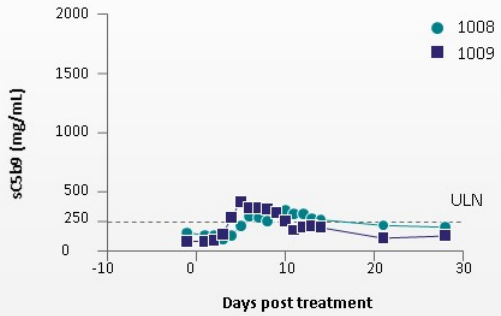
# Manageable Safety Profile

## Enhanced immunomodulatory regimen for pediatric cohort was associated with limited side effects: Mitigation of AEs observed in low- and high-dose adult cohorts

### Limited complement activation
### Low dose pediatric cohort
Rituximab + Corticosteroids + Sirolimus




**Platelets remain in normal range for 2 of 2 pediatric patients**

**Rituximab + Corticosteroids + Sirolimus**

- Minimal complement activation and ↓ potential for TMA
- Early steroid taper and no exacerbation of Danon disease-associated skeletal myopathy

**Enhanced risk management plan: Safety results**

- Infusion well tolerated with no drug-related SAEs
- Mitigation of complement activation as evidenced by normal-range platelets, hemoglobin and creatinine
- Baseline skeletal myopathy was not significantly exacerbated post treatment
- Patients have been clinically stable



AE, adverse event; SAE, serious adverse event; TMA, thrombotic microangiopathies; ULN, upper limit of normal.
Data on file. Rocket Pharmaceuticals. 2022.

# Development Plan

## Moving toward pivotal Phase 2 study

**CURRENT**

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

**PLANNED**

- Pediatric cohort update in late Q3 2022
- Expanded natural history study
- End of Phase 1 Regulatory meeting with FDA
- Initiate Phase 2 Global Pivotal Study Activities
- Initiate female study

**PLANNED GLOBAL REGISTRATIONAL PHASE 2 STUDY**



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

# Ex Vivo Platform: Lentiviral Vector (LV)

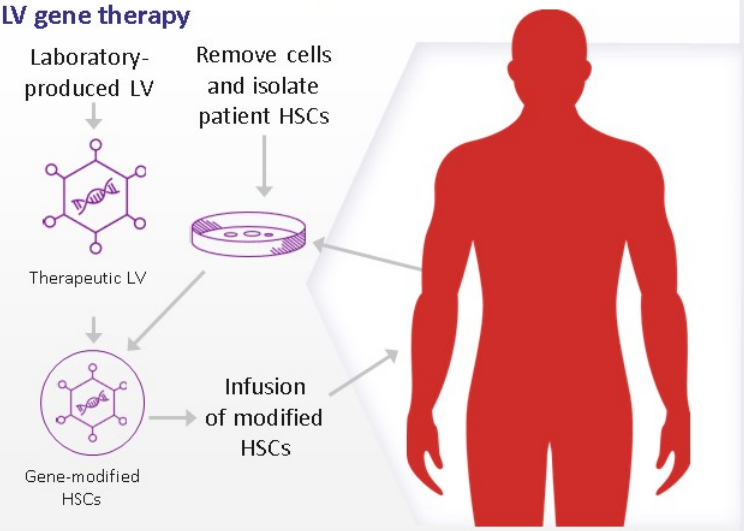
### Fanconi Anemia, Leukocyte Adhesion Deficiency-I and Pyruvate Kinase Deficiency

- HSCs transduced with a lentiviral vector carrying the corrected gene and infused following transduction
- Transduction process occurs ex vivo, ensuring the gene has been properly integrated before the therapy is given to the patient
- Corrected HSCs engraft in bone marrow, and repopulate marrow and blood with functional hematopoietic cells capable of reversing disorder

**IDEAL FOR**
Modifying HSCs to address hematologic and immune disorders

**GOAL**
Promote sufficient quantities of a healthy therapeutic protein to be manufactured by patients' own blood cells

### EX VIVO (outside the body) LV gene therapy






HSC, hematopoietic stem cell; LV, lentiviral vector.
Data on file. Rocket Pharmaceuticals. 2022.

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

**Fanconi Anemia (A, C, & 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 60-70% 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
  - Congenital abnormalities



BMF, bone marrow failure; FA, Fanconi Anemia; FA-A, Fanconi Anemia, group A; FANC, Fanconi Anemia complementation group; GvHD, graft-versus-host disease; HLA, human leukocyte antigen; HSCT, hematopoietic stem cell transplantation; MOA, mechanism of action.

