Rocket Program Updates Following ASGCT 2022

Danon Disease, Pyruvate Kinase Deficiency, Fanconi Anemia, and Leukocyte Adhesion Deficiency-I

Gaurav Shah, MD

Chief Executive Officer

August 2022

rocket pharma

SEEKING GENE THERAPY CURES

NASDAQ: RCKT

Cautionary Statement Regarding Forward-Looking Statements

Various statements in this release concerning Rocket's future expectations, plans and prospects, including without limitation, Rocket's expectations regarding its guidance for 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), Infantile Malignant Osteopetrosis (IMO) and Danon Disease, and the safety, effectiveness and timing of related pre-clinical studies and clinical trials, may constitute forward-looking statements for the purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995 and other federal securities laws and are subject to substantial risks, uncertainties and assumptions. You should not place reliance on these forward-looking statements, which often include words such as "believe," "expect," "anticipate," "intend," "plan," "will give," "estimate," "seek," "will," "may," "suggest" or similar terms, variations of such terms or the negative of those terms. Although Rocket believes that the expectations reflected in the forward-looking statements are reasonable, Rocket cannot guarantee such outcomes. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Rocket's ability to monitor the impact of COVID-19 on its business operations and take steps to ensure the safety of patients, families and employees, the interest from patients and families for participation in each of Rocket’s ongoing trials, our expectations regarding when clinical trial sites will resume normal business operations, our expectations regarding the delays and impact of COVID-19 on clinical sites, patient enrollment, trial timelines and data readouts, our expectations regarding our drug supply for our ongoing and anticipated trials, actions of regulatory agencies, which may affect the initiation, timing and progress of pre-clinical studies and clinical trials of its product candidates, Rocket's dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the section entitled "Risk Factors" in Rocket’s Annual Report on Form 10-K for the year ended December 31, 2020, filed March 1, 2021 with the SEC. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and Rocket undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

rocket pharma

Rocket Pharma: Seeking Gene Therapy Cures

Multi-Platform Gene Therapy Company

4 of 4 programs w/ compelling clinical proof of concept

First, Best and Only-in-Class

Clear MOAs and **clinical endpoints**

Strong Commercial and Manufacturing Capabilities

Value-based and cost-effective pricing strategy; targeting fatal and serious diseases with ***expensive and risky transplants & lifelong treatments as SoC***

In-house AAV manufacturing with capabilities to support commercial product

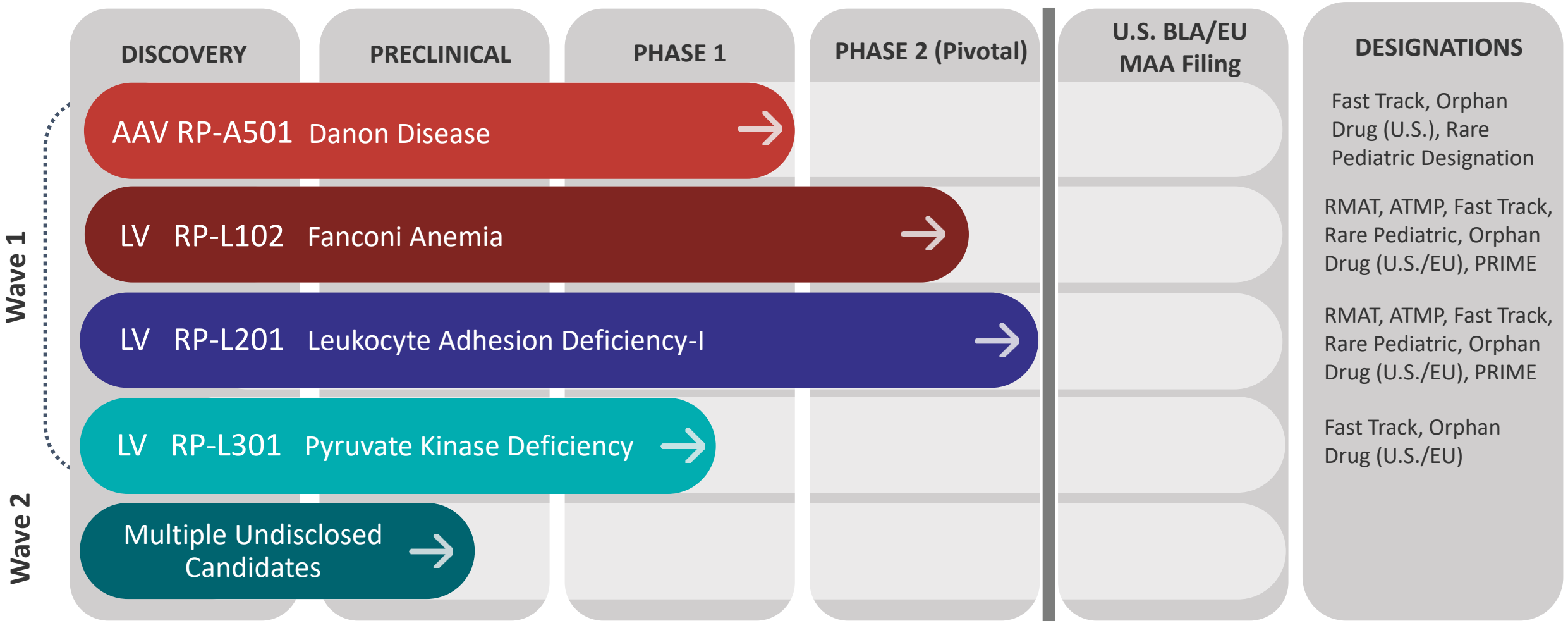
~100,000 sq. ft. facility in Cranbury, NJ

Expert Leadership Team

Seasoned leadership team with a track record of 20+ drug approvals and launches

rocket pharma

Our Multi-Platform Pipeline: Potential for Significant Value Creation Near and Long Term



Note: IMO Program (RP-L401) to be returned to academic sponsors, human and financial resources to be reallocated to building Wave 2 and accelerating Wave 1

Danon Disease:
A Monogenic Heart Failure Syndrome

RP-A501
Danon Disease

RP-L301
Pyruvate Kinase Deficiency

RP-L102
Fanconi Anemia

RP-L201
Leukocyte Adhesion Deficiency-I

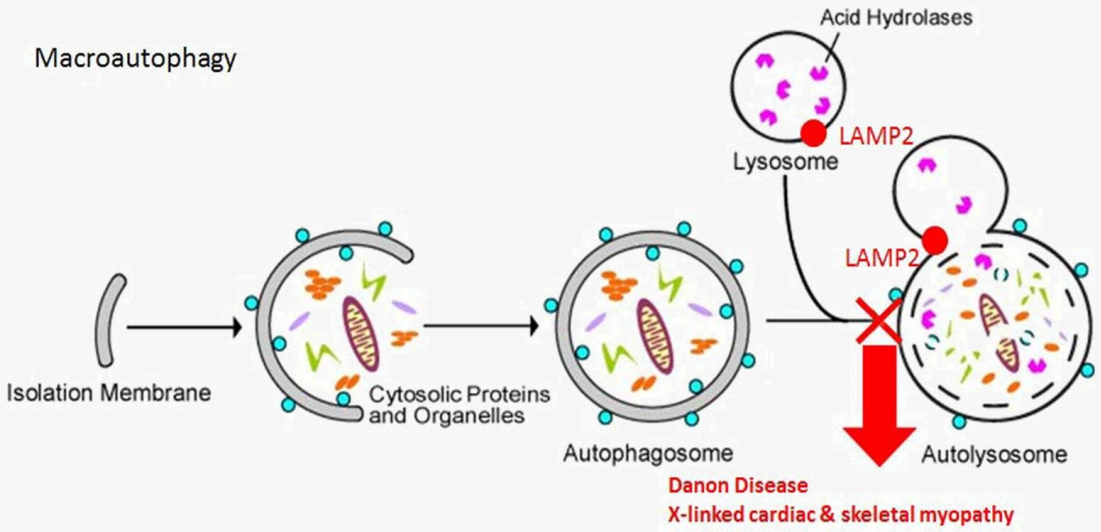
Background: ***Multisystemic disorder*** caused by highly penetrant, X-linked dominant ***LAMP2 mutations;*** progressive cardiomyopathy is predominant cause of early mortality in young adults

- Males: *aggressive* disease course, median OS is 19y
- Females: *generally delayed* presentation due to additional X chromosome

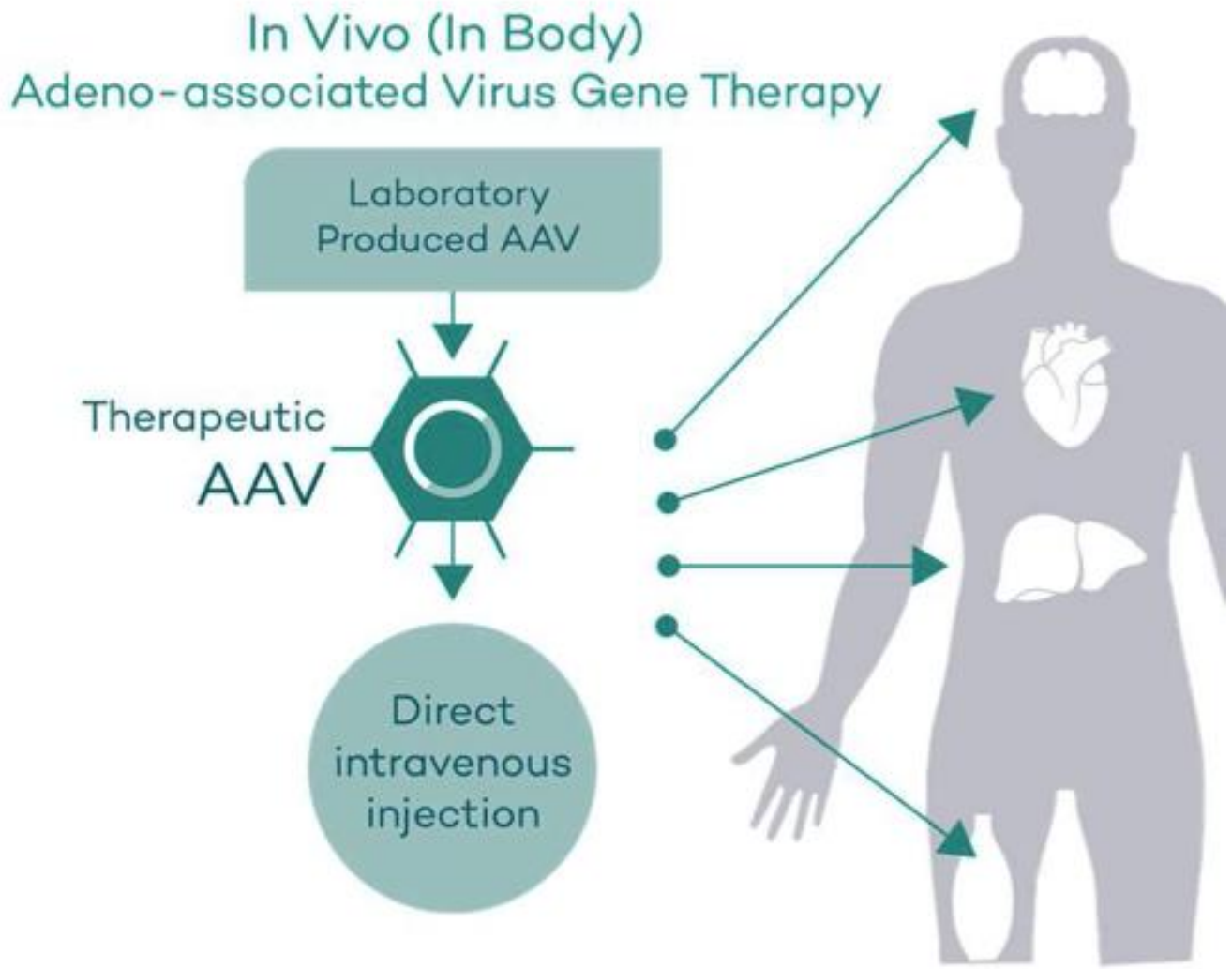
Currently available treatments: Heart transplants associated with considerable morbidity and mortality (10y OS 50%) and available to ~20% of DD pts

Addressable Market: Estimated US + Europe prevalence of ***15,000-30,000***

MECHANISM OF ACTION



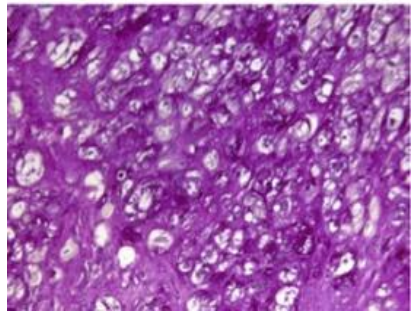
How Does rAAV Gene Therapy (RP-A501) Work in Danon Disease?

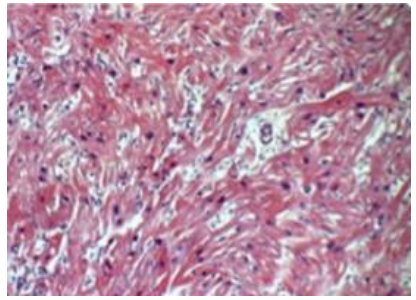


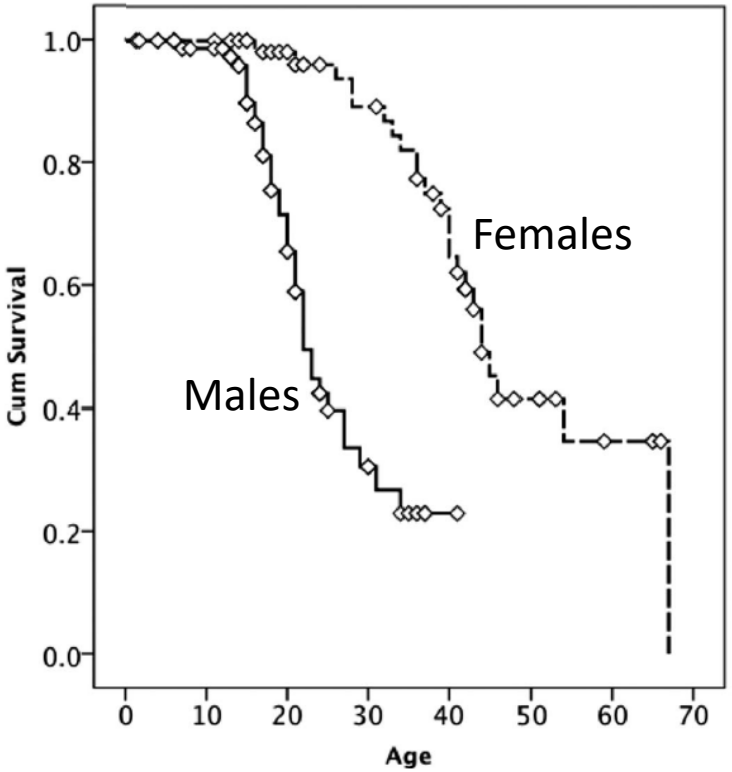
Intravenous Administration of rAAV

- AAV9 demonstrates tropism to:
  - Cardiomyocytes
  - Skeletal muscle
  - Brain tissue
- Non-dividing, terminally differentiated cardiomyocytes can be transduced
- rAAV9 DNA expresses *LAMP2B* gene
- Cardiomyocytes have minimal cell turnover; long-term durable expression anticipated

Danon Disease







Autosomal dominant, monogenic X-linked disease

- *LAMP-2B* gene mutation
  (**L**ysosomal **A**ssociated **M**embrane **P**rotein 2B)
- Impaired autophagy
  - Prominent sarcoplasmic vacuoles
  - Myocardial disarray

Severe Cardiomyopathy (CM 95%)

