Autologous *Ex Vivo* Lentiviral Gene Therapy RP-L201 for Pediatric Patients with Severe Leukocyte Adhesion Deficiency-I Provides Sustained Efficacy with a Favorable Safety Profile

Donald B. Kohn, MD
Departments of Microbiology, Immunology & Molecular Genetics,
Pediatrics, and Molecular & Medical Pharmacology
University of California, Los Angeles

Julián Sevilla, MD, PhD; Gayatri R. Rao, MD, JD; Maria Chitty Lopez, MD; Elena Almarza, PhD; Dayna Terrazas, RN; Josune Zubicaray MD, PhD; Marta González-Vicent MD, PhD; Kritika Chetty, MBBS; Gráinne O'Toole, RN; Jinhua Xu-Bayford, RN; Eileen Nicoletti, MD; Augustine Fernandes, PhD; Caroline Y. Kuo, MD; Satiro de Oliveira, MD; Theodore B. Moore, MD; Grace Choi, BS; Miriam Zeini, PhD; Cristina Mesa-Núñez, PhD; Adrian J. Thrasher, MBBS, PhD; Juan A. Bueren, PhD; Jonathan D. Schwartz, MD; Claire Booth, MBBS, PhD

27th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT)
May 10, 2024
Abstract # 246

American Society of Gene + Cell Therapy

CIRM CALIFORNIA'S STEM CELL AGENCY

UCLA MATTEL Children's Hospital
Children's Discovery & Innovation Institute

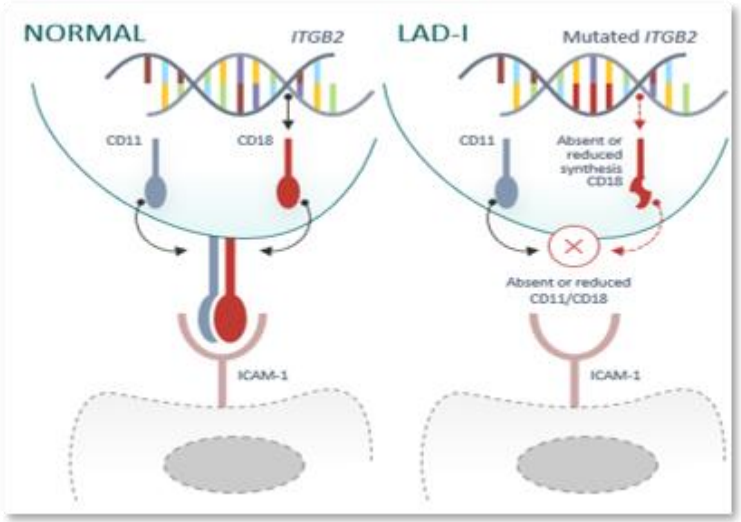
rocket pharma

Disclosures

- Consultant: Allogene Therapeutics, Pluto Therapeutics, ImmunoVec, MyoGeneBio, Be Bio, Cargo Therapeutics, Rarity PBC
- Research funding from Rocket Pharmaceuticals, Inc.

Leukocyte Adhesion Deficiency Type I (LAD-I) is a Rare Autosomal Recessive Inborn Error of Immunity Caused by *ITGB2* Mutations

A heterodimeric complex of CD18 and CD11 is expressed on the surface of leukocytes[1]



Leukocytes have **reduced, absent, or dysfunctional CD18** and are **unable to attach to inflamed endothelium and migrate to tissues to clear infections or facilitate wound repair[2-4]**

Epidemiology

~1 case per 1 million
individuals diagnosed with LAD-I globally[5]

> 60% **of patients are categorized as severe**

1. Deshpande P et al.; *Indian J Pediatr*. 2016;83(8):799-804; 2. Madkaikar, M. et al., *Indian Pediatr.* 2012;49(1):43-45; 3. Abdel-Salam BK, Ebaid H. *Cent Eur J Immunol.* 2014;39(2):209-215; 4. Tan SM. *Biosci Rep.* 2012;32(3):241-269; 5. Almarza E et al. *J Allergy Clin Immunol Pract.* 2018;6(4):1418-1420.

LAD-I is Associated With Poor Clinical Prognosis and Unmet Need

LAD-I Disease Spectrum[1]

Severe
<2% CD18+ PMN

Moderate
2–30% CD18+ PMN

Severe LAD-I is characterized by recurrent disseminated bacterial and fungal infections. Majority of patients will encounter ultimately fatal infections in absence of alloHSCT[1,2]

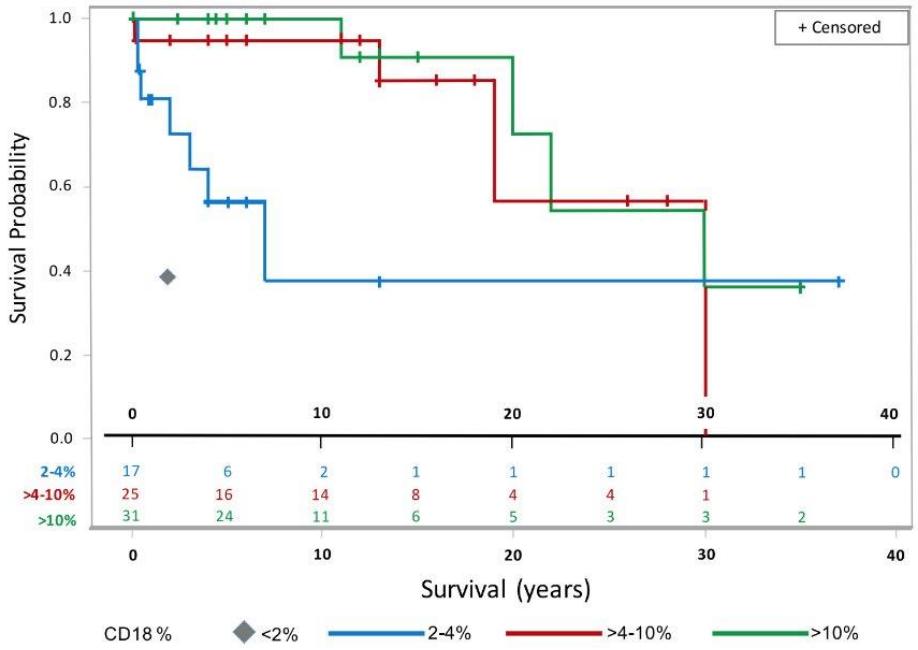
- Severe LAD-I: 60–75% mortality **prior to age 2**
- Moderate LAD-I: >50% mortality prior to age 40