Alter BP et al. *Br J Haematol.* 2010;150(2):179-188.

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# Clinical Studies Overview

## Description

Autologous HSCs transduced with LV carrying *FANCA* transgene
Conditioning is not required because gene-corrected HSCs display proliferative advantage over time

## Clinical studies

- EU FANCOLEN I study (N=9) completed
- US Phase 1 study (N=2) completed
- US Phase 2 study ongoing
- EU Phase 2 study ongoing

## Primary endpoints*:

- Engraftment (VCN)
- Phenotypic correction (BM MMC-resistance)
- Prevention of BMF (blood count stability)

## Safety

- No conditioning
- No dysplasia, clonal dominance or oncogenic integrations
- 1 RP-L102 related SAE: infusion-related reaction (transient, Grade 2)

## Key efficacy data

**12 patients**
Enrolled and treated

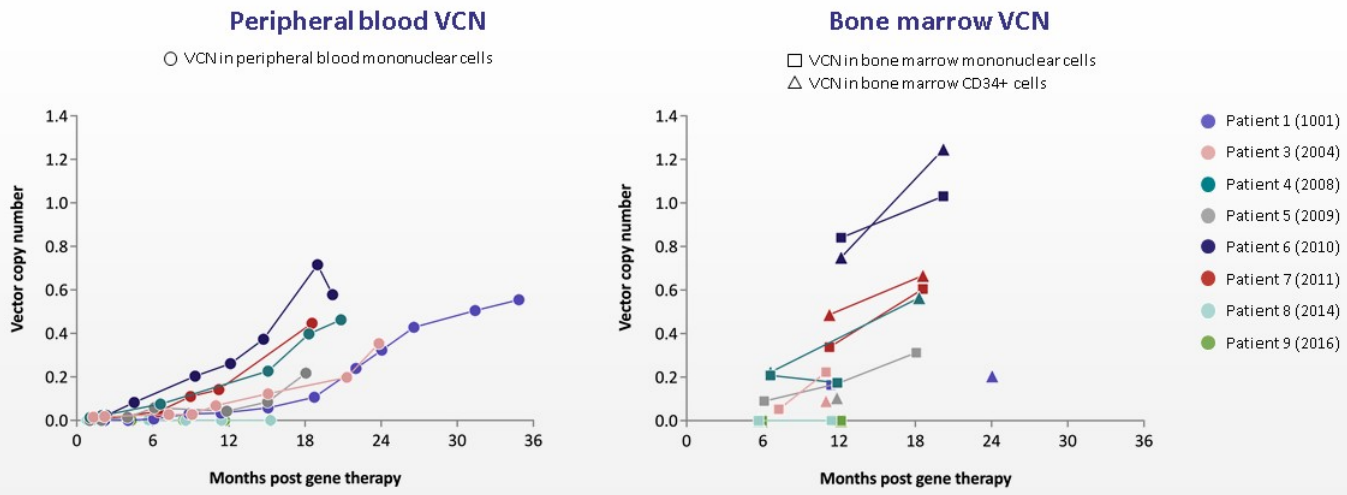
- **9 patients**
  With ≥12 months follow-up
  - **6 patients**
    Sustained peripheral blood and bone marrow genetic correction (VCN)
    → **5 patients**
    Sustained, increasing MMC resistance in BM CFCs:
    - 51% to 94% at 18 to 24 months, and
    - ≥20% at 2 consecutive timepoints
  - **2 patients**
    Potential for engraftment 12 to 24 months post RP-L102
  - **1 patient**
    Progressive BMF and underwent successful allogeneic transplant
- **3 patients**
  <12 months follow-up †

***Evidence of confirmed phenotypic & genetic correction and hematologic stability identified in 5 of initial 9 evaluable patients***

*Efficacy in ≥5 patients (observed over >1 year post prescription) required to reject null hypothesis. † In absence of conditioning, ≥12 months follow-up required to identify engraftment and MMC-resistance.
BM CFC, bone marrow colony forming cell; BMF, bone marrow failure; FA, Fanconi Anemia; HSC, hematopoietic stem cell; MMC, mitomycin-C; VCN, vector copy number.
Data on file. Rocket Pharmaceuticals. 2022.