- Mortality secondary to heart failure
- **Males**:
  - Hypertrophic CM with arrhythmias
  - Mortality in 2nd to 3rd decades
- **Females:**
  - Dilated/hypertrophic CM and arrhythmias
  - Mortality in 4th to 5th decades

Other Clinical Manifestations

- Skeletal Myopathy
- CNS manifestations
- Ophthalmologic manifestations

Heart transplant is current standard of care

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

RP-A501: Gene Therapy Has Potential to Alter Natural History of Danon Disease Patients

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

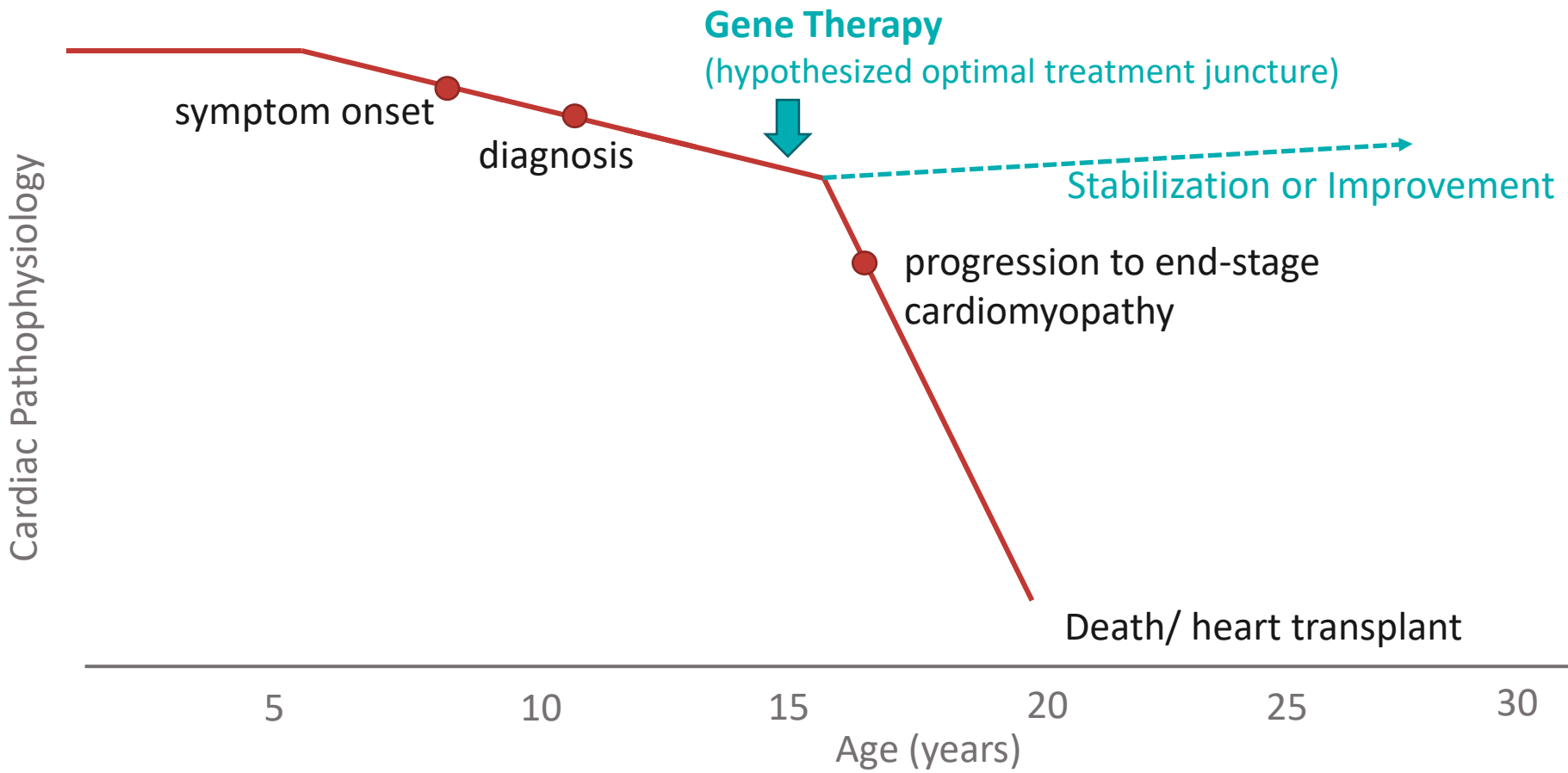


Figure modified from disease progression by age data in Boucek et al. Natural history of Danon disease. Genet Med. 2011 Jun;13(6):563-8, Brambatti et al. J Cardiac Failure. 2019. Aug;25(8):1-7, and Feingold et al. Am J Transplant. 2015 Nov;15(11):2978-85

RP-A501: Danon Disease Gene Therapy Clinical Trial Overview

Design

Non-Randomized Open Label Phase 1 Study

- Male Danon Disease patients
  - Adults (& Adolescents): ≥15 years
  - Pediatric: 8-14 years
- Single Intravenous Dose of **RP-A501 (AAV9.LAMP2B)**
  - Low Dose: 6.7×10^{13} GC/kg
  - High Dose*: 1.1×10^{14} GC/kg

Primary Outcomes

- **Safety at each dose level**
- Target tissue transduction & *LAMP2B* expression
- Effect on cardiomyocyte morphology
- Clinical stabilization or improvement

Key Patient Entry Criteria**

Inclusion

- Male
- Confirmed *LAMP2B* mutation
- Cardiac involvement confirmed by imaging or ECG
- New York Heart Association (NYHA) Class II or III
- Able to walk >150 meters unassisted during 6-minute walk test (6MWT)

Exclusion

- Anti-AAV9 neutralizing antibodies
- Cardiopulmonary instability
- Prior organ transplantation

*** No further enrollment at this dose.**
**** Additional details at ClinicalTrials.gov**

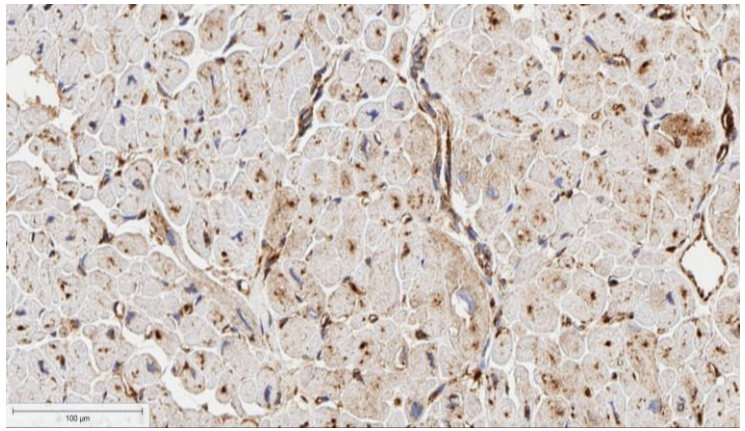
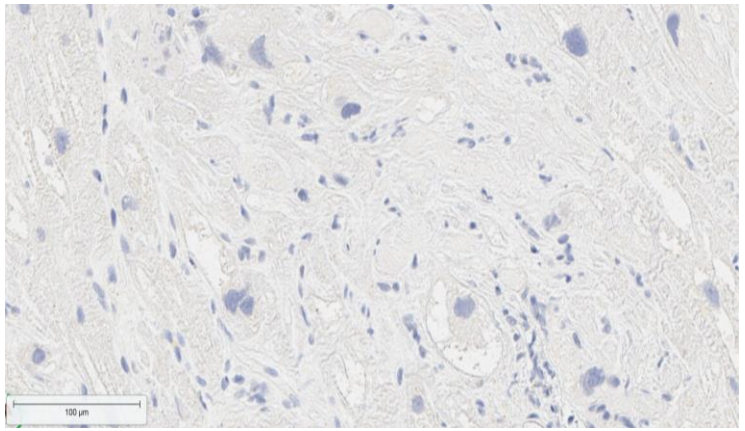
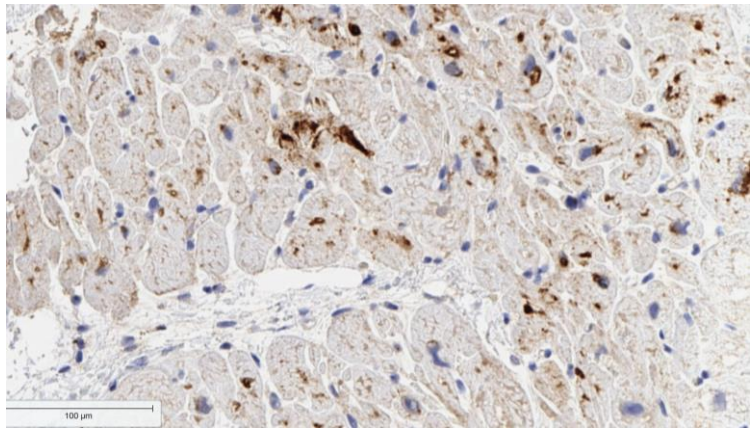
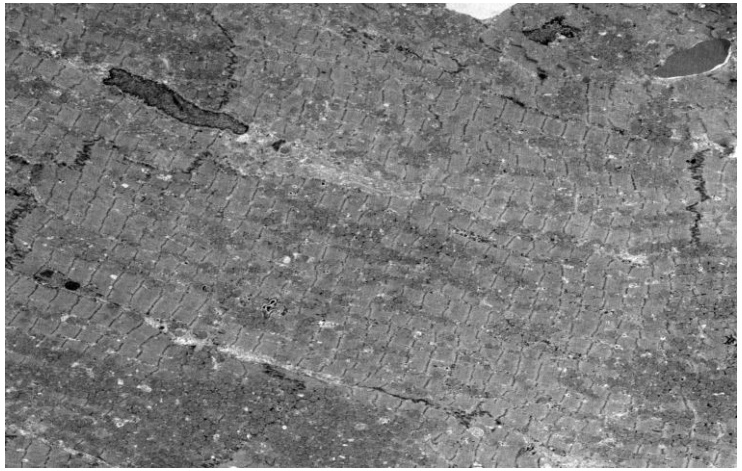
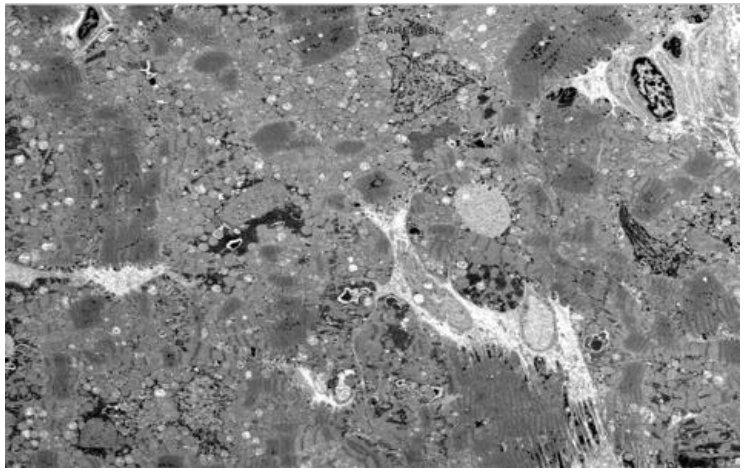
GC/Kg: Genome copies/kilogram

RP-A501: Baseline Status of Adult Cohorts

Cohort	Patient ID	Age at Enrollment (years)	Weight (kg)	Clinical Status		Cardiac Status	
				NYHA Class	Six Minute Walk (meters)	BNP (pg/mL)	LV Ejection Fraction* (%)
Adult - Low Dose 6.7×10^{13} GC/kg	1001	17.5	52.5	II	443	70	62
	1002	20.4	89.1	II	405	942	59
	1005	18.3	91.8	II	427	176	59
Adult - High Dose 1.1×10^{14} GC/kg	1006	21.1	82.7	II	436	123	47
	1007	20.7	96.7	II	434	630	35

*All echocardiographic parameters are from local laboratory assessment by a single reader.
BNP = Brain Natriuretic Peptide
NYHA = New York Heart Association

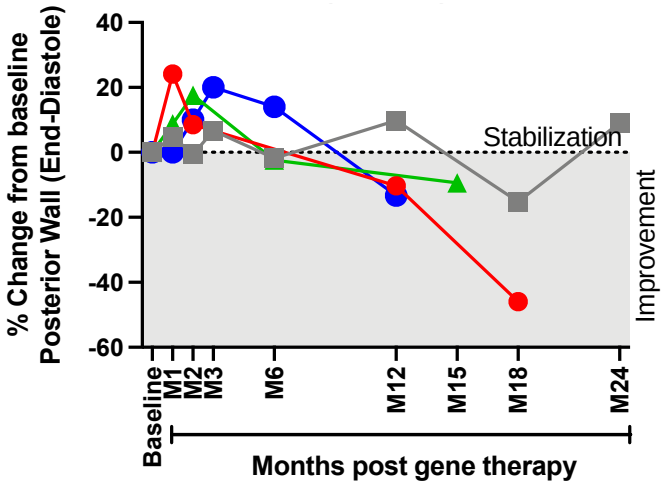
RP-A501: LAMP2 Cardiac Protein Expression by Immunohistochemistry and Myofibrillar Structure by Electron Microscopy

	Normal Control	Baseline*	Month 9*
Immunohistochemistry			
Electron Microscopy			

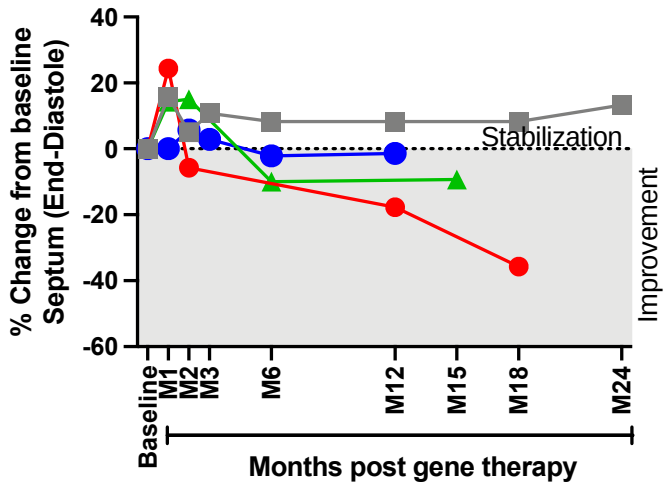
*Representative images from patient 1005 from endomyocardial.