Current treatment: allogeneic HSCT (allo-HSCT)[3]

- Limited by donor availability
- Most of allo-HSCT **occurs within 1 year of diagnosis**; however, it is associated with **frequent GvHD and graft failure**

Kaplan-Meier Survival Estimates by Neutrophil CD18 Expression[1]

Patients with severe & moderate LAD-I not receiving allo-HSCT



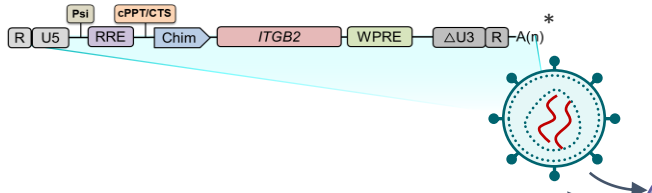
39% survival to age 2 years for 66 evaluable patients with severe LAD-I not receiving allo-HSCT

GVHD=graft versus host disease; HSCT=hematopoietic stem cell transplantation; PMN=polymorphonuclear neutrophil.

1. Almarza E et al. *J Allergy Clin Immunol Pract.* 2018;6(4):1418-1420; 2. Fisher A et al. *Immunodefic Rev.* 1998;1(1):39-54; 3. Bakhtiar S, et al. *Blood Adv.* 2021;5(1):262-273.

Ex vivo Gene Therapy for LAD-I: RP-L201 (Marnetegragene autotemcel; Marne-cel)

Autologous CD34+ cells transduced with a lentiviral vector* encoding for functional *ITGB2*



3 TRANSDUCTION
with Lentiviral Vector Chim-CD18-WPRE

2 SELECTION
CD34+ Stem Cells

4 HARVEST & FINAL FORMULATION
and cryopreserve for final formulation

Unmanipulated back-up
≥2.0×10^6 CD34+ cells/kg

<2.0×10^6 CD34+ cells/kg

1 MOBILIZATION & APHERESIS COLLECTION
G-CSF and Plerixafor;
Apheresis Collections
Ustekinumab (2 weeks prior)

Apheresis 1
Apheresis 2
RP-L201

≥2.0×10^6 CD34+ cells/kg

2nd SEQUENCE: MOBILIZATION, COLLECTION, & RP-L201 MANUFACTURE

5 INFUSE
with Antecedent Busulfan Conditioning (AUC 65-75mg/L*hour)
Ustekinumab (1-2 week(s) prior)

*The lentiviral vector was developed at CIEMAT, in partnership with UCL-GOSICH.
AUC=area under *curve*.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Marne-cel was Evaluated in Nine Patients With Severe LAD-I Without Allo-HSCT Over a ≥1-yr period*

TRIAL DESIGN

Non-Randomized, Single-Arm, Global Phase 1/2 (N = 9)†

long-term follow-up 15 years post-infusion

ELIGIBILITY CRITERIA

- Age **≥ 3 months**
- Diagnosis of **severe LAD-I**

CD18 expression on <2% PMNs, OR <2% CD11a or CD11b expressing PMNs	Documented *ITGB2* mutations	Clinical or family history consistent with LAD-I

- **≥1** prior significant **bacterial or fungal infection** (CTCAE Grade ≥2)
- Appropriate **candidate for auto- or allo-HSCT but without available/eligible HLA-identical sibling donor**

PRIMARY OUTCOMES

HSCT-free survival

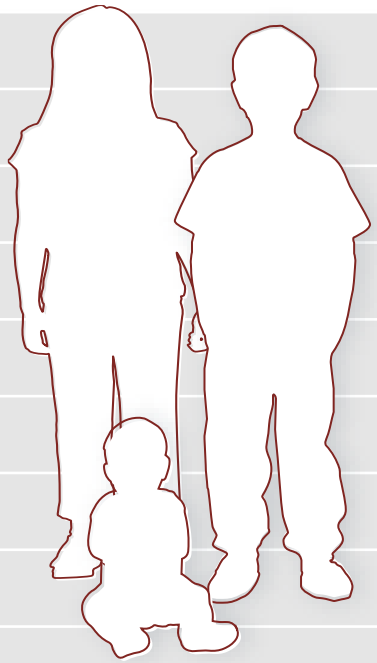
- **Alive at least 1-year post-Marne-cel infusion** without allo-HSCT, **and/or**
- **Alive at the age of 2 years** without allo-HSCT in patients <1 year of age at enrollment

SECONDARY OUTCOMES

- **Overall Survival**
- **Event-Free Survival** (survival in the absence of graft failure and acute GvHD grades II-IV)
- Reduction in **significant infections†**, **infection-related hospitalizations**, and **prolonged (≥7 days) infection-related hospitalizations**
- Partial or complete resolution of LAD-I related **skin rashes or periodontal abnormalities**
- Change in PMN **CD18 expression,** including percentage of patients with PMN **CD18 expression ≥10% of normal and CD11a/b co-expression**
- **VCN in blood and BM cells**, including percentage of patients with PBMC and PB CD15+ granulocytes **VCN of ≥0.1**
- Improvement of LAD-I associated **leukocytosis** and **neutrophilia**

*Clinicaltrials.gov ID NCT03812263.
†2 patients were enrolled in a Phase 1 trial first, then 7 additional patients were enrolled as part of the Phase 2 continuation.
allo-HSCT=allogeneic hematopoietic stem cell transplant; CTCAE=common terminology criteria for adverse events; HLA=human leukocyte antigen; LAD-I: leukocyte adhesion deficiency-I; PMN=polymorphonuclear neutrophil; yr=year.
Data on file. Rocket Pharmaceuticals. RP-L201-0318 CSR. 2023, data cut 24 Jul 2023.