# Progressive Increase in **Peripheral Blood and Bone Marrow VCNs**

## Progressive increases in gene markings in peripheral blood and bone marrow cells in 6 patients

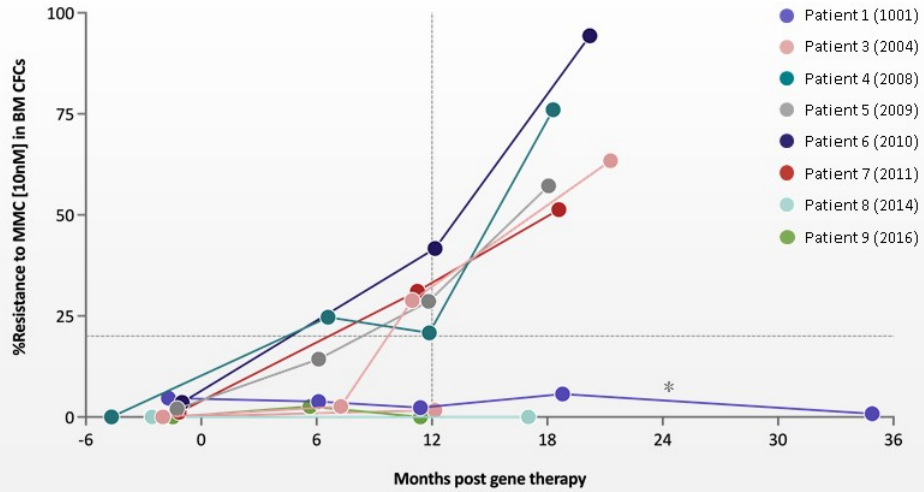





FA, Fanconi Anemia; VCN, vector copy number.
Data on file. Rocket Pharmaceuticals. 2022. Data Cut-off: April 4, 2022

# Strong Evidence for **Phenotypic Reversal**

## Increasing phenotypic correction over 1 to 2 years post RP-L102* in 5 of initial 9 evaluable patients

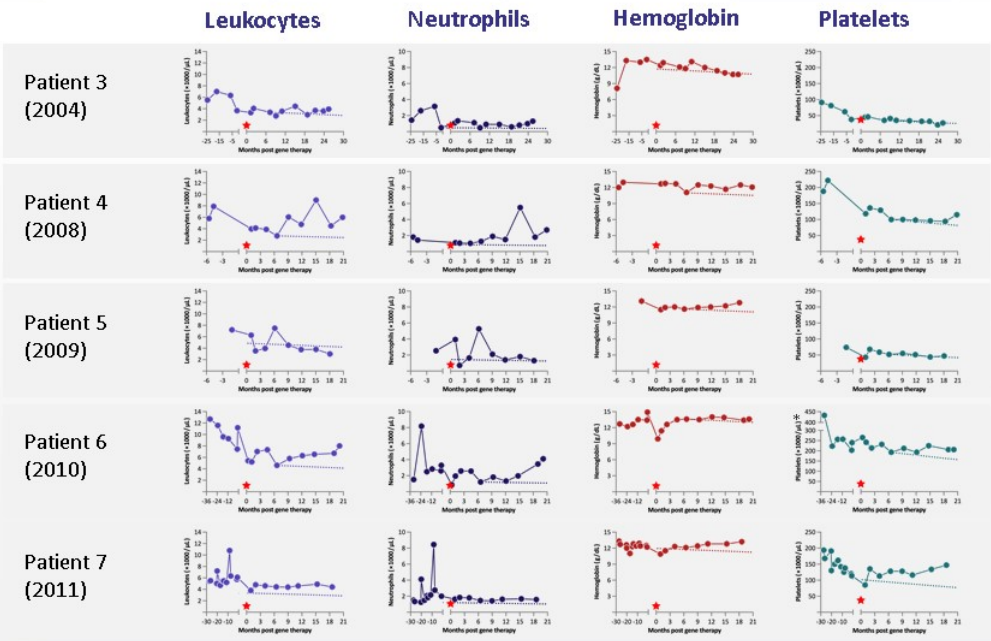



**For 5 patients, increased BM CFC MMC resistance ranging from 51% to 94% observed at 18 to 24 months post–RP-L102 administration**

*MMC resistance of >20% achieved at 2 consecutive timepoints ≥12 months for n=5*

*BM MMC-res for Patient 1 (1001)'s 24-month assessment was not performed at one of the study's central laboratories and is not included. Not shown: BM MMC-res in Patient 2 (1002), who was withdrawn from the study at 18 months post–RP-L102 infusion.
BM CFC, bone marrow colony forming cell; FA, Fanconi Anemia; MMC, mitomycin-C; VCN, vector copy number.
Data on file. Rocket Pharmaceuticals. 2022. Data Cut-off: April 4, 2022