RP-A501: Remodeling of Left Ventricular Hypertrophy in Adult Cohorts

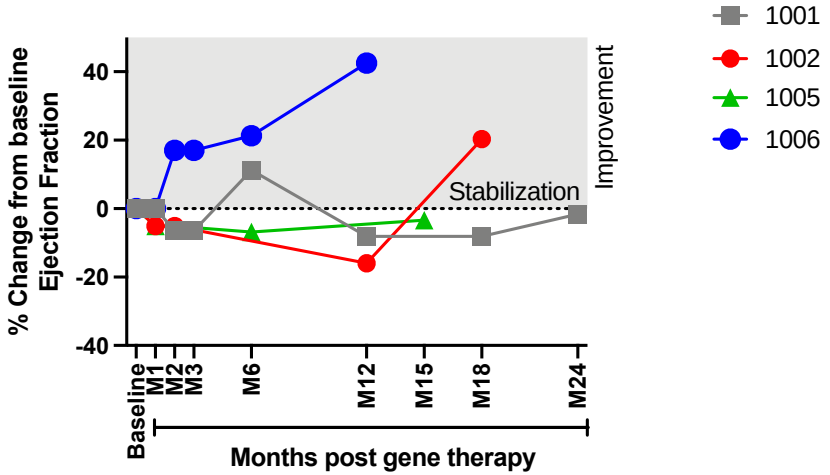
Posterior Wall Thickness (LVPWd)

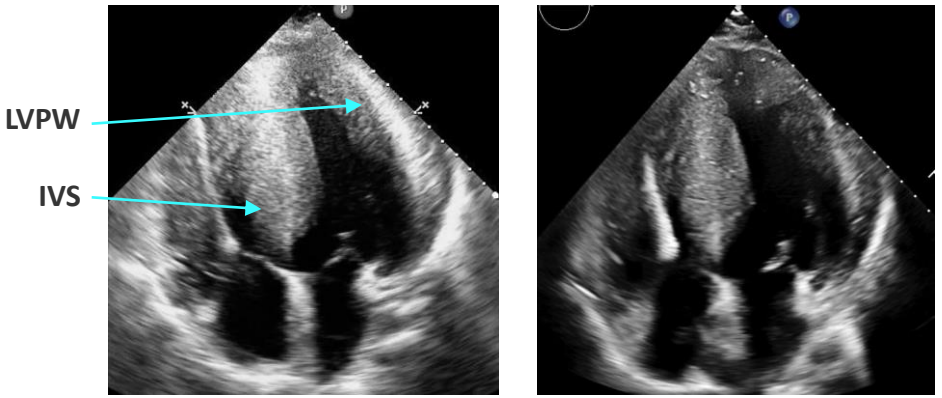


Septum Thickness (IVSd)



Ejection Fraction (LV EF)





Baseline

Month 15

Representative images from patient 1005

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

RP-A501: Functional Clinical Status of Adult Cohorts

Cohort	Patient ID	Variable	Baseline	Most Recent Follow-up	Time of Follow-up
Adult – Low Dose	1001*	NYHA class	II	II	24 Months
		BNP (pg/mL)	70	30	
	1002	NYHA class	II	I	18 Months
		BNP (pg/mL)	942	200	
	1005	NYHA class	II	I	15 Months
		BNP (pg/mL)	176	44	
Adult – High Dose **	1006	NYHA class	II	I	12 Months
		BNP (pg/mL)	123	41	

* Corticosteroid compliance uncertain.
** Patient 1007 underwent heart transplant at 5 months for progressive DD, thus no subsequent data reported.
BNP = Brain Natriuretic Peptide
NYHA = New York Heart Association

RP-A501: Grade 3 and 4 Serious Adverse Events (SAEs) in Adult Cohorts (As Previously Disclosed)

RP-A501 Related*:

Thrombotic microangiopathy (TMA) [grade 4] associated with

- thrombocytopenia [grade 4]
- acute kidney injury & renal failure [grade 4]

Transaminase increase [grade 3]

n=3; transient and resolved with immunosuppression

→ **Pt 1007 (received highest dose secondary to baseline weight and 1.1 x 10^{14} GC/kg dose level)**

Resolved fully with eculizumab and transient hemodialysis

Corticosteroid Related*:

Skeletal myopathy [grade 3]

- n=3; resolved with steroid taper

Salmonella sepsis [grade 3]

- n=1; resolved with antibiotics

Danon Disease Progression Likely Related*:

Acute cardiac failure with ventricular arrhythmia [grade 4]

→ **Pt 1007 (LVEF 35% at enrollment)**

Based on MedDRA v23; the highest severity for each event (per NCI-CTCAE v.5.0) is presented.
*Indicates events for which the relationship was definitely, probably, or possibly related.

RP-A501: Risk Mitigation Strategies Implemented Prior to Pediatric Enrollment

Enhanced prophylactic immunosuppressive regimen

- Sirolimus to inhibit complement activation
- Steroid-sparing regimen to decrease skeletal myopathy
  - Initial dose 0.5 to 0.8 mg/kg/day (compared to ≥ 1mg/kg/day in adult cohort)
  - Early initiation of taper (Day 10) and discontinuation (goal Month 3)
- Frequent monitoring for early signs of TMA for potential early use of Eculizumab
  - Clinical Monitoring Team included 2 independent monitors with expertise in TMA

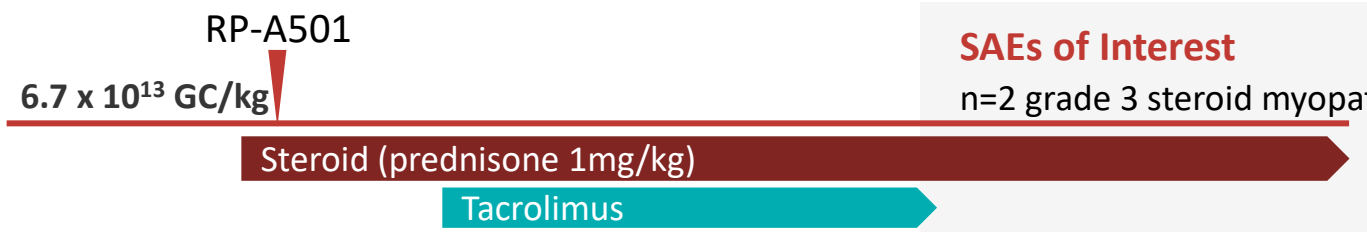
Dose-dependent toxicity

- No further enrollment at higher dose level

RP-A501: Immunosuppression, Patient Characteristics & Safety in Phase 1

Cohort 1: Low-dose adult

Pt	Age	Wt
1001	17.5	52.5
1002	20.4	89.1
1005	18.3	91.8

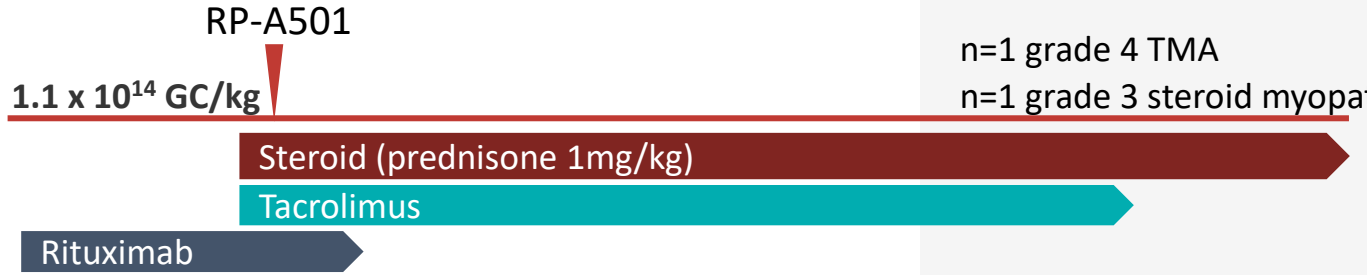


SAEs of Interest
n=2 grade 3 steroid myopathy

Platelets
n=2 decreases to LLN range

Cohort 2: High-dose adult

Pt	Age	Wt
1006	21.1	82.7
1007	20.7	96.7

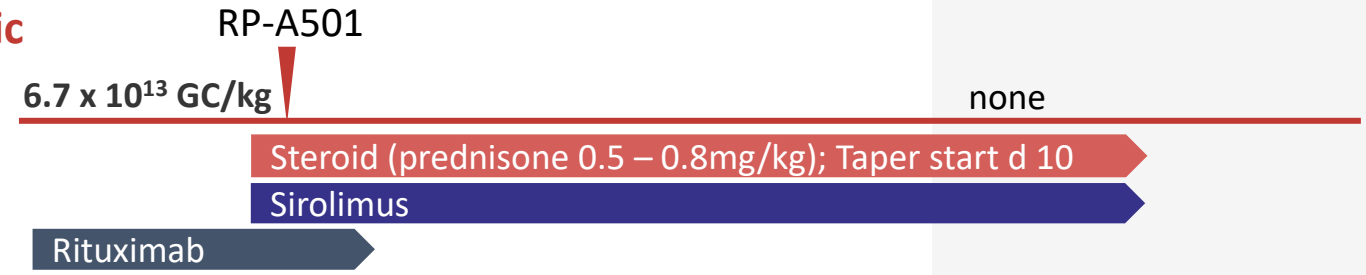


n=1 grade 4 TMA
n=1 grade 3 steroid myopathy

n=1 grade 4 decrease

Cohort 3: Low-dose pediatric

Pt	Age	Wt
1008	12.3	70.5
1009	11.5	55.7



none

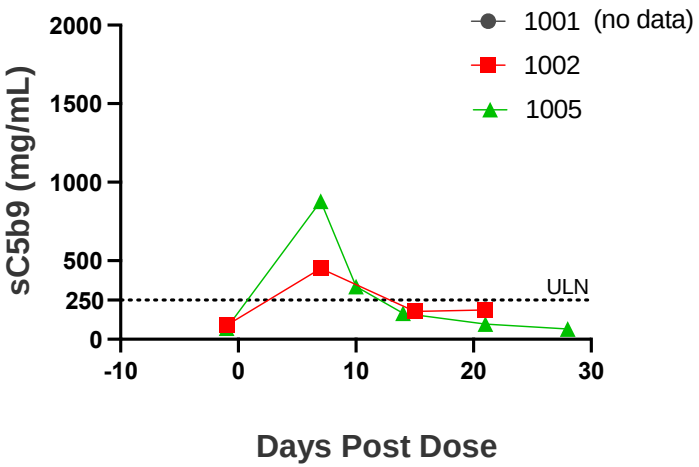
n=2 normal range

Age in years; weight in kg

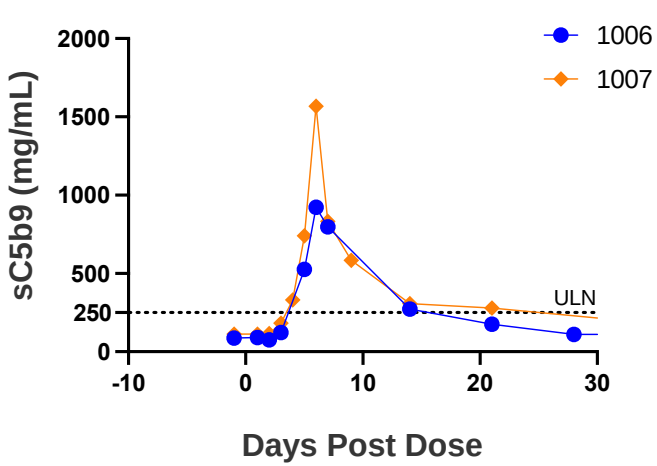
RP-A501: Inhibition of Complement Activation with Modified Immunosuppression

sC59b (terminal soluble complement complex)

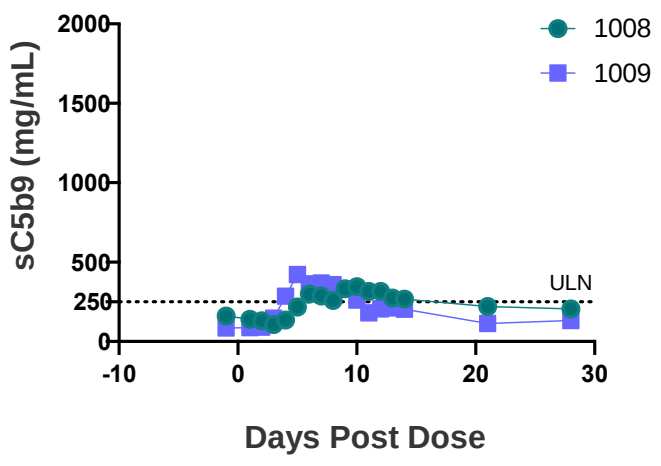
Low Dose Adult
Corticosteroids



High Dose Adult
Rituximab + Corticosteroids + Tacrolimus



Low Dose Pediatric
Rituximab + Corticosteroids + Sirolimus



Platelets	2 of 3 patients had platelet decreases to LLN range	1 of 2 patients (Pt 1007) had grade 4 thrombocytopenia (transient)	**2 of 2 patients had platelets remain within normal range**

RP-A501: Summary of Results from Adult and Pediatric Cohorts

Adult Cohort:

- RP-A501 was generally well tolerated
- Increased *LAMP2* protein expression with signals of disease stabilization and improvement including NYHA class, BNP, wall thickness and cardiac histology

Pediatric Cohort: RP-A501 was well tolerated in both patients with modified protocol

- T- and B-cell directed immunosuppression associated with markedly reduced complement activation relative to adult cohorts
  - **Minimal complement activation**
  - **Platelets remained within normal range**
  - **No complement-related clinical or laboratory AEs**
- Absent or limited worsening of skeletal myopathy with initial steroid dose-reduction and more rapid taper, and introduction of sirolimus
- No immediate, early or delayed RP-A501 related toxicities observed to date

RP-A501: Conclusion and Future Direction

- RP-A501 was generally well tolerated in adult and pediatric patients with Danon disease
- Modified immunosuppressive regimen appears well tolerated and effective in pediatric cohort
- Phase 1 efficacy signal in age ≥15 cohort: RP-A501 stabilizes and potentially improves Danon disease cardiomyopathy
- These findings support phase 2 evaluation of RP-501 in Danon disease

RP-A501: Overview of Development Plan

Current Status

- ✓ Adult High- and Low-dose cohorts completed
- ✓ First patient dosed in pediatric cohort
- ✓ Orphan Drug, Rare Pediatric & Fast Track designations in the US (Eligible for PRV)

Planned Next Steps

- ❑ Completion of pediatric cohort dosing and follow-up
- ❑ End of Phase I Regulatory meeting with FDA
- ❑ Initiation of European study sites (for Phase II)
- ❑ Expanded natural history with additional longitudinal patient data in EU

Additional Life-cycle Management Activities:

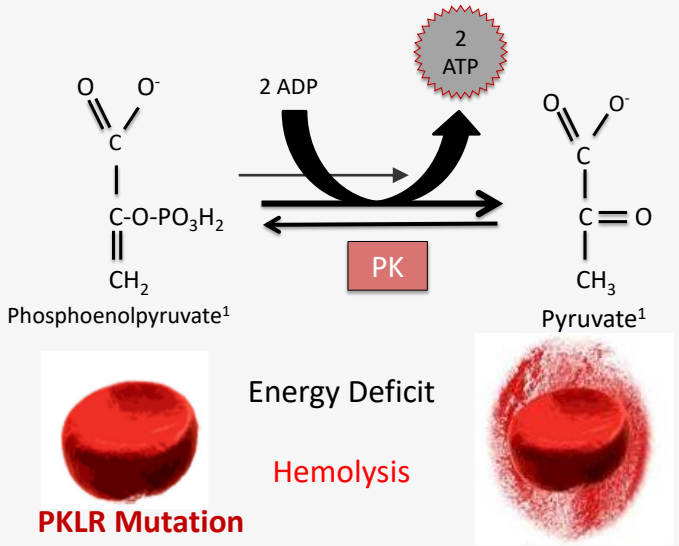
- Potential label expansion to include female Danon patients

Planned US & EU Registrational Phase II Study

Pyruvate Kinase Deficiency (PKD):
A Monogenic Red Blood Cell Hemolytic Disorder

RP-A501	**RP-L301**	RP-L102	RP-L201
Danon Disease	**Pyruvate Kinase Deficiency**	Fanconi Anemia	Leukocyte Adhesion Deficiency-I

MECHANISM OF ACTION:



Current Available Treatments: ***Chronic*** blood transfusions and splenectomy—side effects include iron overload and extensive ***end-organ damage***

Addressable Market[2]: ***~250-500*** patients/year for transfusion-dependent post-splenectomy patients