Demographics and Investigational Product Metrics



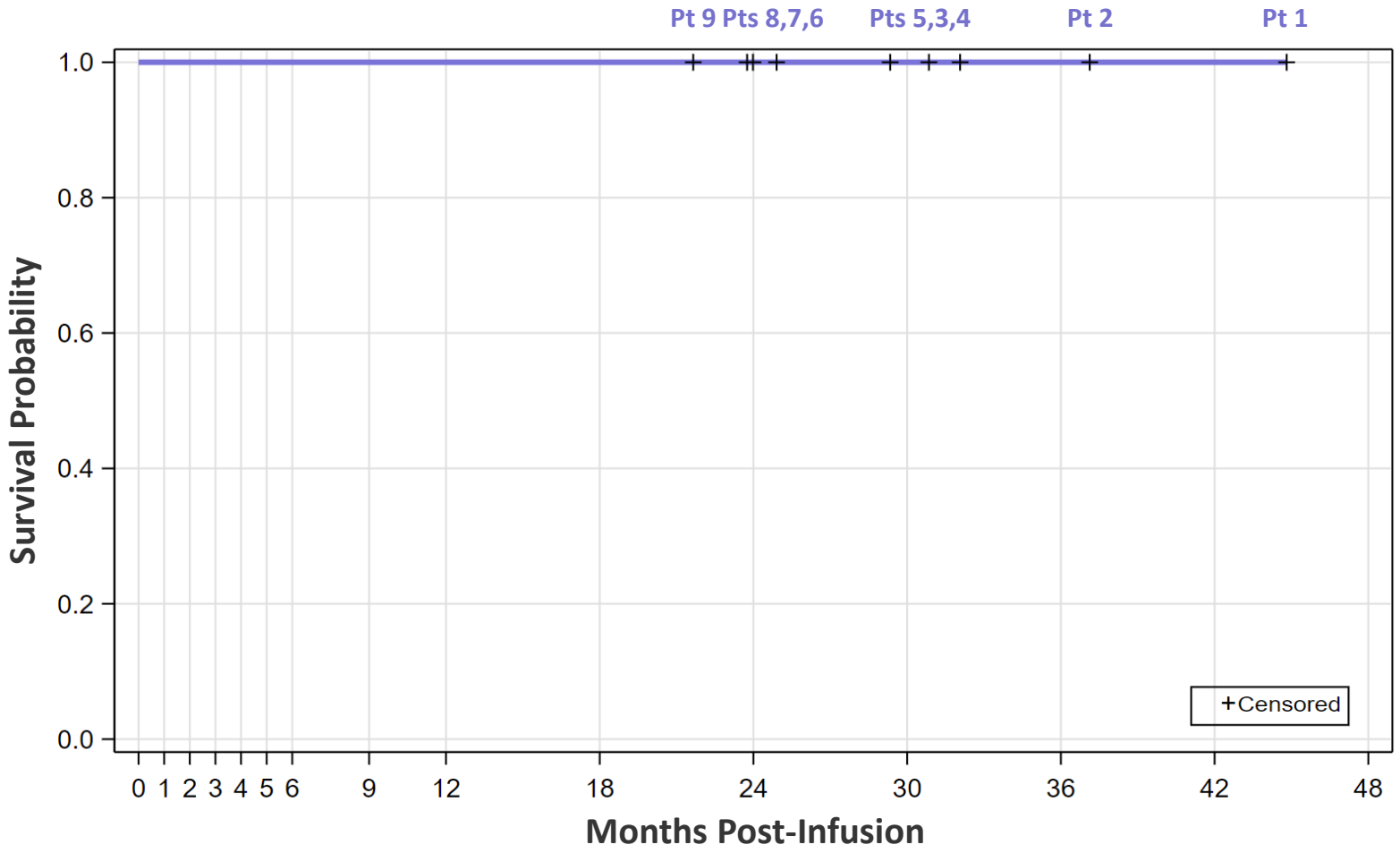
PATIENT NUMBER	GENDER	NATION	AGE AT SCREENING (YEARS)	IP VCN	CD34+ Cell Dose (× 10^6 cells/kg)
Patient 1	Female	USA	9.3	3.8	4.2
Patient 2*	Female	USA	3.8	2.5	2.8
Patient 3	Male	USA	0.6	2.9	4.3
Patient 4	Female	USA	3.0	1.8	6.5
Patient 5	Male	USA	0.3	3.6	5.0
Patient 6	Male	Great Britain	0.4	3.8	3.3
Patient 7	Male	Sri Lanka	3.3	2.0	4.5
Patient 8	Female	India	2.2	3.8	3.8
Patient 9	Female	Turkey	4.1	3.5	10.0