# Blood Count Stabilization and Sustained Phenotypic Reversal




Increased MMC resistance in BM CFCs associated with hematologic stabilization at ≥1 year post RP-L102

**Concomitant blood count stabilization over 12 to 24 months seen in all 5 patients with sustained and increasing BM CFC MMC resistance**

☆ Time of RP-L102 Infusion

···· Projected blood counts based on FA-A natural history



BM CFC, bone marrow colony forming cell; FA, Fanconi Anemia; MMC, mitomycin-C.
Data on file. Rocket Pharmaceuticals. 2022. Data Cut-off: April 4, 2022

* Y-axis for Pt 2010 platelet counts is different scale to incorporate pre-treatment values

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# Development Plan

## Moving toward BLA/MAA filing

### INITIAL EFFICACY AND HIGHLY FAVORABLE SAFETY PROFILE

- Initial comprehensive efficacy in 5/9 evaluable patients (≥12-month f/u)
- No cytotoxic conditioning, only 1 transient RP-L102 related SAE (Grade 2)

### REGULATORY DESIGNATIONS

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

### 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

### ANTICIPATED SIMULTANEOUS BLA/MAA FILING

**Additional life-cycle management activities:**

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



ATMP, advanced therapy medicinal product; BLA, Biologics License Application; FA, Fanconi Anemia; 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. 2022.

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# 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 HSC transplant
- **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 y in absence of alloHSCT
  - Moderate LAD-I: Death prior to age 40 in >50% of patients, extensive morbidity with recurrent infections and inflammatory lesions



GvHD, graft-versus-host disease; HSC, hematopoietic stem cell; ITGB2, integrin subunit beta 2; LAD-I, Leukocyte Adhesion Deficiency-I; MOA, mechanism of action.
Almarza E et al. *J Allergy Clin Immunol Pract.* 2018;6(4):1418-1420.

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# Clinical Study Overview

## Description

Autologous HSCs transduced with LV carrying *ITGB2* transgene

## Clinical study

*Treatment completed*

Phase 1/2 (N=9)

**Primary endpoints:**

- Safety (Phase 1)
- Survival and safety (Phase 2)

**Selected secondary endpoints:**

- CD18 expression
- Genetic correction
- Incidence of infections
- Overall survival

## Safety

- Well tolerated; no drug product-related SAEs
- No graft rejection, no GvHD
- Initial ISA indicates highly polyclonal patterns without evidence of dominant integrations in proximity to oncogenic loci

## Key efficacy data

- 100% overall survival
- Efficacy evident in 9/9 patients – genetic, laboratory and clinical reversal of disease course
- Sustained ≥ 10% CD18 neutrophil expression, concomitant sustained CD11 expression, VCN of ≥ 0.1 in PB neutrophils and leukocytosis resolution
- Significant reduction in all hospitalizations, including infection- and inflammatory-related hospitalizations, prolonged hospitalizations and severe infections
- Spontaneous resolution of LAD-I–related skin rash and restoration of wound repair capabilities



GvHD, graft-versus-host disease; HSC, hematopoietic stem cell; ISA, Insertion site analysis; LAD-I, Leukocyte Adhesion Deficiency-I; PMN, polymorphonuclear neutrophils; SAE, serious adverse event; VCN, vector copy number.

ClinicalTrials.gov. NCT03812263. Accessed May 9, 2022. https://clinicaltrials.gov/ct2/show/NCT03812263

Data Cut-Off March 9, 2022

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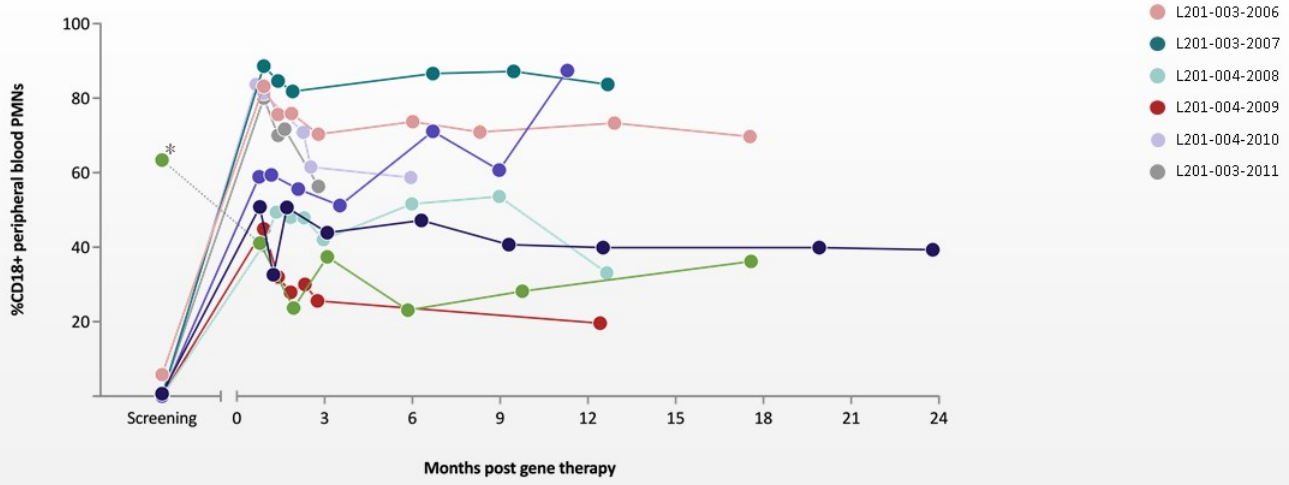
# Sustained **CD18 Expression in Peripheral Blood PMNs**