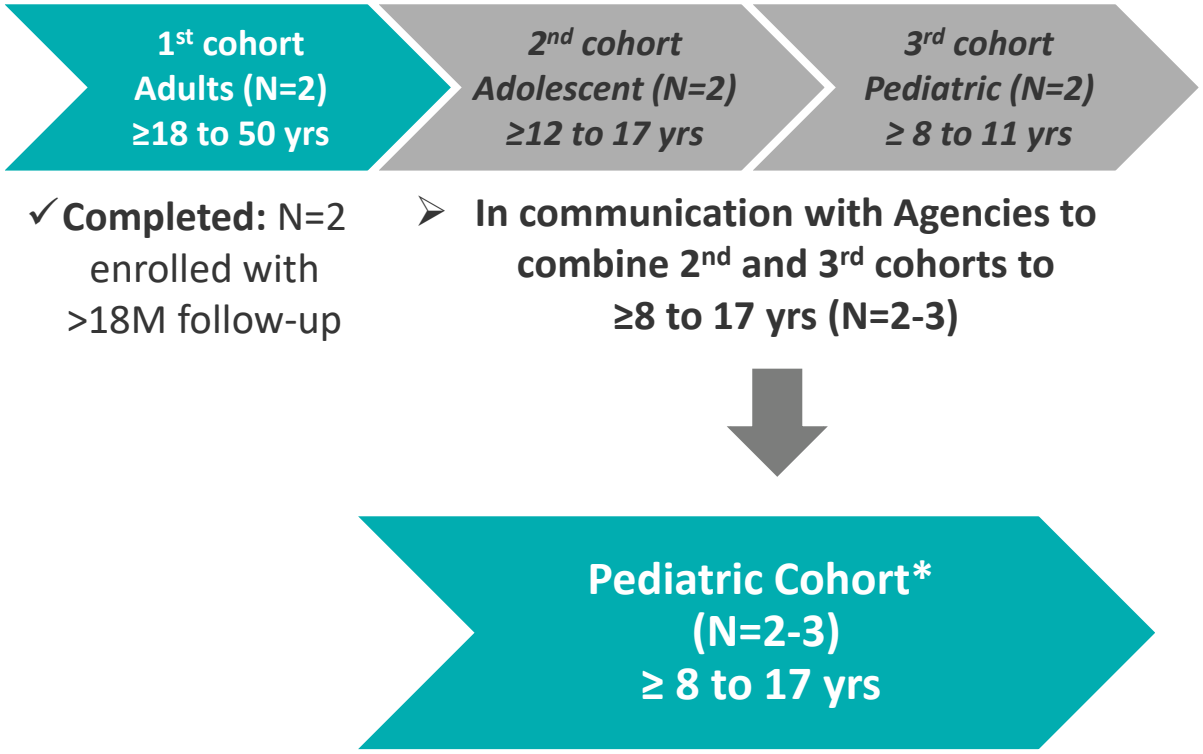
- Conservative estimates indicate a total number from ***3,000*** to ***8,000*** in the US, Europe and RoW combined
- Largest LV program in Rocket's Wave 1 pipeline

[1]One glucose molecule is metabolized into two Phosphoenolpyruvate and ultimately two Pyruvate (pyruvic acid) molecules; this final enzymatic step yields two additional ATPs from each glucose molecule

RP-L301 (PKD): Phase 1 Overview of Clinical Study Design

- Patients with ***prior splenectomy*** and ***severe and/or transfusion-dependent anemia***
- Primary Endpoint: Safety and toxicity of RP-L301
- Secondary Endpoints:
  - Clinically significant reduction of anemia
  - ***Transfusion independence*** at 12 months
  - 50% reduction in transfusion requirements
  - ***PB and BM*** genetic correction (VCN)
  - Reduction of hemolysis

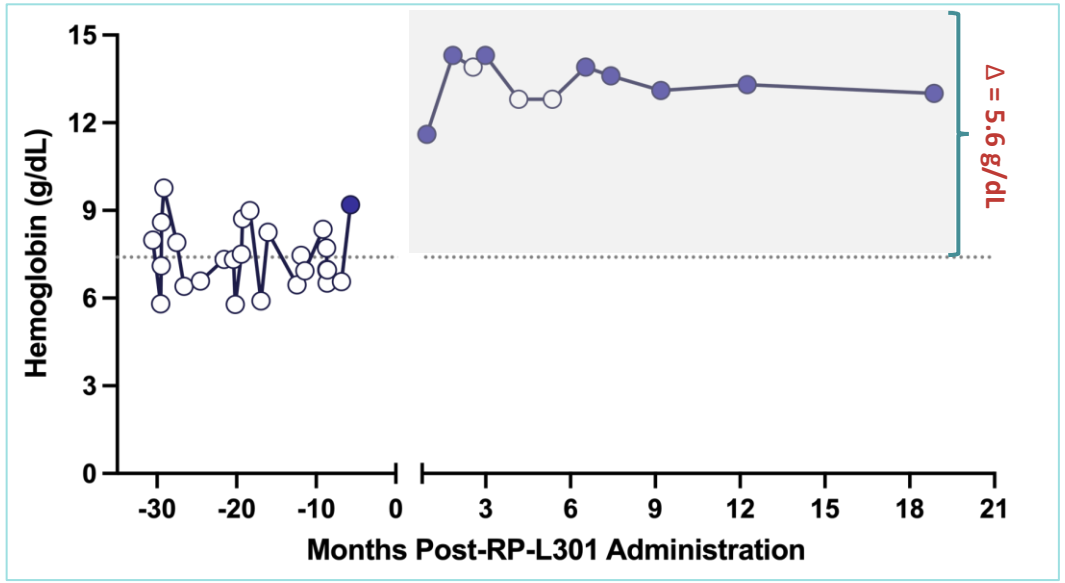
Phase I Cohort Dosing Plan



*Discussions ongoing w/ Agency

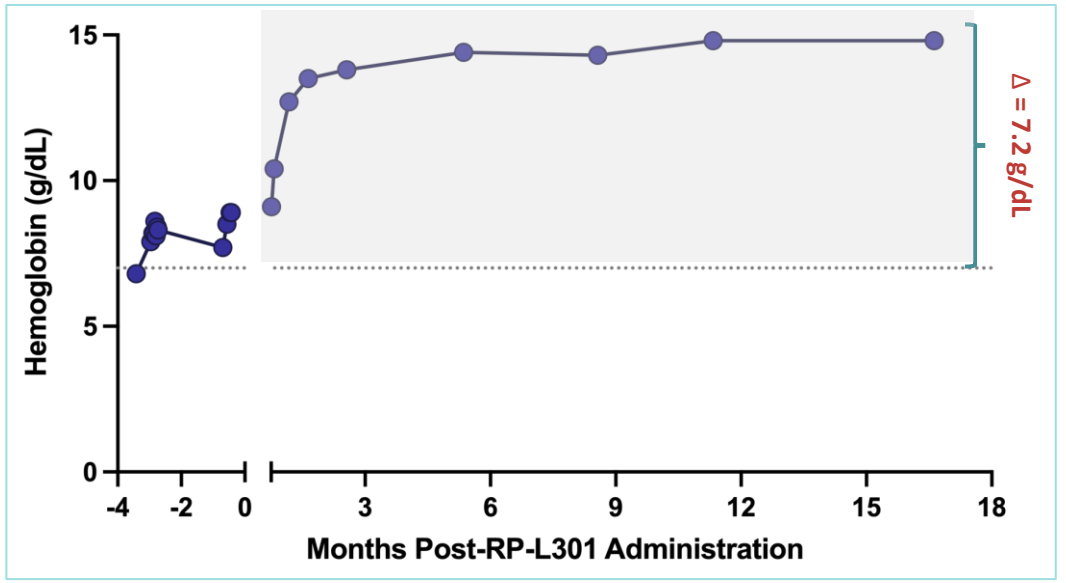
RP-L301 (PKD): Patients 1001 & 1002 Efficacy Results at 18 Months

Patient 1001



- Marked hemoglobin improvement (~7.4 g/dL to 13.0 g/dL) sustained at 18 months post-infusion
- No transfusion requirements following engraftment

Patient 1002



- Hemoglobin normalized to 14.8 g/dL at ~18 months post-infusion
- No transfusion requirements following engraftment

Accompanied by sustained pVCN in 1-3 range and improvement of hemolysis markers

Note: Lab Values during mobilization/apheresis & post-conditioning period were not included

Data as of December 2021

RP-L301 (PKD) Conclusion: Sustained Safety and Efficacy Observed in First 2 Patients at 1 Year

- Safety profile of RP-L301 ***appears favorable*** with no IP-related SAEs
- Insertion site analyses in PB and BM for both adult patients up to 12 months post-RP-L301 demonstrated highly polyclonal patterns and no demonstrable insertions in proximity to potential oncogenic loci
- Preliminary efficacy sustained to date
  - Normalized Hgb and improving hemolysis markers
  - No red blood cell transfusion requirements post-engraftment
- Commercial-grade drug product and centralized testing for all treated patients

RP-L301 (PKD): Development Plan

PKD Study Progress to Phase II and Launch

✓ Key Endpoints selected
- Hgb increase
- ↓50% transfusions or transfusion independence

✓ Well delineated natural history in recent PKD NHS publications

❑ Complete Phase I pediatric cohort dosing (N=2-3)

❑ End of Phase I Regulatory meeting with FDA

❑ Approve & Launch RP-L301 seek regulatory approval in the U.S. and EU

Life-Cycle Management

❑ Expansion study to pre-splenectomy patients anticipated in 2023

❑ Exploration of non-genotoxic conditioning

rocket pharma

Fanconi Anemia (FA): *Monogenic DNA-repair disorder*

RP-A501
Danon Disease

RP-L301
Pyruvate Kinase Deficiency

RP-L102
Fanconi Anemia

RP-L201
Leukocyte Adhesion Deficiency-I

Background: 80% of patients experience BMF within the ***1st decade of life.*** Patients have a predisposition to ***hematologic malignancies*** and solid tumors

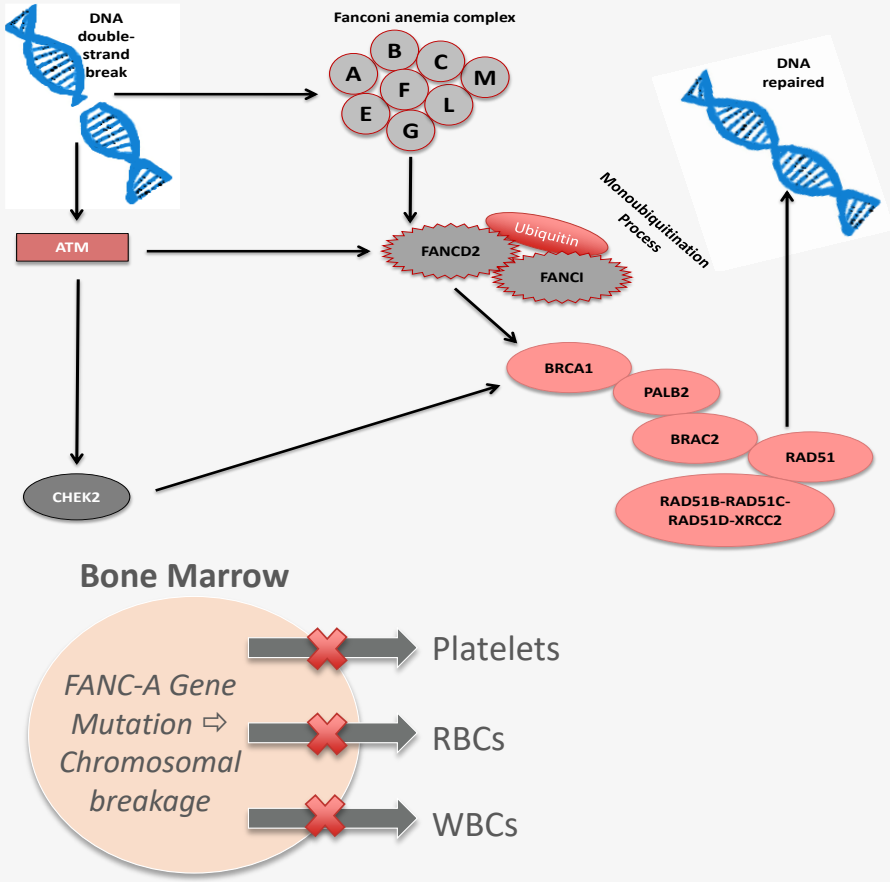
- Acute Myeloid Leukemia
- Head and Neck Cancer[1]

} ↑ Risk 30-50x

Current available treatments: Allogeneic hematopoietic stem cell transplant associated with 100-day mortality, GVHD, and additional increased cancer risk

Addressable Market[2]: Estimated US + Europe ~***4000*** *patients (prevalence),* ***500 patients/year***

MECHANISM OF ACTION



[1] Alter Br J Hametol 2010.
[2] 4,000 based on a detailed population analysis of FA genomic variants. 500 per year extrapolated by actual transplants per year plus patients from prevalence

RP-L102 (FA): Clinical Program Overview

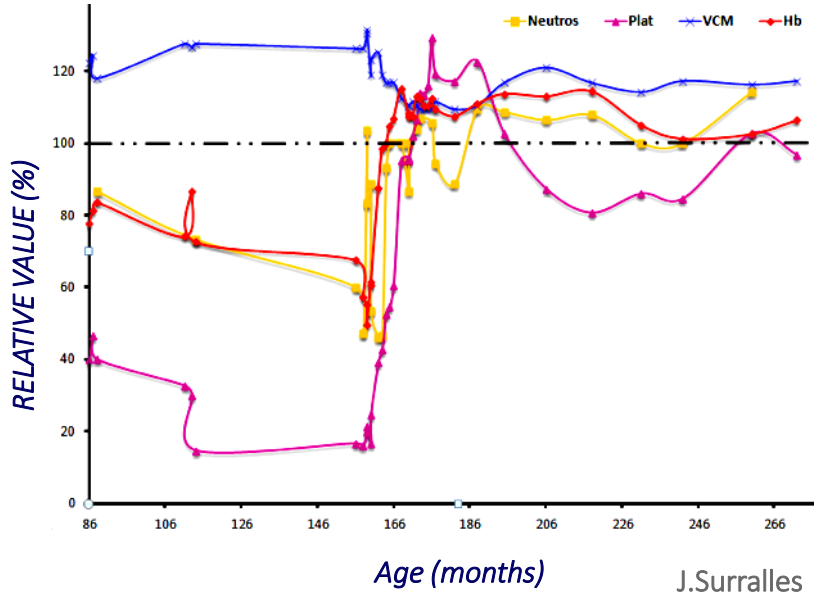
RP-L102 Studies	Non-randomized, open label studies: US Phase 1, US Phase 2, and EU Phase 2 (FANCOLEN-II)	
CMC/Drug Product	**"Process B"** includes cell enrichment, transduction enhancers, commercial-grade vector and modified cell processing	
Clinical Studies	✓ EU FANCOLEN-I study (n=9) completed ✓ US Phase 1 study (n=2) completed at Stanford University ❑ US Phase 2 study ongoing at Stanford and Minnesota University ❑ EU Phase 2 study ongoing at Hospital Infantil Universitario Niño Jesús and UCL/GOSH	
Endpoints	**Efficacy**	**Engraftment**: Peripheral blood (PB) and BM vector copy number (VCN) **Phenotypic correction**: Increased resistance of BM and PB cells to MMC and DEB **Clinical response**: Prevention of BMF
	Primary Endpoint: ***Efficacy in at least 5 patients (defined as >10% increase in MMC resistance at 2 time points observed between 12-36M post-rx) required to reject null hypothesis***	
	Safety profile of RP-L102	

Post rx = Post-treatment

RP-L102 (FA): Potential to Correct Bone Marrow Defect Without Conditioning to Prevent Hematologic Failure

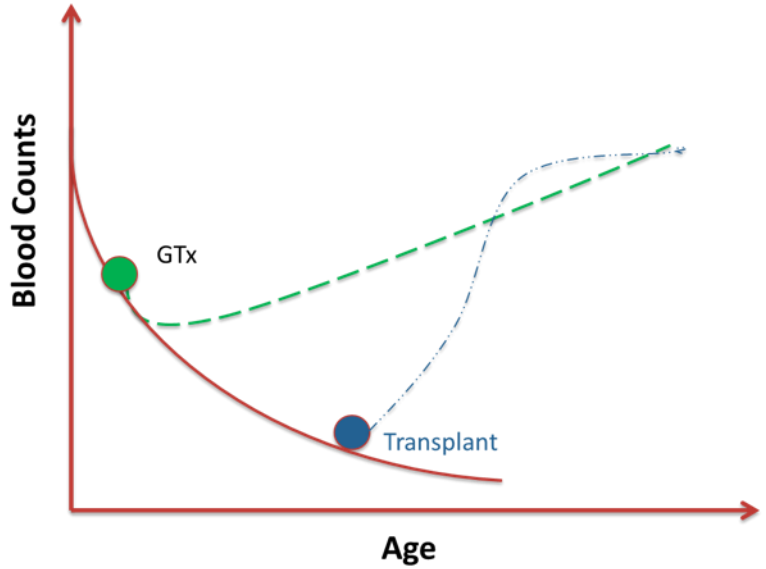
Rationale for GTx in FA Based on Somatic Mosaicism

- Small proportion of FA patients ***spontaneously revert*** to normal phenotype
- ***Proliferative advantage*** favors gene-corrected cells



Gene Therapy Value Proposition:

- Potential to ***correct*** blood & bone marrow defect ***without conditioning***
- GTx implemented as preventative measure to ***avert bone marrow failure***



Potential for single-corrected cell to repopulate to healthier bone marrow[1,2]

[1] Soulier, J., et al. (2005) Detection of somatic mosaicism and classification of Fanconi anemia patients by analysis of the FA/BRCA pathway. *Blood* 105: 1329-1336; [2]Data on file: Showing a single patient with a spontaneous correction of blood counts, no therapy administered.