*Patient 2 received the investigational gene therapy that had been collected via two separate apheresis sequences and was administered sequentially, with a 73-minute observation period between infusions without incidence, as per protocol that stipulated a 60-minute minimum observation between such infusions. Cell product for all other patients was obtained from a single mobilization/collection sequence.
IP=investigational product; VCN=vector copy number.
Data on file. Rocket Pharmaceuticals. RP-L201-0318 CSR. Listing 16.2.4.1. 2023, data cut 24 Jul 2023.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Marne-cel Changes Course of Severe LAD-I, With All Patients Surviving in the Absence of Allo-HSCT Post-infusion; With Longest Follow-up of >42 Months

Kaplan-Meier Curve of Allogeneic Transplant-Free Survival



100% HSCT-free survival[1]

All 9 patients met the primary endpoint: survival at 1-year post-Marne-cel infusion (and to >2 years for those <1 year old) without allo-HSCT

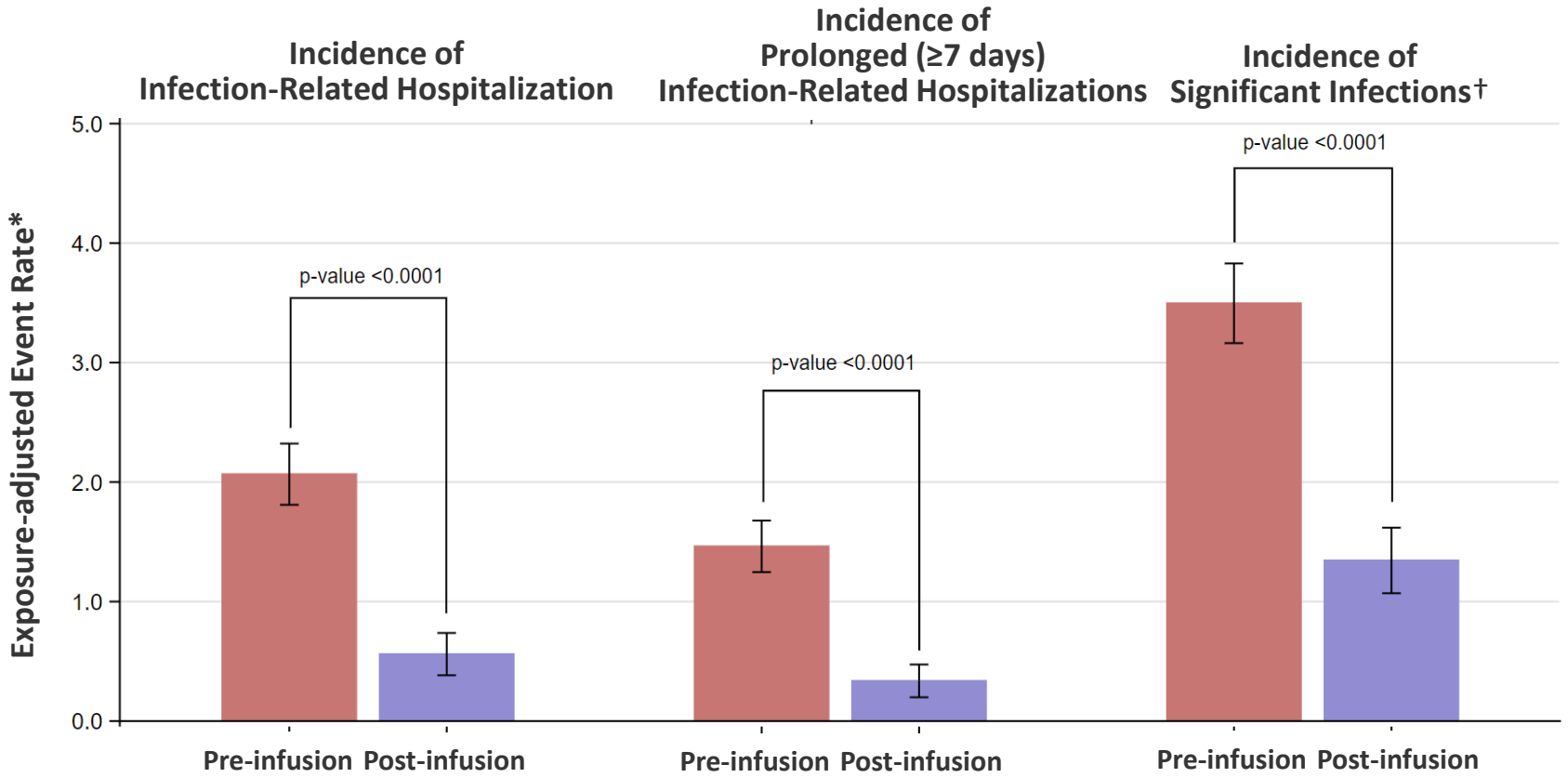
No Incidences of Graft Failure or GvHD

allo-HSCT=allogeneic hematopoietic stem cell transplant; GvHD=graft versus host disease; LAD-I=leukocyte adhesion deficiency type-I.
Data on file. Rocket Pharmaceuticals RP-L201-0318 and RP-L201-0121-LTFU, BLA 120d Efficacy Update Figure 1 (Source Figure 1.2.1) and Safety Update, data cut 24 Jul 2023.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Meaningful Reduction in Infection Related Hospitalizations Following Immune Reconstitution

All rates of **infection-related** outcomes were **significantly reduced** after RP-L201:

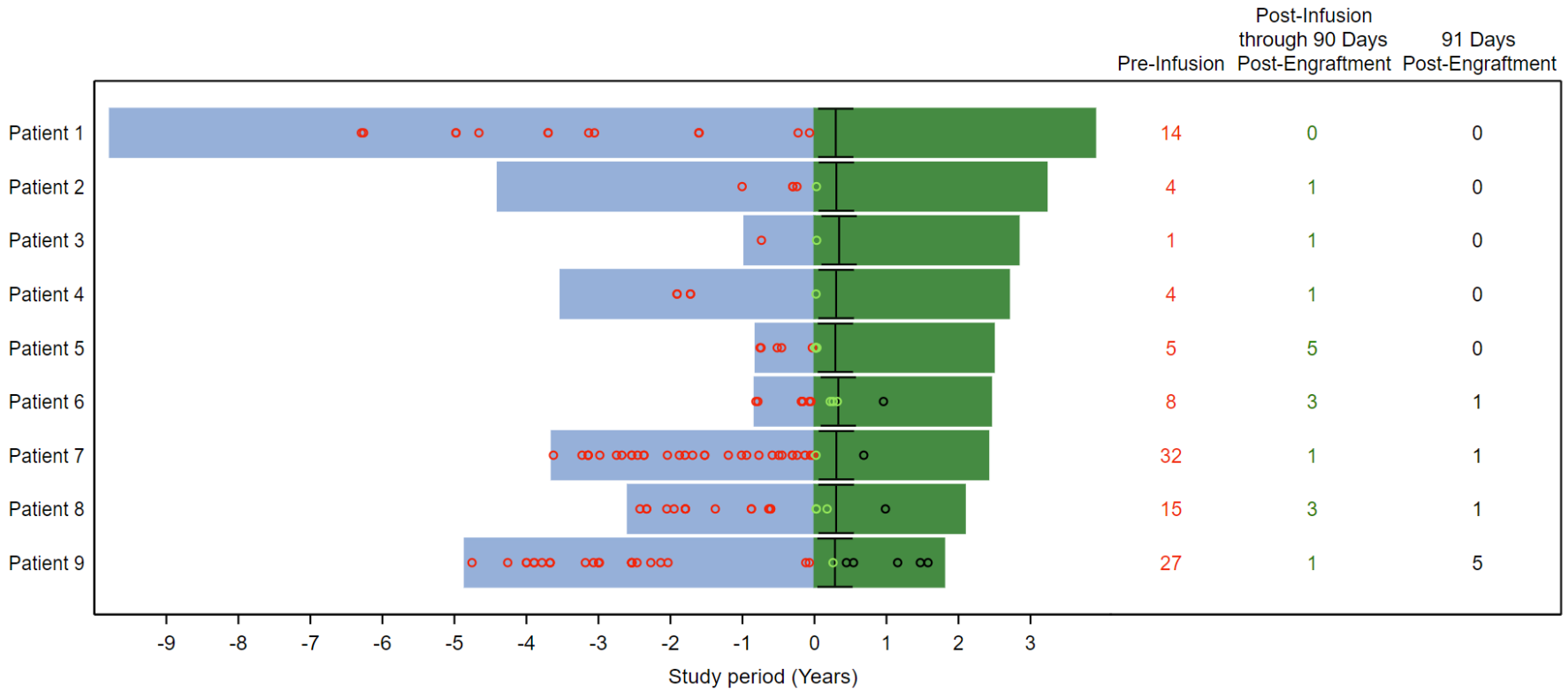


Infections that developed post-infusion (beyond 90 days post-engraftment) were consistent with **typical childhood infections** frequently observed in immunocompetent (healthy) children

*Annualized event rate is calculated as the Total Number of Events / Total time in each Time Period for all subjects. Results are adjusted event rate per year. Pre-infusion includes all lifelong medical history prior to infusion. p-value from Poisson regression with even and time period in the model with an offset of log exposure.
†Significant infections are defined as those requiring hospitalizations or I.V. antimicrobial therapy.
I.V.=intravenous.
Data on file. Rocket Pharmaceuticals, Inc. RP-L201-0318 and RP-L201-0121-LTFU, BLA 120d Efficacy Update Report Figure 2 (Source Table 2.3.5.1), data cut 24 Jul 2023.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Marne-cel Treatment Significantly Reduced the Incidence of Significant Infections*



Bar represents the timeline in years; blue bar is life-long history pre-infusion and green bar is post-infusion.

Circles represent significant infection events

Red circles are events occurring pre-infusion

Green circles are events occurring post-infusion and within 90 days post-engraftment

Black circles are events occurring 91 days post-engraftment

*Significant infections are defined as those requiring hospitalizations or I.V. antimicrobial therapy.

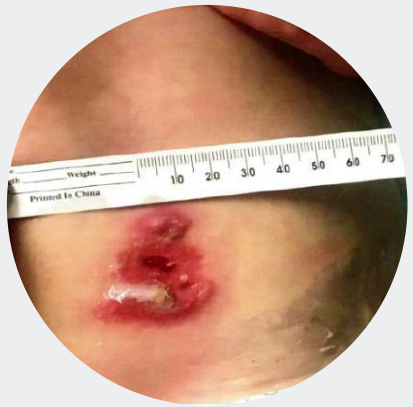
I.V.=intravenous.

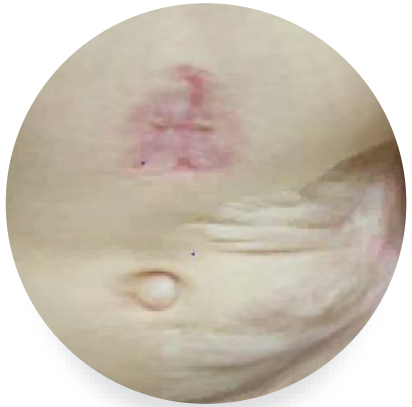
Data on file. Rocket Pharmaceuticals RP-L201-0318 and RP-L201-0121-LTFU, BLA 120d Efficacy Update Report Figure 3 (Source figure 2.1.6), data cut 24 Jul 2023.