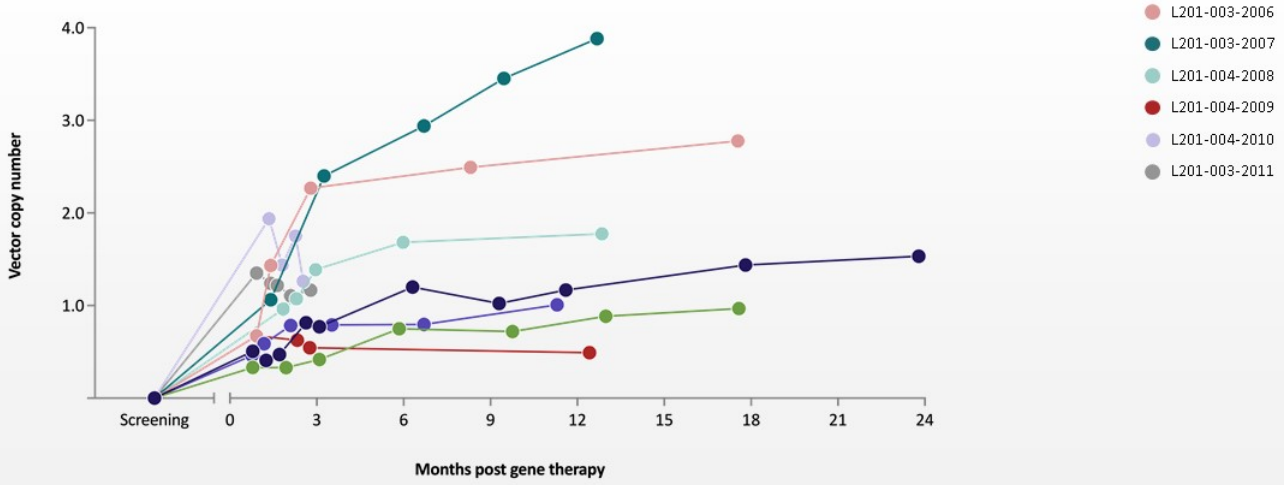
**At 3 to 24 months after infusion, 9/9 patients sustained stable CD18 expression (median: 56%) with no therapy-related serious adverse events**




*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. 2022. Data Cut-Off: March 9, 2022

# Sustained VCN in PBMCs

**At 3 to 24 months after infusion, 9/9 patients sustained stable CD18 expression (median: 56%) with no therapy-related serious adverse events**

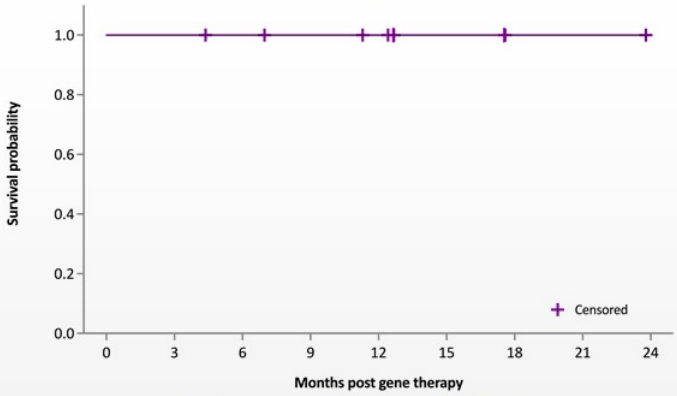





LAD-I, Leukocyte Adhesion Deficiency-I; PB, peripheral blood; PBMCs, peripheral blood mononuclear cells; VCN, vector copy number.
Data on file. Rocket Pharmaceuticals. 2022. Data Cut-Off: March 9, 2022