RP-L102 (FA): Highly Favorable Safety and Initial Efficacy Observed

Safety Data

Safety results appear *highly favorable* and RP-L102 well positioned as *potential first-line treatment option

- Patients treated **without conditioning**
- No signs of dysplasia
- Therapy does not preclude later allogeneic transplant

Efficacy Data

12 patients received RP-L102
6 of 9 show preliminary evidence of engraftment

N = 9 with ≥ 12M follow-up (12-36M)

To date, **5 of 9** show increasing evidence of engraftment with BM MMC resistance ranging from **51-94%** and **≥20%** at **two consecutive timepoints**

N = 3 with < 12M follow-up

Longer term data to follow

*RP-L102 related SAE: 1 patient experienced a Grade 2 transient infusion-related reaction; resolved without any additional clinical sequelae

12 Patients Treated: Demographics and Investigational Product Metrics for Initial n=9

Subject #	Age at Enrollment (years)	Follow Up (months)	CD34+ Cells/kg	CFCs/kg	Mean VCN: Liquid Culture	Mean VCN: CFCs	Transduction Efficiency (%)	CFC Survival MMC 10nM (%)
1 (1001)	5	36	$2.0 \times 10^{5*}$	$5.2 \times 10^{4*}$	2.08	0.62**	67	33
2 (1002)	6	18†	$3.7 \times 10^{5*}$	$5.0 \times 10^{4*}$	2.21	0.92**	72	47
3 (2004)	3	24	4.8×10^{5}	$1.3 \times 10^{5‡}$	1.70	0.73	100	63
4 (2008)	2	21	3.2×10^{6}	$5.5 \times 10^{5‡}$	1.65	1.56	97	63
5 (2009)	3	18	1.9×10^{6}	$3.1 \times 10^{5‡}$	2.16	0.76	61	45
6 (2010)	3	21	$4.1 \times 10^{6*}$	n/a	0.62	n/a	n/a	n/a
7 (2011)	5	18	$2.8 \times 10^{6*}$	n/a	1.46	n/a	n/a	n/a
8 (2014)	6	15	$5.4 \times 10^{5*}$	$3.6 \times 10^{4*}$	3.68	pending	pending	31
9 (2016)	2	12	$3.0 \times 10^{5*}$	$2.5 \times 10^{4*}$	1.96	0.64	88	64

All patients ≤6 years at enrollment

9 patients have ≥12–36 months of follow-up

3 patients recently treated

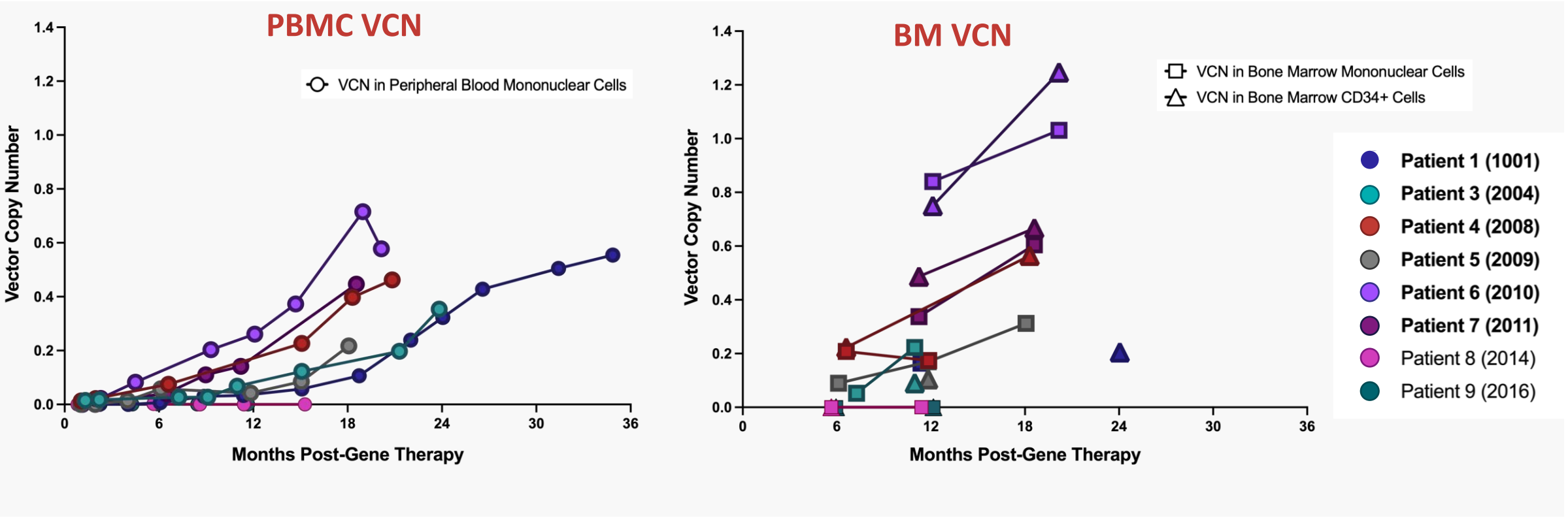
(<1 yr follow up; CD34+ cells/kg: 2.5×10^{5} to 2.3×10^{6}/kg; other metrics pending validation)

Mean Values

VCN (liquid culture): 1.95
VCN (CFC): 0.87
Transduction eff: 81%
CFC MMC-resistance: 49%

m: months; CFCs: colony forming cells; VCN: vector copy number; n/a: not available
* Per NC200 automated count (results in ~50% lower count vs. manual count used in FANCOLEN-I).
** Mean CFC VCN was assessed from a cryopreserved drug product sample.
† Patient withdrawn from the study at 18 months post-RP-L102 infusion; received successful allogeneic HSCT. ‡ Revised value following data validation.
Data cut-off: April 4, 2022; Preliminary interim results are presented from the ongoing clinical studies.

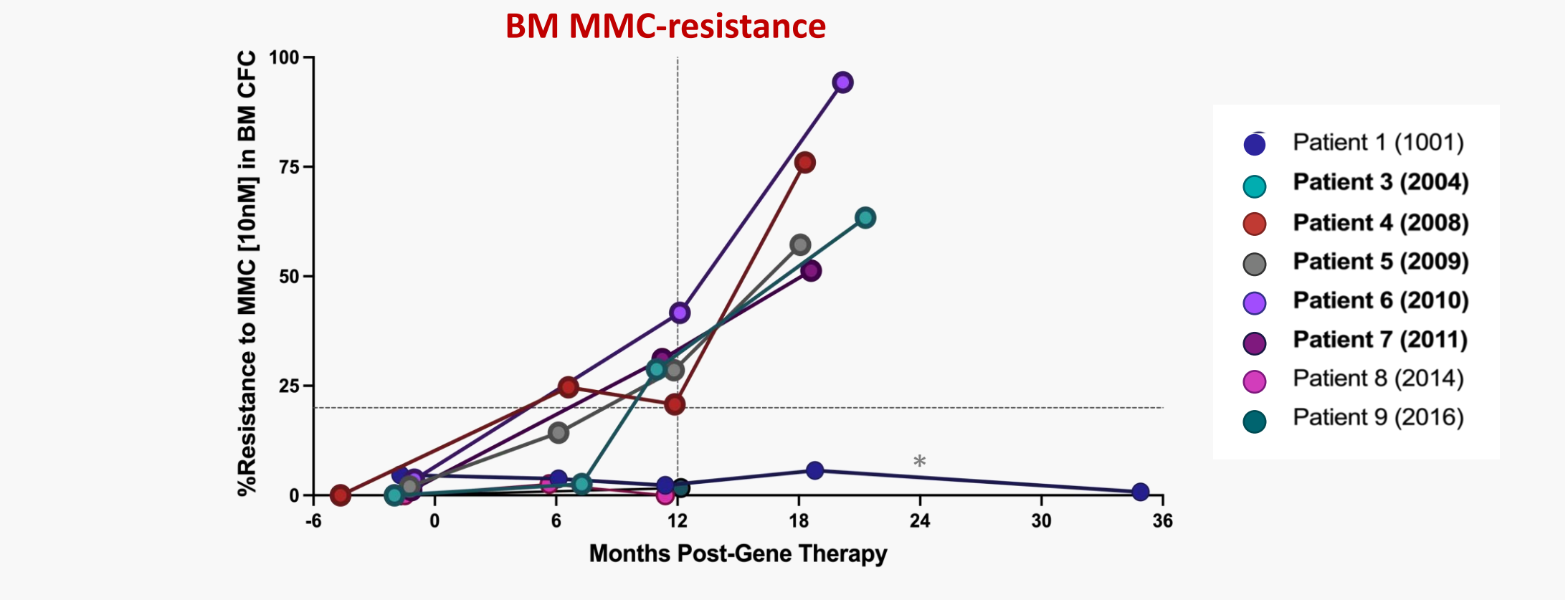
Sustained Genetic Correction in 6 of 9 Patients ≥1 year post-RP-L102



Progressive increases in gene markings in PB and BM in 6 patients

Not shown: PB and BM VCN in Patient 2 (1002), who was withdrawn from the study at 18 months post-RP-L102 infusion

Increasing Phenotypic Correction over 1-2 years post-RP-L102



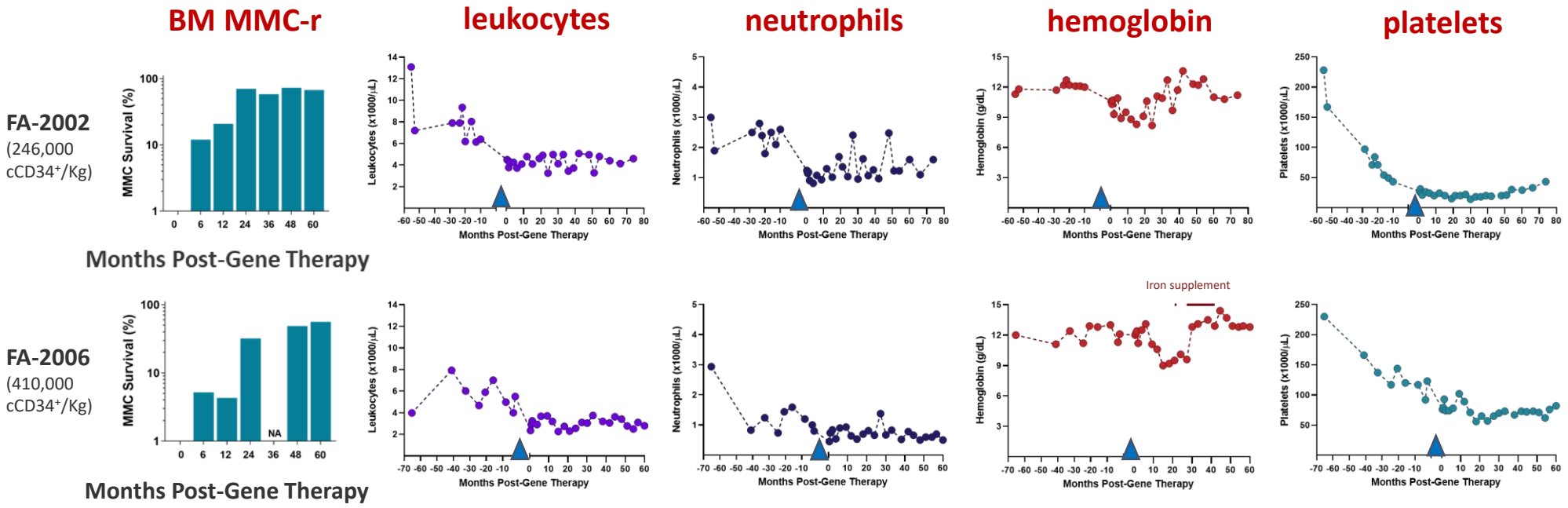
For 5 pts, increased BM CFC MMC resistance ranging from 51% to 94% observed at 18–24 months post-RP-L102 administration

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

* BM MMC-res for patient 1 (1001)'s 24 m assessment was not performed at one of the study's central laboratories and are 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 MMC Resistance is Associated with Long-term Hematologic Stability

FANCOLEN-I (investigator-initiated) long-term follow-up:



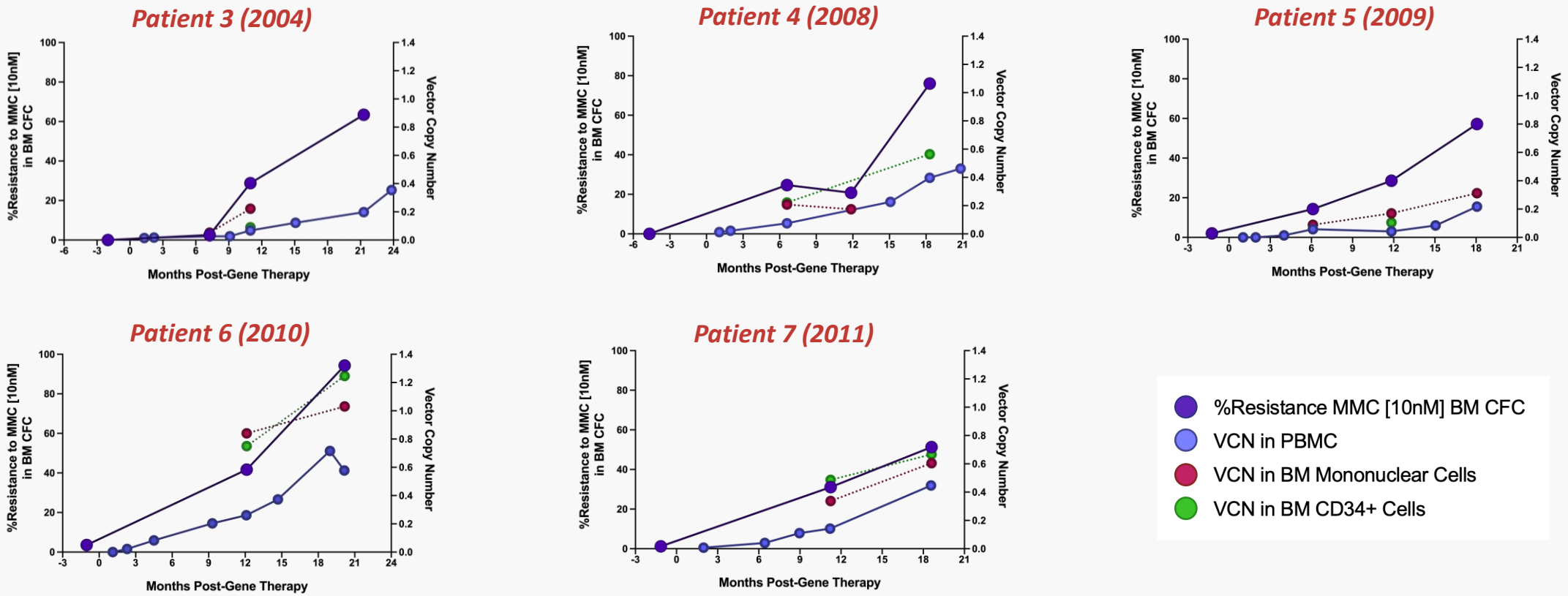
≥20% BM CFC MMC resistance is associated with long-term hematologic stability (up to 6 years post-gene therapy) as demonstrated by FANCOLEN-I patients FA-2002 and FA-2006