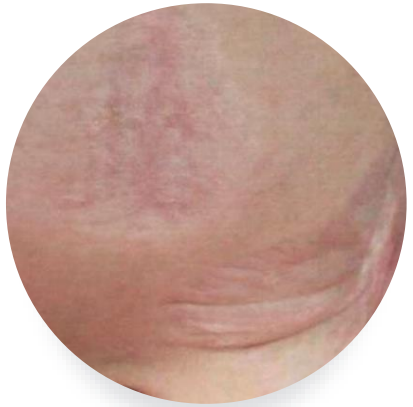
Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

All Patients with LAD-I-related Skin and Periodontal Lesions at Baseline Showed Improvement: *Illustrative Clinical Trial Patient Experiences*

Spontaneous resolution of **abdominal** LAD-I-associated **skin rash**





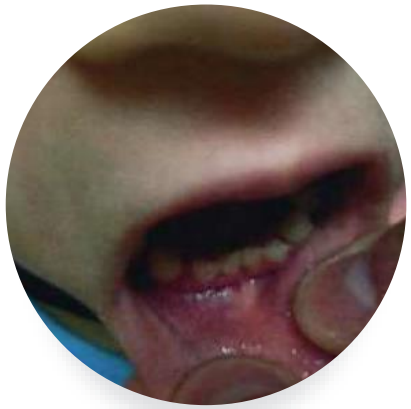


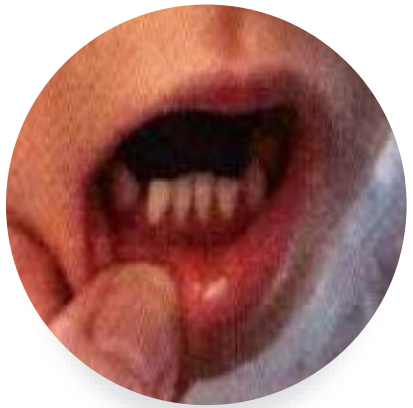
BASELINE

MONTH 3 post-infusion

MONTH 9 post-infusion

Spontaneous resolution of LAD-I-associated **periodontal lesions**





All pre-existing cases of serious skin rashes (n = 7) and periodontal lesions (n = 2) resolved post-infusion

No new cases of serious lesions or rashes developed post-infusion

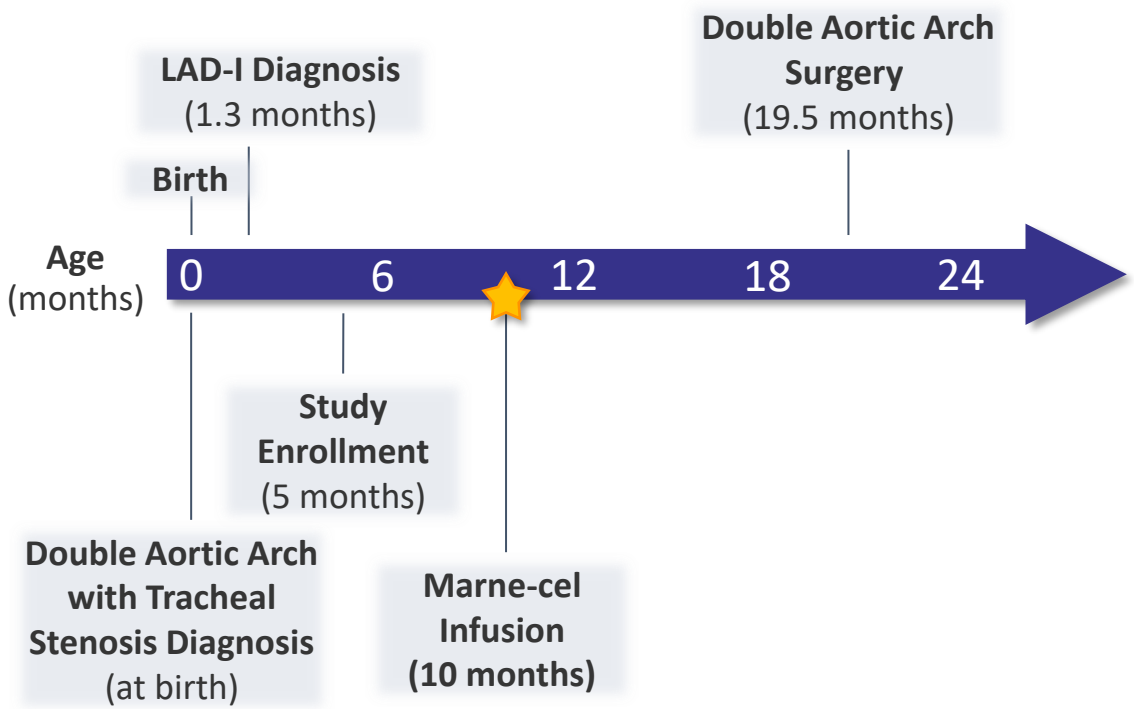
LAD-I=leukocyte adhesion deficiency type-I

Data on file. Rocket Pharmaceuticals, Inc. RP-L201-0318 Clinical Study Report, data cut 24 Jul 2023.