# Significant Reduction in Hospitalizations and 100% Overall Survival

## 100% overall survival Kaplan–Meier estimate

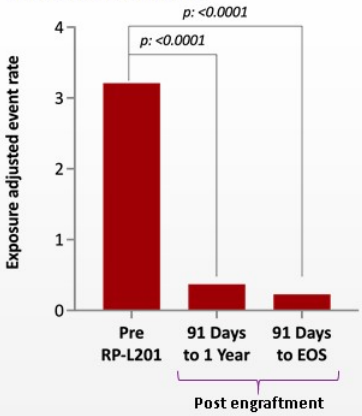



## Survival without allogeneic HSCT

### Primary outcomes

- ≥2 years of age AND
- ≥1-year post–RP-L201 infusion

## Significant reduction in incidence of hospitalizations






EOS, end of study; HSCT, hematopoietic stem cell transplantation; LAD-I, leukocyte adhesion deficiency-I.
Data on file. Rocket Pharmaceuticals. 2022. Data Cut-Off: March 9, 2022

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# Development Plan

## Moving toward BLA/MAA filing

### ENROLLMENT AND INITIAL EFFICACY

- Enrollment completed; 9/9 patients treated
- Efficacy observed in 9/9 patients with 3 to 24 months follow-up
- Efficacy is comprehensive, across all efficacy parameters including CD18 expression and survival

### REGULATORY DESIGNATIONS

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

### TOP-LINE DATA READOUT 2Q 2022

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

Guiding H1 2023 **BLA/MAA Filing**

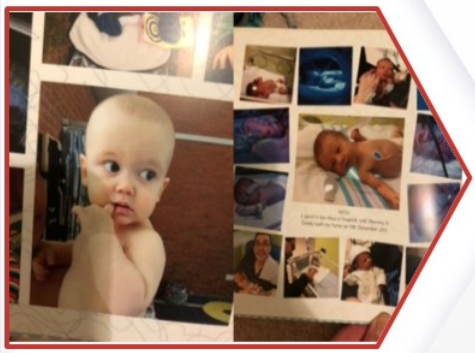
**Life-cycle management**

- Potential label expansion to include moderate LAD-I population
- Potential study initiation in 2023



ATMP, advanced therapy medicinal product; BLA, Biologics License Application; H1, first half of the year; LAD-I, leukocyte adhesion deficiency-I; MAA, Market Authorization Application; PRIME, PRIority MEdicines; PRV, priority review voucher; RMAT, Regenerative Medicine Advanced Therapy.
Data on file. Rocket Pharmaceuticals. 2022. Data Cut-off: March 9, 2022

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



### 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

**Market Opportunity – US and EU**

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

Annual Incidence of **75 to 125** individuals



LV, lentiviral vector; MOA, mechanism of action; PKD, pyruvate kinase deficiency; PKLR, pyruvate kinase L/R; RBC, red blood cell.

Zanella A et al. *Br J Haematol.* 2005;130(1):11-25.

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# Clinical Study Overview

## Description

Autologous HSCs transduced with LV containing human *PKLR* transgene

## Clinical study

N = 4-5 (Phase 1)

**Primary endpoints:**

- Safety
- Toxicity

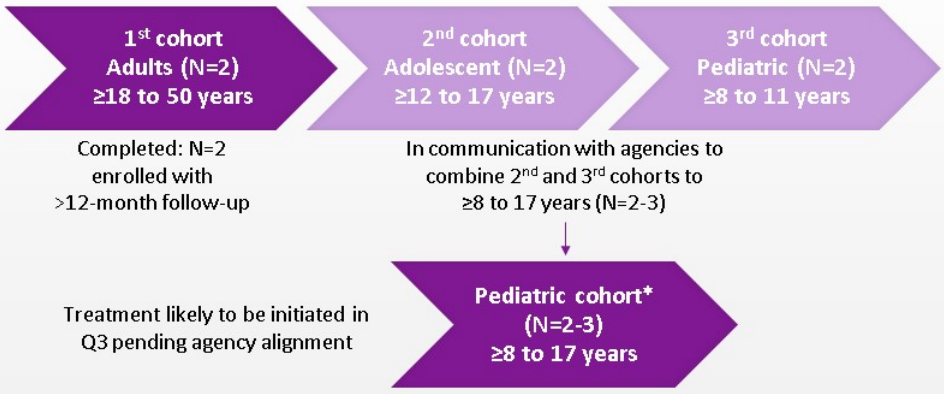
**Selected secondary endpoints:**

- Genetic correction
- Transfusion independence
- Reduction in anemia
- Reduction of hemolysis