- FA-2002 has had concomitant sustained blood count stabilization, with trends suggesting increases in Hb and platelets after 24 and 30 m, respectively
- FA-2006 has had blood count stabilization with hemoglobin improvement

* Source data verification has not yet been performed on most recent visits. Data cut-off April 26, 2022

Genetic Correction Correlates with Phenotypic Improvement

- PB VCN strongly correlates with BM CFC MMC-Res at 12 months post-RP-L102 (r = 0.83)+*
- BM Mononuclear cell VCN strongly correlates with BM CFC MMC-Res at 12 months post-RP-L102 (r = 0.81)**

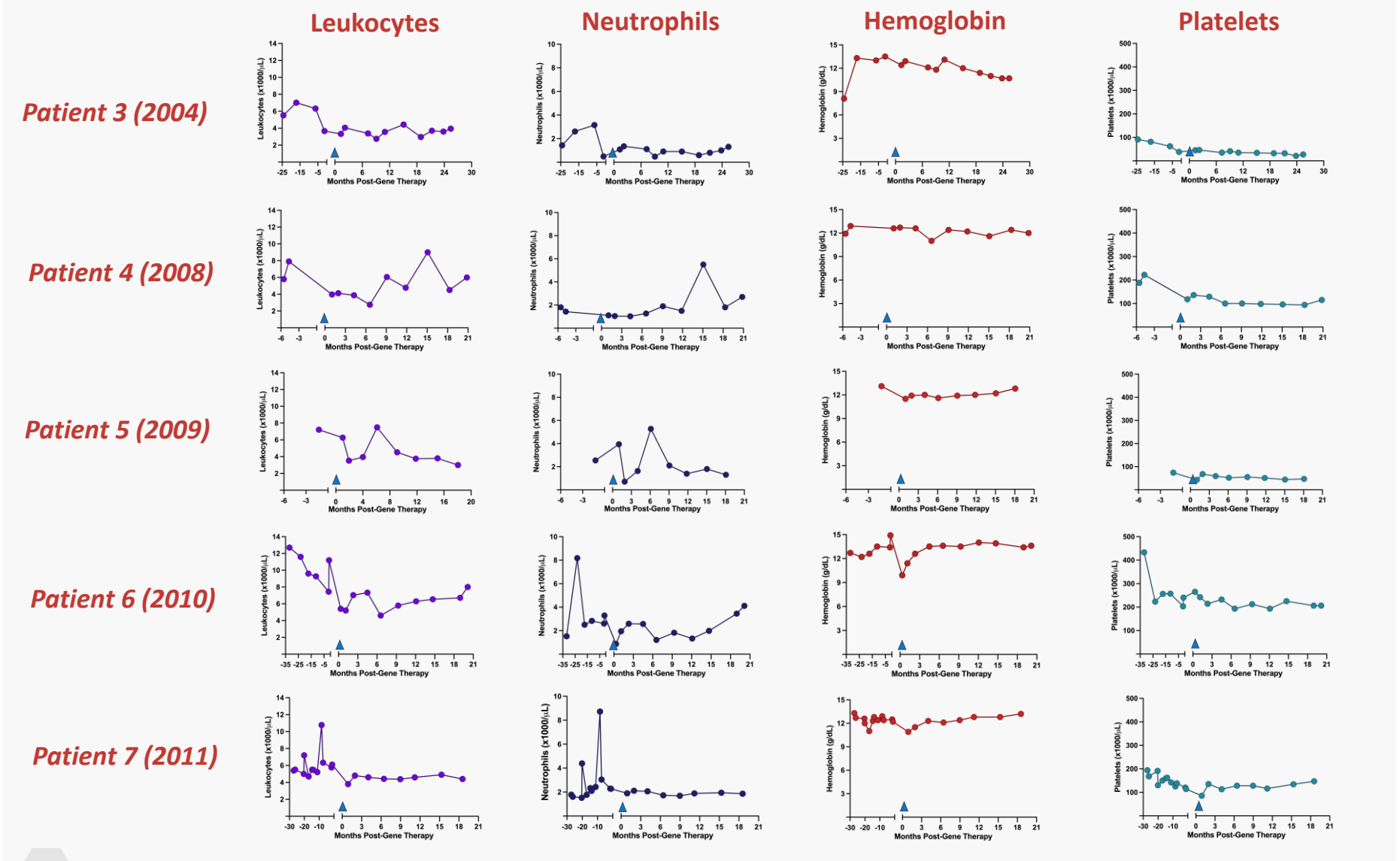


*r correlation calculated using data from n=7 patients (PB VCN data from patients 2 [1002] and 4 [2008] not available); **r correlation calculated using data from n=9 patients

+ Patient 1 (1001) has to-date demonstrated more limited correlation between VCN and MMC-Resistance

- Genetic correction has been evident via PB VCN (0.55 at 36 m study visit) and BM CD34+ VCN (0.21 at 24 m study visit).
- BM MMC-Resistance Δ was ~11% at 24 m study visit (not performed at central lab), but BM MMC-Resistance was 0.8% at 36 m study visit (central study lab).
- Patient required RBC transfusion at ~35 m post-RP-L102 in setting of potential intercurrent viral illness and recent vaccination.

Increased BM CFC MMC Resistance Associated with Hematologic Stabilization at ≥1 year post RP-L102



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

Conclusions from Initial 9 Patients with ≥1 Year of Follow-Up

Comprehensive efficacy in multiple patients with >1 year of follow-up

- **5 patients have sustained, increasing BM CFC MMC resistance ranging from 51 to 94% at 18–24 months, and ≥20% at two consecutive timepoints**
- **Increasing BM CFC MMC resistance is accompanied by concomitant genetic markings and hematologic stabilization**
- 6 patients with sustained peripheral blood and BM genetic correction (VCN)
- 2 additional patients with 12 months follow-up, potential for engraftment 12–24m post RP-L102
- 1 patient had progressive BMF & underwent successful allogeneic transplant

Safety profile of RP-L102 is favorable

- Engraftment and phenotypic correction achieved in the ***absence of conditioning***
- No signs of dysplasia, clonal dominance or oncogenic integrations
- RP-L102 related SAEs: 1 patient experienced an infusion-related reaction (transient, Grade 2)

**** Efficacy in ≥5 patients (observed over >1 year post rx) required to reject null hypothesis***

Data cut-off: April 4, 2022; Preliminary interim results are presented from the ongoing clinical studies.

Leukocyte Adhesion Deficiency-I (LAD-I): A *Monogenic Immunodeficiency*

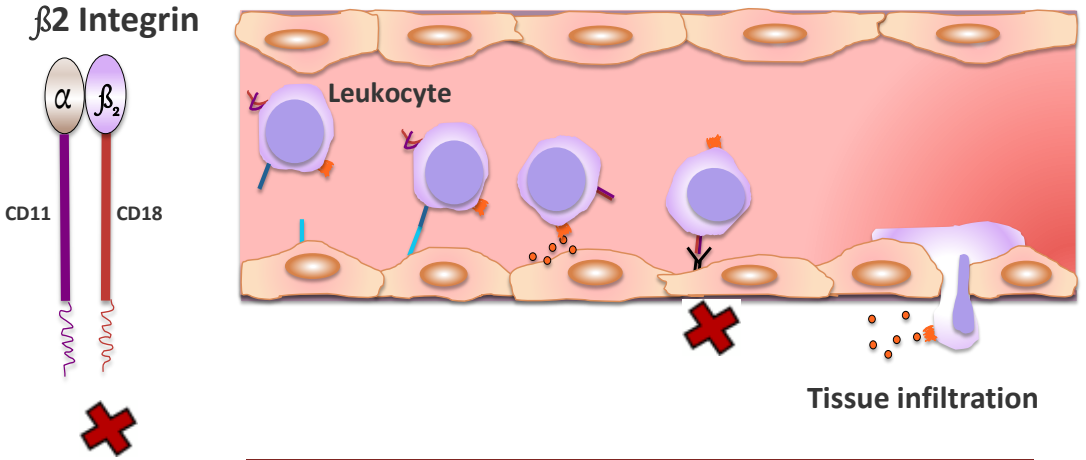
RP-A501
Danon Disease

RP-L301
Pyruvate Kinase Deficiency

RP-L102
Fanconi Anemia

RP-L201
Leukocyte Adhesion Deficiency-I

MECHANISM OF ACTION



LAD-I Disease Spectrum

Moderate: 2–30% CD18⁺ PMN

Severe: <2% CD18⁺ PMN

Background: Autosomal recessive disease characterized by recurring and ultimately fatal infections; caused by mutations in *ITGB2* encoding for CD18 - essential for leukocyte adhesion and subsequent migration; ***>50%*** of patients present with severe phenotype: ***60-75% mortality by age 2***[1]

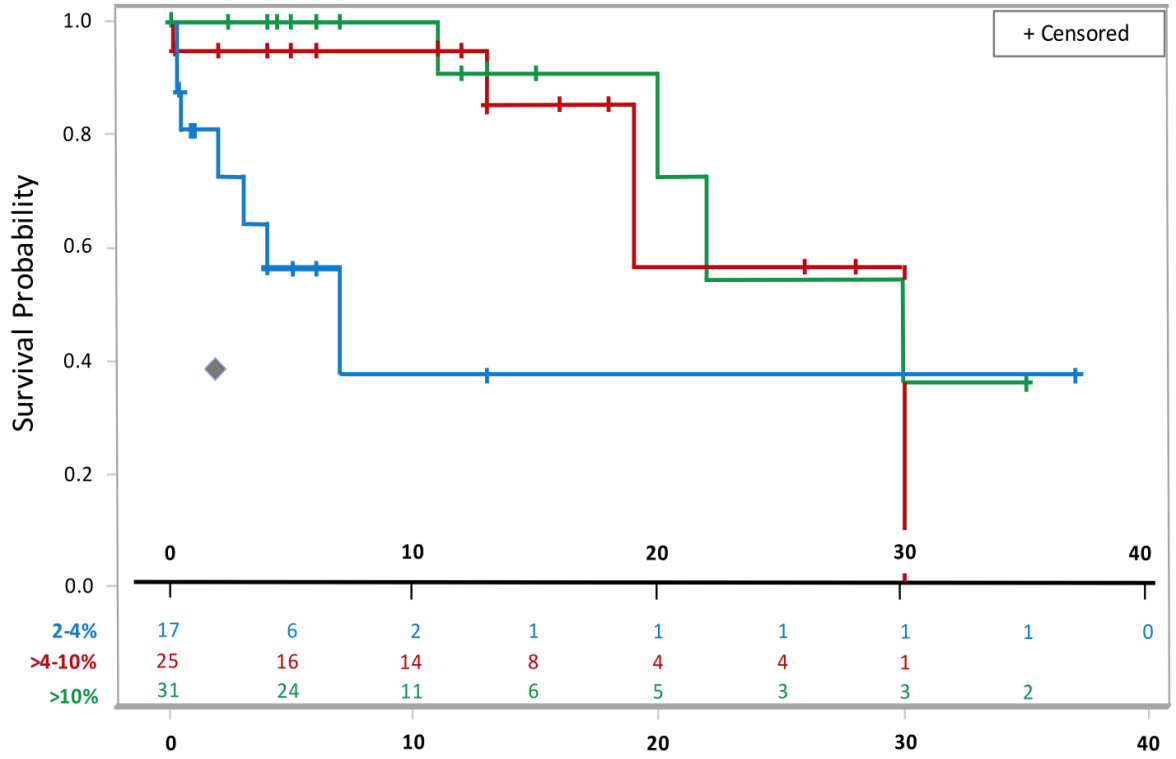
Current Available Treatments: Allogeneic hematopoietic stem cell transplant associated with significant graft failure and acute GvHD

Addressable Market: Estimated ***25-50 pts*** treatable per year for severe LAD-I population; ***up to 100*** for potential expansion into moderate LAD-I population

[1]Almarza E et al. J Allergy Clin Immunol Pract. 2018 July-August (6) 1418-1420.
PMN: polymorphonuclear leukocytes
Additional funding for the LAD-I clinical trial is supported by the California Institute for Regenerative Medicine (CIRM)

Rationale for Gene Therapy in LAD-I: CD18 Expression Correlates to Patient Survival

Kaplan-Meier Survival Estimates by Neutrophil CD18 Expression



Patients with severe and moderate LAD-I not receiving allogeneic HSCT[1]

CD18 % ◆ <2% — 2-4% — >4-10% — >10%

Clinical Spotlight Presentation at ASGCT May 2022

Almarza E et al. J Allergy Clin Immunol Pract. 2018 July-August (6) 1418-1420

Natural history studies show the ***correlation*** between ***higher CD18*** expression and longer patient ***survival,*** supporting gene therapy's potential in LAD-I patients

CD18 > 10% results in survival of severe LAD-I patients for decades

◆ : **39% survival to age 2 years** for 66 evaluable patients with severe LAD-I not receiving HSCT

RP-L201 Clinical Trial, Subject and Cell Product Characteristics

Trial Design

- Non-Randomized Global Phase 1/2 Study (n=9)

Key Eligibility Criteria

- Severe LAD-I; CD18 expression <2% neutrophils, or CD11a/b <2% with documented *ITGB2* mutation
- Age ≥ 3 months
- At least one prior significant bacterial of fungal infection

Primary Outcomes

Phase 1:

- Safety & preliminary efficacy

Phase 2:

- Survival: Proportion of patients alive at age 2 and at least 1-year post infusion (& not requiring allogenic HSCT)
- Safety