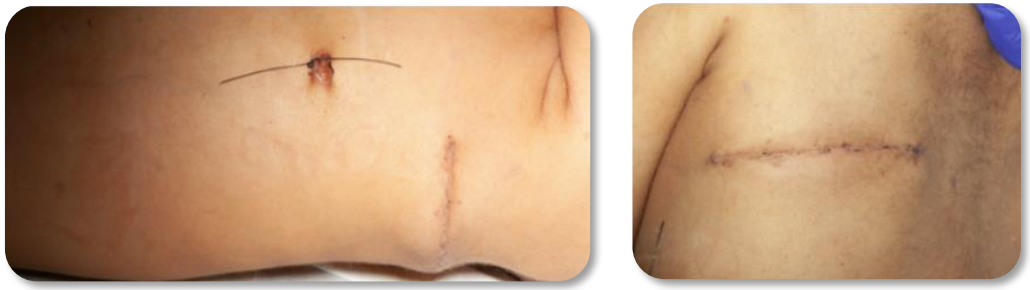
Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Marne-cel Restored Wound Healing Capabilities

Illustrative Clinical Trial Patient Experiences



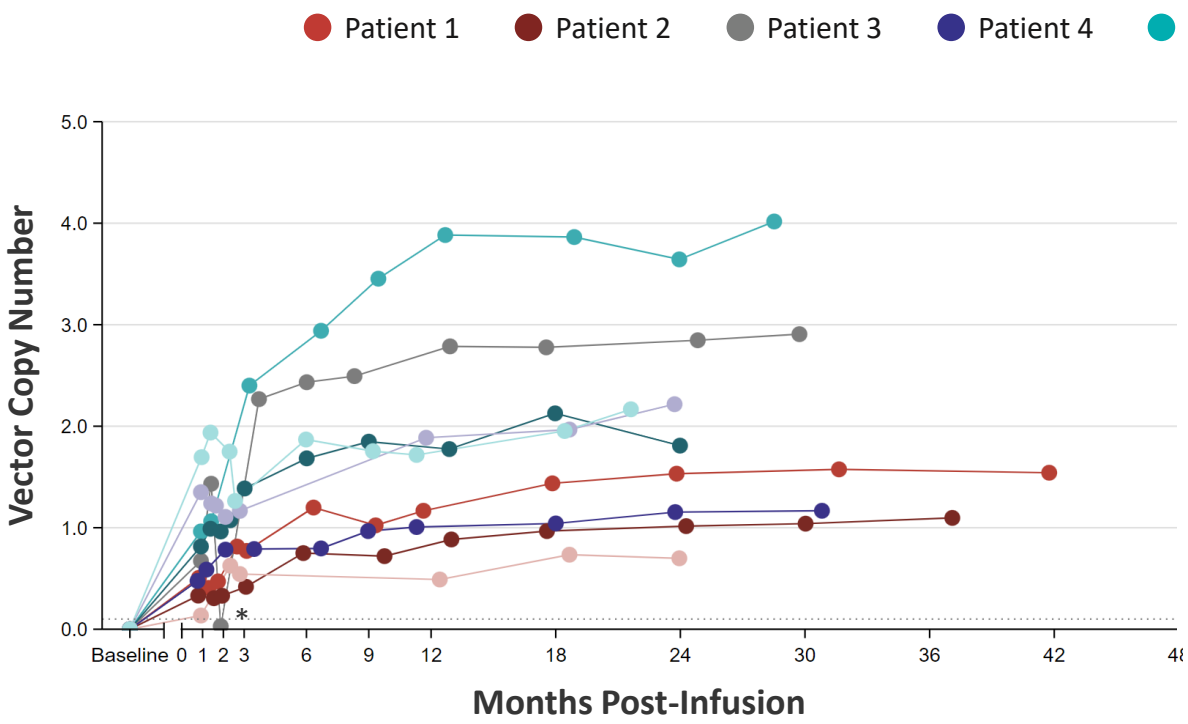
Wound repair at thoracotomy site after surgical correction of double aortic arch



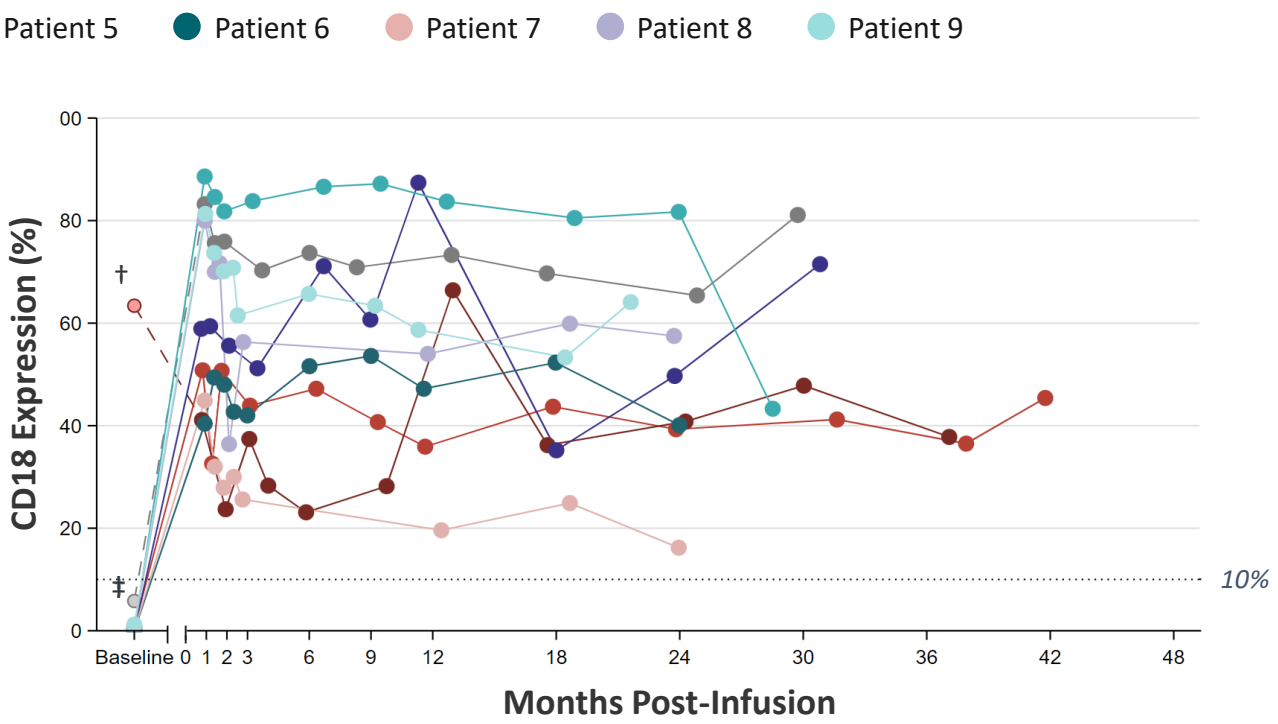
LAD-I=leukocyte adhesion deficiency type-I.
Data on file. Rocket Pharmaceuticals, Inc. RP-L201-0318 Clinical Study Report, data cut 24 Jul 2023.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Marne-cel Resulted in Sustained Genetic Correction and CD18 Expression in Peripheral Blood Neutrophils Throughout Follow-up