## Safety

Appears favorable with no IP-related SAEs

### Phase 1 cohort dosing plan






*Discussions ongoing w/ agency.
HSC, hematopoietic stem cell; IP, investigational product; LV, lentiviral vector; PKD, Pyruvate Kinase Deficiency; Q2, second quarter of the year; SAE, serious adverse event.
ClinicalTrials.gov. NCT04105166. Accessed May 9, 2022. https://clinicaltrials.gov/ct2/show/NCT04105166

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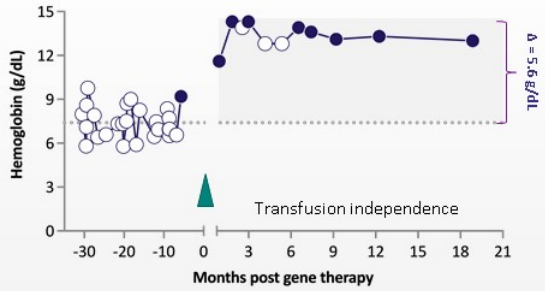
# Hemoglobin Normalization and Transfusion Independence

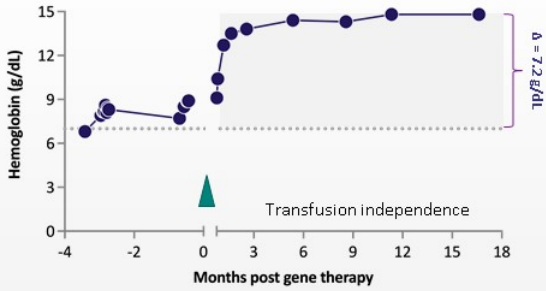
**Hemoglobin improvement to normal range (from baselines in severe (<8g/dL range)**
**Transfusion independence (extensive transfusion requirements prior to RP-L301)**
**Sustained improvement of hemolysis markers (LDH, bilirubin) and PB VCNs in 1.0 – 3.0 range**

PATIENT 1001




- Hemoglobin normalized (from ~7.4 to 13.0 g/dL) sustained at 18 months post infusion
- No transfusion requirements following engraftment

PATIENT 1002




- Hemoglobin normalized (from ~7.0 to 14.8 g/dL) sustained at ~18 months post infusion
- No transfusion requirements following engraftment
- Prior therapy with mitapivat: no Hb significant increase

Dotted lines indicate average Hb for each patient prior to gene therapy



PKD, Pyruvate Kinase Deficiency; pVCN, peripheral vector copy number.
Data on file. Rocket Pharmaceuticals. 2022. Data Cut-off: April 13, 2022

▲ Time of RP-L301 infusion

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# Development Plan

## Moving toward pivotal Phase 2 study

### PKD STUDY PROGRESS TO PHASE 2 AND LAUNCH

**Key endpoints selected**

- Hemoglobin increase
- ↓ 50% transfusions or transfusion independence

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

- Complete Phase 1 pediatric cohort dosing (N=2-3)
- End of Phase 1 regulatory meeting with FDA
- Approve and launch RP-L301; seek regulatory approval in the US and EU

### REGULATORY DESIGNATIONS

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

### LIFE-CYCLE MANAGEMENT

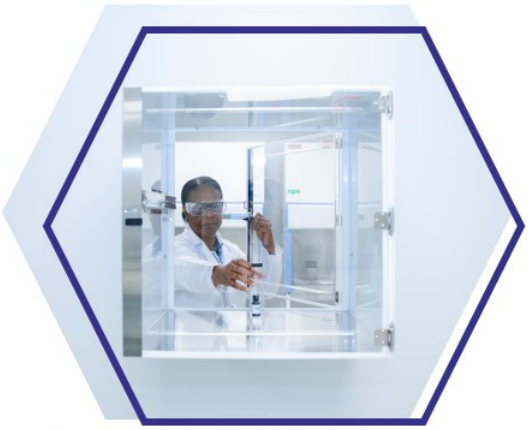
ANTICIPATED EXPANSION STUDY TO PRE-SPLENECTOMY PATIENTS IN 2023

EXPLORATION OF NON-GENOTOXIC CONDITIONING



FDA, Food and Drug Administration; NHS, National Health Service; PKD, pyruvate kinase deficiency.
Data on file. Rocket Pharmaceuticals. 2022.