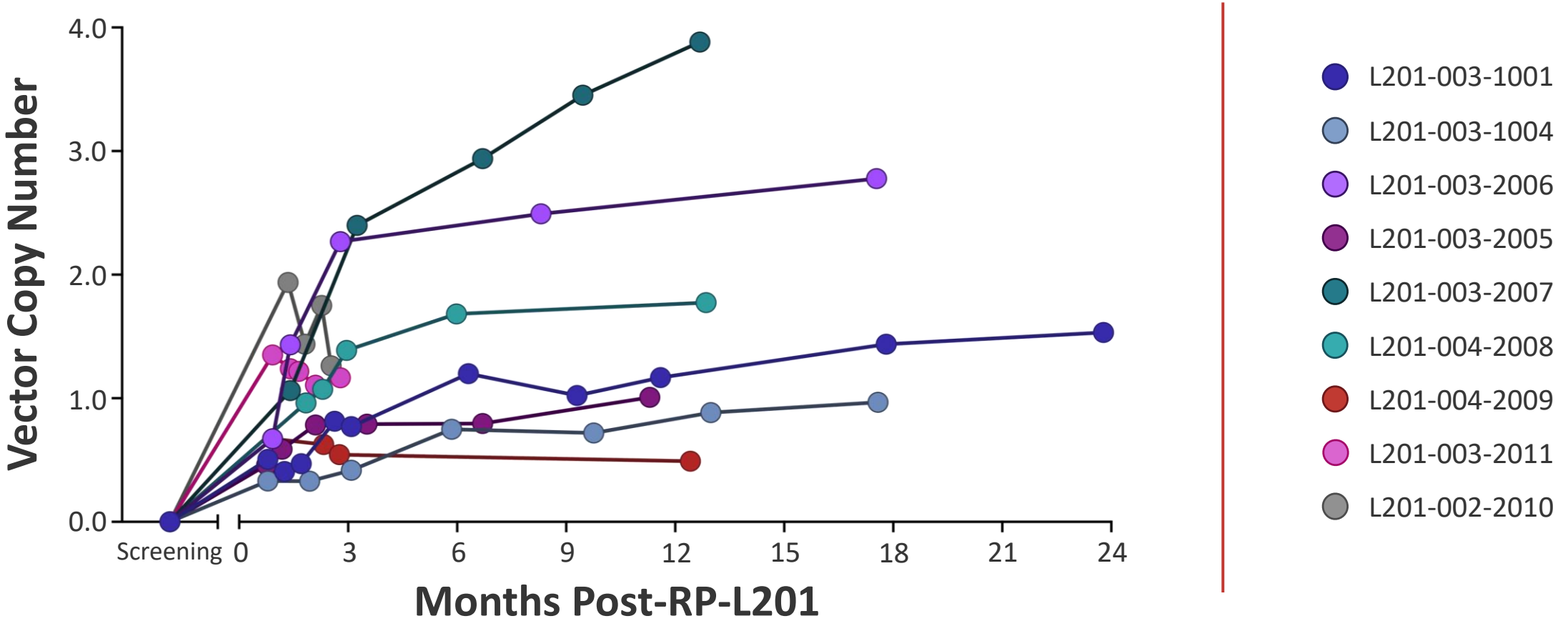
Secondary Outcomes

- **Incidence and severity of infections** (e.g., incidence of severe infections, hospitalizations and prolonged hospitalizations)
- % of pts **w/neutrophil CD18 expression at least 10% of normal**
- % of pts w/neutrophil **VCN** of at least 0.1 at 6m post-infusion
- Improvement/**normalization of leukocytosis**
- Resolution (partial or complete) of underlying **skin rash or periodontal abnormalities**

Patient	Sex	Age at enrollment	Drug Product VCN	CD34+ Cell Dose
L201-003-1001	F	9 years	3.8	4.2×10^6 cells/kg
L201-003-1004	F	3 years	2.5	2.8×10^6 cells/kg
L201-003-2005	F	3 years	1.8	6.5×10^6 cells/kg
L201-003-2006	M	7 months	2.9	4.3×10^6 cells/kg
L201-003-2007	M	3 months	3.6	5.0×10^6 cells/kg
L201-004-2008	M	5 months	3.8	3.3×10^6 cells/kg
L201-004-2009	M	3 years	2.0	4.5×10^6 cells/kg
L201-002-2010	F	4 years	3.5	10.0×10^6 cells/kg
L201-003-2011	F	2 years	3.8	3.8×10^6 cells/kg

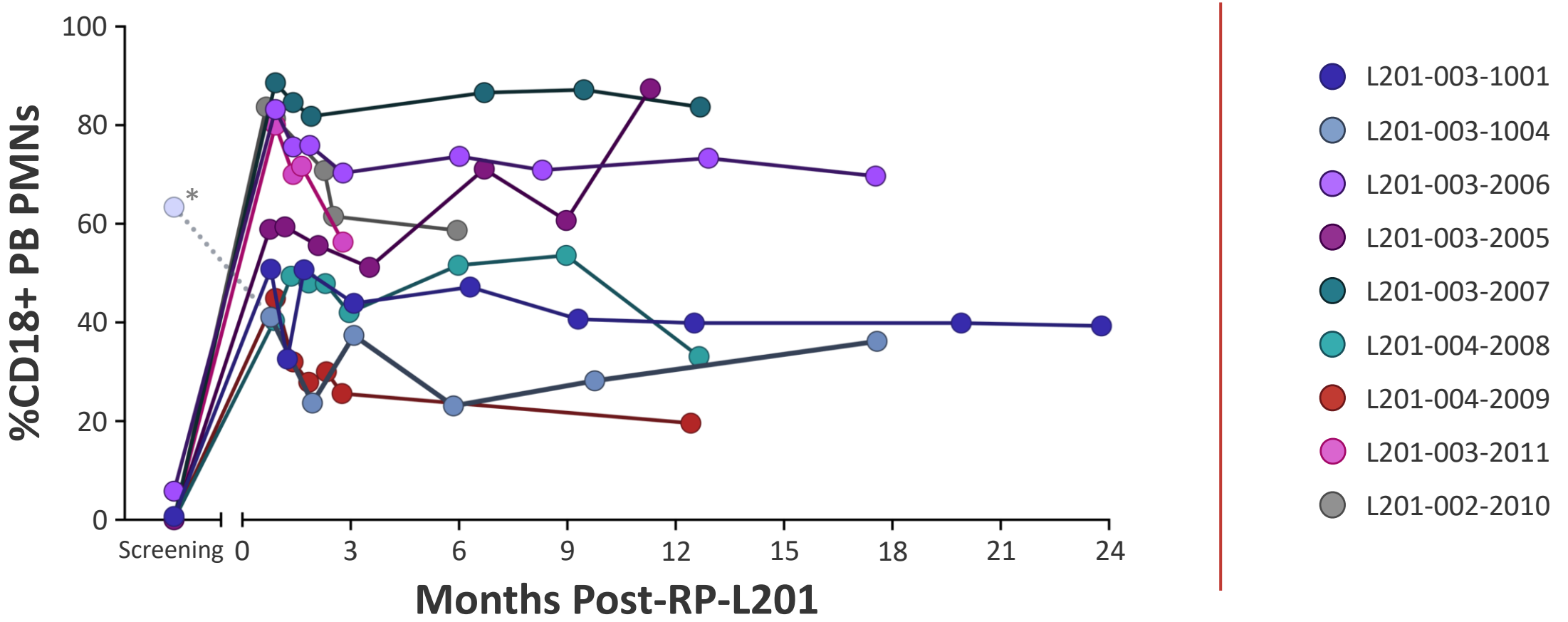
As of March 9, 2022: Data reported from 9 of 9 patients (3–24m follow-up)
Study enrollment is completed. All subjects have been treated.

RP-L201 (LAD-I): VCN in Peripheral Blood Mononuclear Cells (PBMCs)



All 9 of 9 patients with durable VCN integration

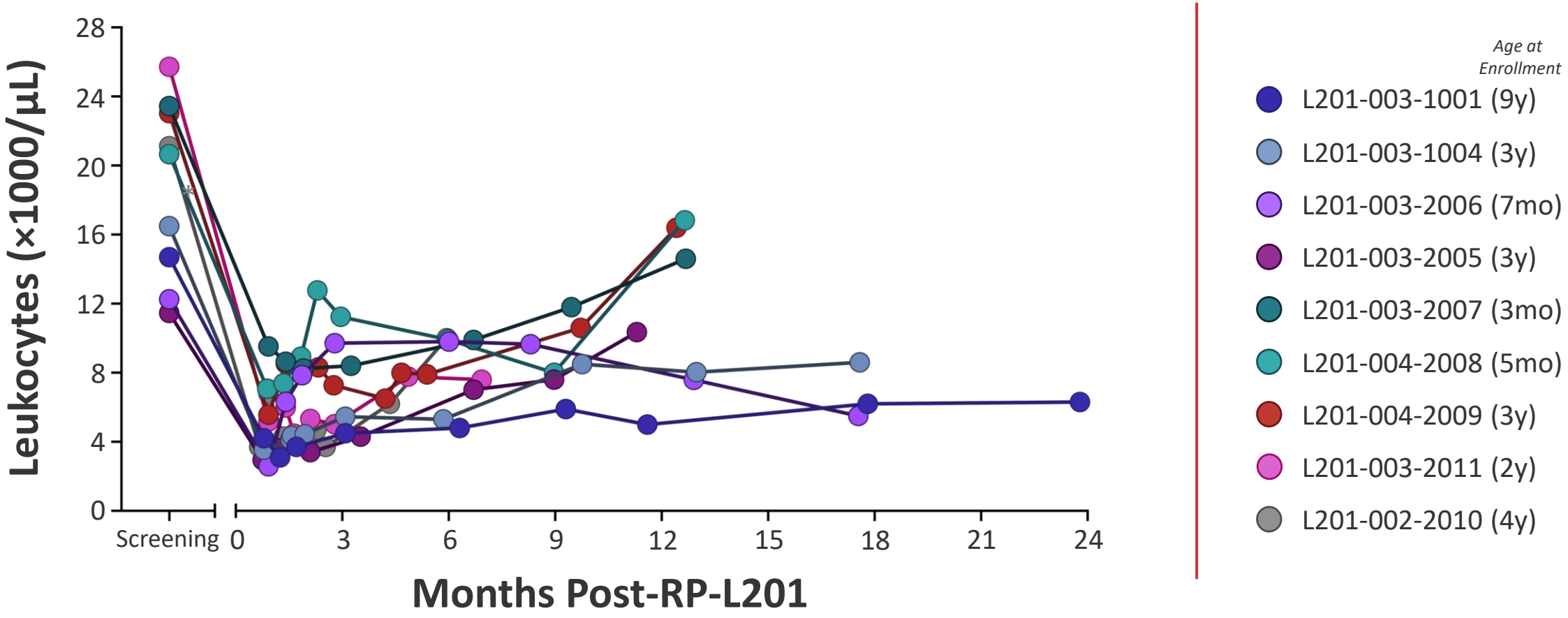
RP-L201 (LAD-I): CD18 Expression in PB Polymorphonuclear Cells (PMNs)



All 9 of 9 patients with >10% CD18 PMNs expression

* Dim/weak CD18 expression reported at baseline for Subject L201-003-1004 in ~63% of cells in conjunction with <2% CD11a/CD11b pression, likely indicating abnormal/unstable protein

RP-L201 (LAD-I): Resolution of LAD-I Related Abnormal Leukocytosis
A clinical biomarker of a normalized phenotype

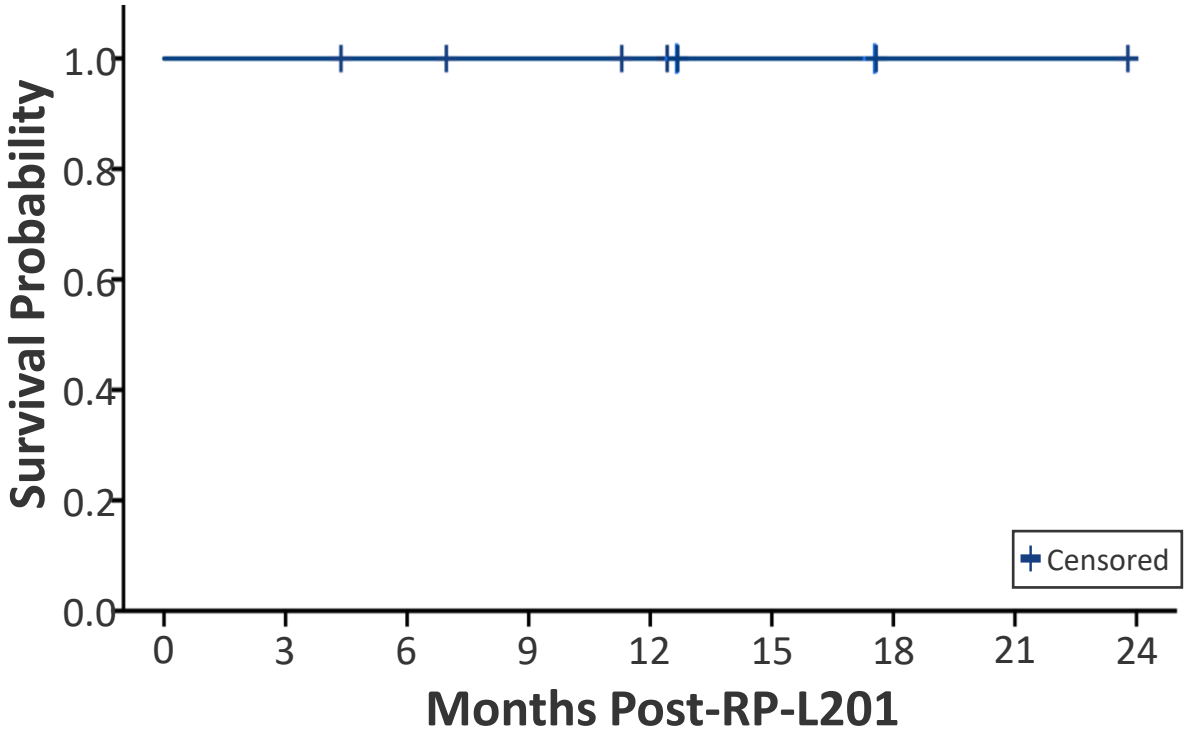


All 9 of 9 patients with leukocytosis resolution

Normal Leukocyte Ranges per Age Group: *0 months to <3 months: 7.20–18.00×1000/µL; ≥3 months to <6 months: 6.70–14.00×1000/µL; ≥ 6months to 12 months: 6.40–13.00×1000/µL; 12 months to <2 years: 6.40–12.00×1000/µL; ≥2 to <6 years: 5.20–11.00×1000/µL; ≥6 years to <12 years: 4.40–9.50×1000/µL; ≥12 years to <18 years: 4.40–8.10×1000/µL*

RP-L201 (LAD-I): Clinical Outcomes - Overall Survival & Incidence Reduction of All Hospitalizations

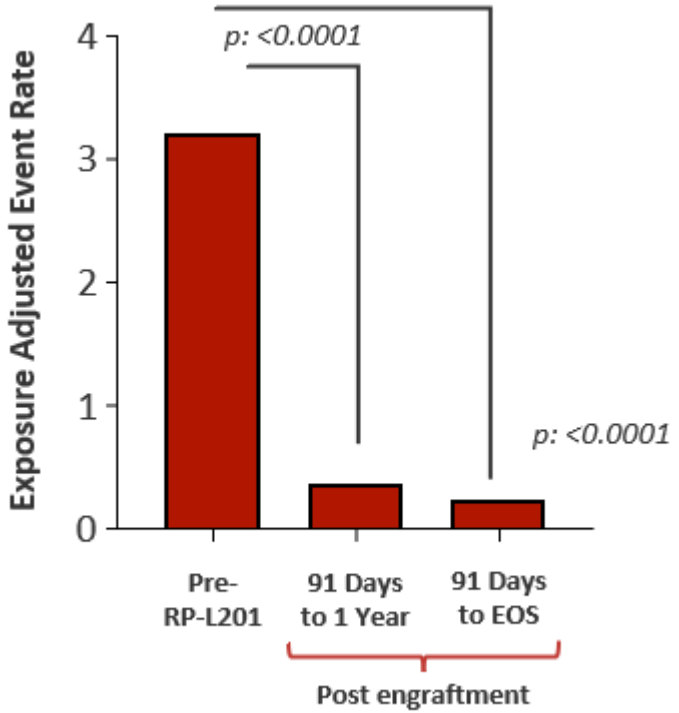
Overall Survival (OS) Kaplan-Meier Estimate



Survival without allogeneic HSCT

- >2 years of age
- 1-year post-RP-L201 infusion

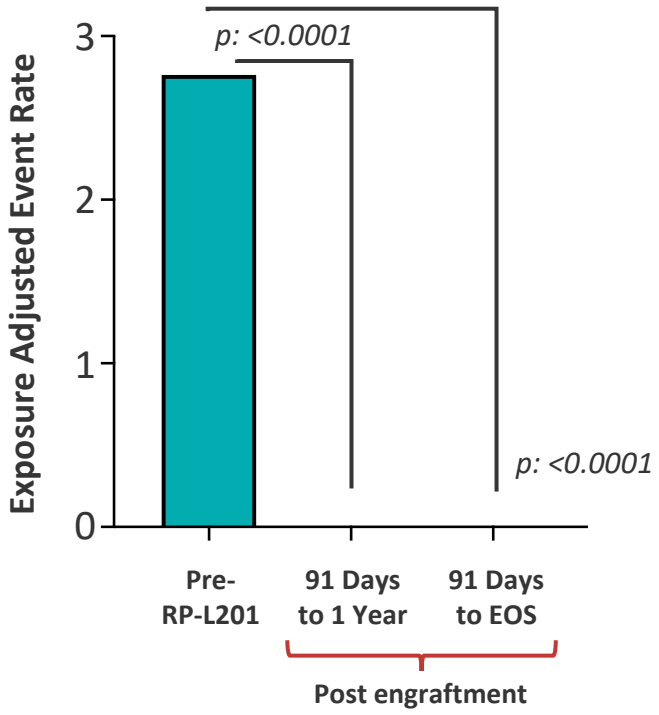
Incidence of All Hospitalizations



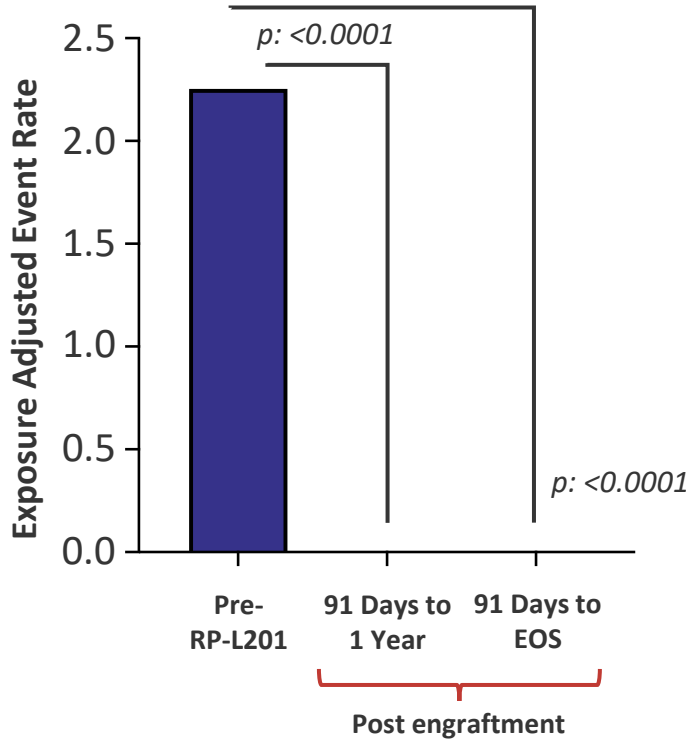
EOS: end of study

RP-L201 (LAD-I): Clinical Outcomes: Incidence Reduction of Infection and Inflammatory Related Hospitalizations, Prolonged Hospitalizations and Severe Infections

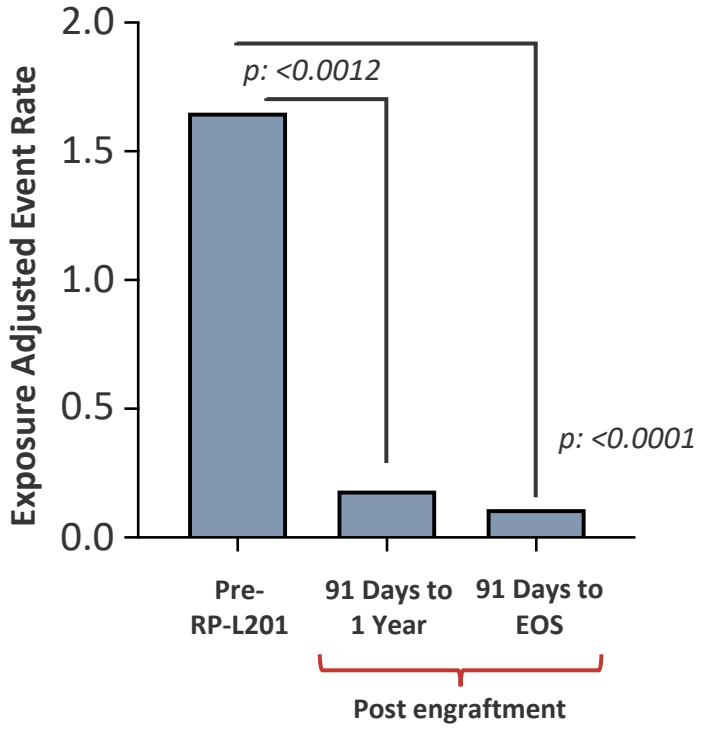
Incidence of Infection and Inflammatory Related Hospitalizations



Incidence of Prolonged (>7 days) Hospitalization



Incidence of Severe Infections



EOS: end of study

RP-L201 (LAD-I): Spontaneous LAD-I Related Skin Rash Resolution and Restoration of Wound Repair Capabilities after RP-L201

Spontaneous resolution of abdominal lesion

L201-003-1001

Baseline

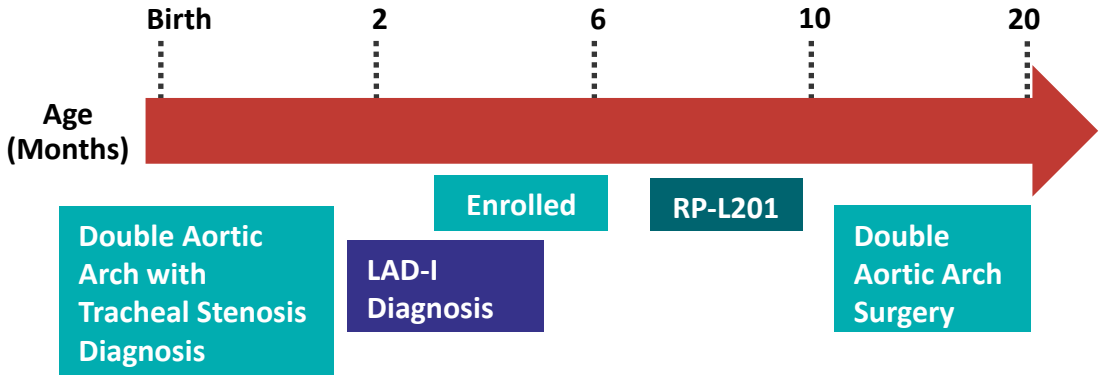
3 months Post-IP

6 months Post-IP

12 months Post-IP

Wound repair at thoracotomy site after surgical correction of double aortic arch

L201-004-2008



RP-L201 (LAD-I): Data Summary

- **Phase 1/2 study enrollment complete: 9 of 9 severe LAD-I patients successfully treated**
- **Safety profile of RP-L201 appears favorable: No drug product-related SAEs**. Initial **ISA** indicates highly **polyclonal** patterns without evidence of dominant integrations in proximity to oncogenic loci
- **Efficacy evident in all 9 severe LAD-I patients with available follow-up of 3-24m**
  - Seven (7/9) patients with ≥ 12-months of follow-up
  - **Durable** >0.1 **VCN integration** across the cohort
  - **100% engraftment and CD18 reconstitution across all treated patients (achieved <34 days post-infusion)** with CD18+ PMN expression ranging from ~19.6% to ~87.4%
  - **Leukocytosis resolution** in all treated subjects
  - **100% overall survival by Kaplan-Meier estimate** one-year post-RP-L201 and ≥ 2 years of age
  - **Significant reduction in** LAD-I disease-related **hospitalizations and severe infections** in **all** (9/9) patients following RP-L201 gene therapy
  - Evidence of spontaneous **resolution** of LAD-I related **skin rash** and **restoration of wound repair** capabilities

RP-L201 (LAD-I): Global Registrational Plan

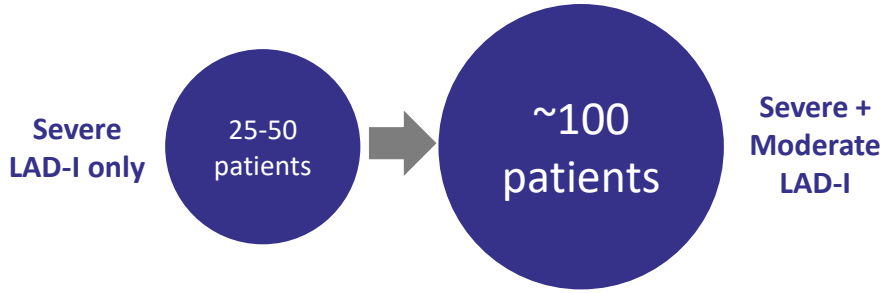
- ✓ **Enrollment Completed; 9 of 9 patients treated**
- ✓ **Efficacy Seen in All 9/9 Patients with 3-24 months of Follow-Up**
- ✓ **Regulatory Designations:**
  - ➢ Fast Track and Advanced Therapy Medicinal Product (ATMP)
  - ➢ **Rare Pediatric Disease (eligible for PRV)**
  - ➢ Orphan Drug designation in the U.S./EU
  - ➢ **Regenerative Medicine Advanced Therapy (RMAT), PRIority MEdicines (PRIME)**
- ❑ **Topline Data Readout Anticipated 2Q-2022**
  - ➢ 100% overall survival (OS) by Kaplan-Meier estimate one-year post-RP-L201 and ≥ 2 years of age, across the cohort

BLA / MAA Filing

Life-cycle Management

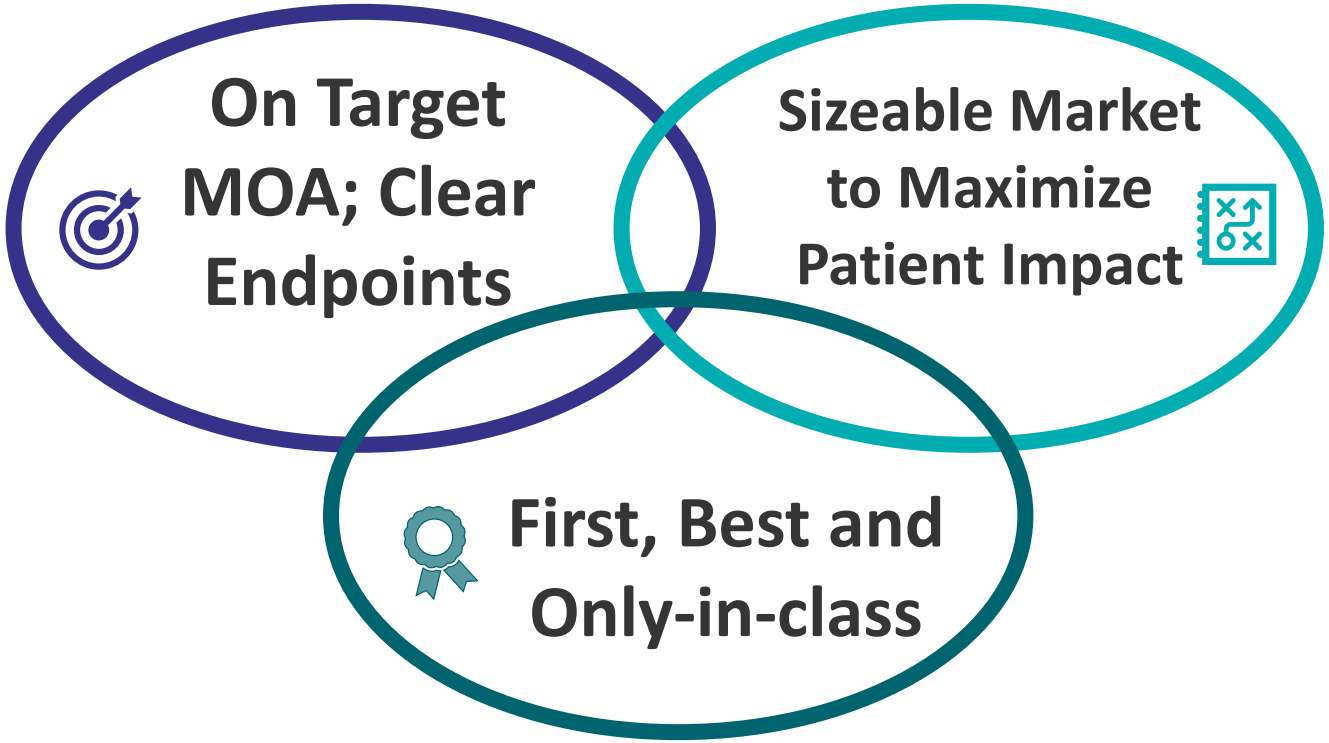
- **Potential label expansion** to include moderate LAD-I population
- Potential study initiation in 2023

LAD-I Addressable Market



Replicating Core R&D Strategy for “Wave 2” Programs

We continue to build our pipeline based on our core R&D strategy; identify the “right” indications for the most efficient development path



Anticipated Program Milestones (2022 – 2024)
Our Path from Clinical to Commercial-Stage

2022

2023-2024

2Q 2022

- **LAD-I:** Top line data
- **FA:** Top line data (early)
- In-house **AAV cGMP manufacturing**

3Q 2022

- **Danon:** Pediatric Cohort Data

4Q 2022

- **Danon:** Initiate Phase 2 pivotal study activities
- **FA:** Additional data
- **PKD:** Preliminary Phase 1 data readout
- **PKD:** Initiate Phase 2 pivotal study activities

- **LAD-I & FA:** Approvals & Launches in U.S. & EU
- **Wave 2 pipeline** enters clinic
- Label expansion studies for **Danon (Female), FA (C & G), LAD-I (Moderate) and PKD (Moderate)** programs

Expert Leadership Team

Gaurav Shah, MD
Chief Executive Officer

- Novartis
- Eli Lilly
- Columbia University
- Harvard University

Kinnari Patel, PharmD, MBA
President and Chief Operating Officer

- AstraZeneca
- Bristol Myers Squibb
- Novartis
- Roche

Jonathan Schwartz, MD
Chief Medical Officer and Clinical Development, SVP

- Stemline Therapeutics
- ImClone Systems (Eli Lilly)
- Mount Sinai Medical Center
- NewYork-Presbyterian Hospital

Raj Prabhakar, MBA
Chief Business Officer, SVP

- Caladrius Biosciences
- Celsion Corporation
- Protiveris
- Osiris Therapeutics

Isabel Carmona, JD
Chief Human Resources Officer, SVP

- Teva Pharmaceuticals
- Shire
- Ichnos Sciences

Mayo Pujols
Chief Technology Officer

- Andelyn Biosciences
- Novartis
- Celgene
- Advaxis

Gayatri R. Rao, MD, JD
Chief Development Officer of LVV, SVP

- FDA
- Sidley Austin LLP

Martin Wilson, JD
General Counsel and Chief Compliance Officer, SVP

- Ichnos Sciences
- Teligent
- Endo Pharmaceuticals
- Par Pharmaceuticals

Carlos Martin
Chief Commercial Officer, VP

- Novartis
- Advanced Accelerator Applications

John Militello, CPA
Principal Accounting Officer, VP

- Immune Pharmaceuticals
- Retrophin
- Volt Information Sciences
- BDO USA, LLP

Jessie Yeung, MBA
Investor Relations and Corporate Finance, VP

- Legend Biotech
- Bank of America
- Wells Fargo Securities
- J.P. Morgan

FDA, Food and Drug Administration; LVV, lentiviral vector.

Rocket Values & Partnerships

TRUST

GENEROSITY

CURIOSITY

ELEVATE

ciber
Centro de Investigación Biomédica en Red

Ciemat

FRED HUTCH

iis FJD INSTITUTO DE INVESTIGACIÓN SANITARIA FUNDACIÓN JIMÉNEZ DÍAZ

Penn

LUND UNIVERSITY

Hospital Infantil Universitario Niño Jesús

REGENXBIO

UCL

UNIVERSITY OF MINNESOTA

UCLA

Stanford MEDICINE

UC San Diego

Hospital Universitario Fundación Jiménez Díaz
Grupo quirónsalud

CIRM
CALIFORNIA'S STEM CELL AGENCY