# FUTURE DIRECTIONS



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# Rocket Pharmaceuticals: **Elevating Gene Therapy to New Heights**

- Recognized as a premier gene therapy company
- Specialized against monogenic diseases
- Pioneer in the development of both *ex vivo* LV and *in vivo* AAV therapies
- AAV9-based gene therapy for Danon disease, a major value driver based on size of indication and lack of other therapies
- LV-based programs to provide near term commercialization

- Commercial company with initial therapies and revenue build for Danon disease, FA, LAD-I and PKD
- Broad pipeline of additional new therapies targeting potentially larger opportunities for rare and orphan diseases
- Potential new technologies employed (gene editing and non-viral gene therapies)



AAV, adeno-associated virus; FA, Fanconi Anemia; LAD-I, Leukocyte Adhesion Deficiency-I; LV, lentiviral vector; PKD, Pyruvate Kinase Deficiency.
Data on file. Rocket Pharmaceuticals. 2022.

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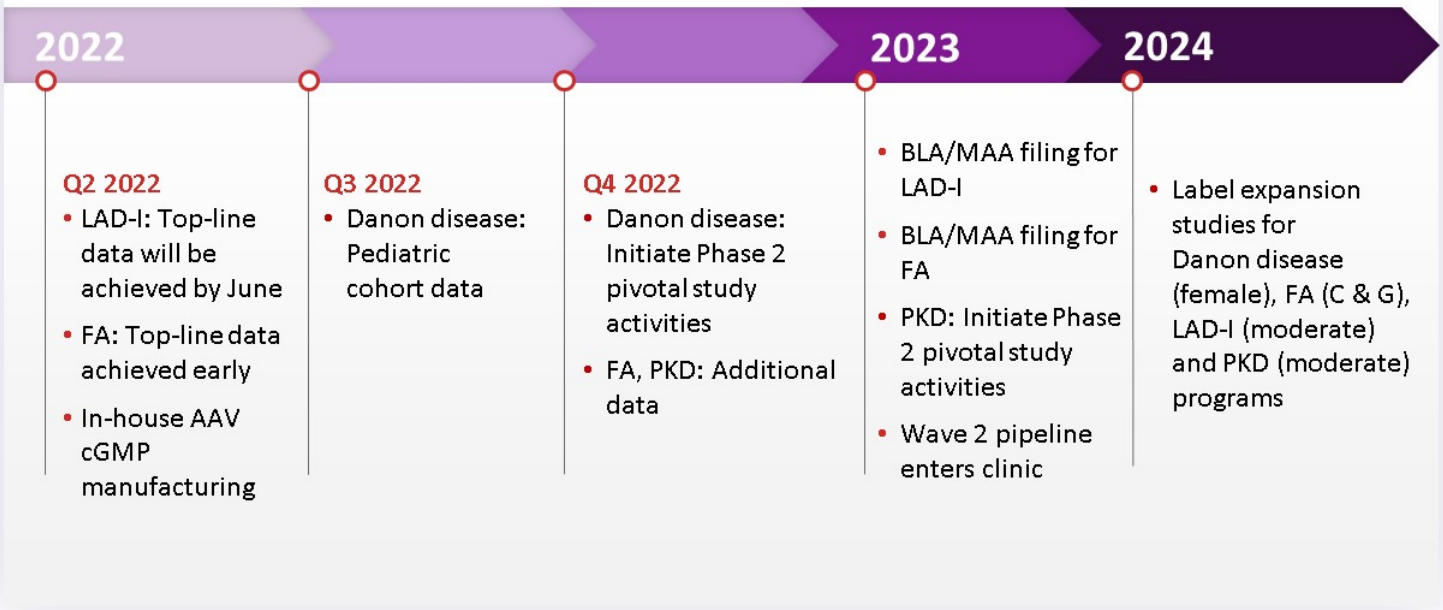
# Anticipated Milestones and **Wave 2**






AAV, adeno-associated virus; BLA, Biologics License Application; cGMP, current Good Manufacturing Processes; FA, Fanconi anemia; H1, first half of the year; LAD-I, leukocyte adhesion deficiency-I; PKD, pyruvate kinase deficiency; Q2, second quarter of the year; Q3, third quarter of the year; Q4, fourth quarter of the year.
Data on file. Rocket Pharmaceuticals. 2022.

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# Future Therapies: Wave 2 (AAV)


**Focused R&D Strategy for Sustainable Innovation**

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

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



MOA, mechanism of action; R&D, research & development
Data on file. Rocket Pharmaceuticals. 2022.

# THANK YOU!

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