Durable provirus integration following gene-modified cell infusion across the entire cohort



Sustained >10% PMN CD18 expression§ following gene-corrected cell infusion across the entire cohort

*VCN in PBMC for Patient 3 at the Week 8 visit (Study Day 57) is likely an outlier, particularly in the context of stable VCN in PB CD15+ cells at this timepoint and stable neutrophil CD18, CD11a, and CD11b expressions at the same timepoint. This is especially the case because PB neutrophils (CD15+) comprise the majority of PB mononuclear cells. Subsequent timepoints show a sustained increase in VCN in PBMC which closely corresponds to both neutrophil CD18+ expression and VCN in CD15+ (as well as CD11a/b expression).

†Baseline dim/weak neutrophil CD18 expression in Patient 2 in ~63% of cells with neutrophil CD11a/CD11b expression <2%, likely indicating abnormal/unstable protein.

‡Baseline neutrophil CD18 expression in Patient 3 in ~5.8% of cells with neutrophil CD11a/CD11b expression <2%, likely indicating abnormal/unstable protein.

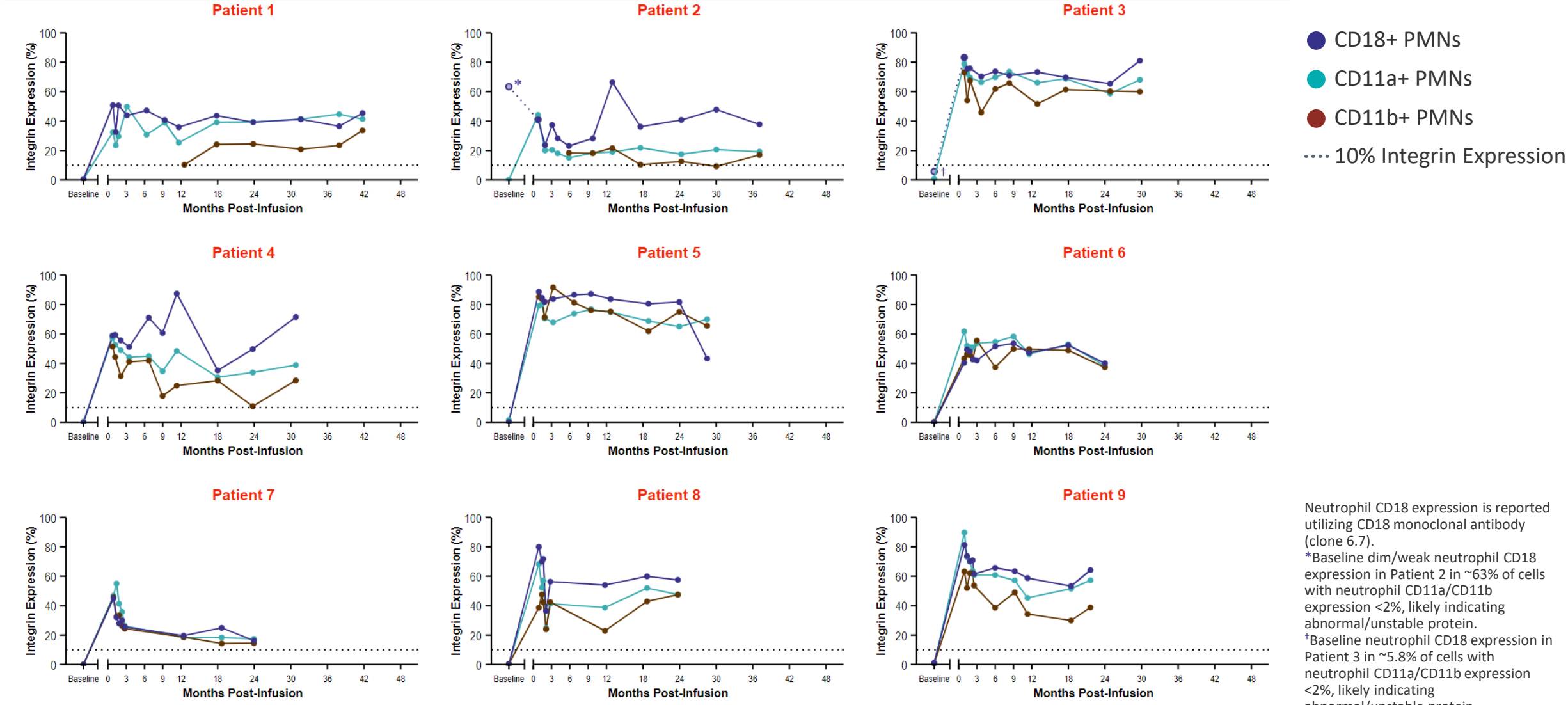
§Neutrophil CD18 expression is reported utilizing CD18 monoclonal antibody (clone 6.7).

PB=peripheral blood; PBMC=peripheral blood mononuclear cells; PMN=polymorphonuclear neutrophil; VCN=vector copy number.

Data on file. Rocket Pharmaceuticals, Inc. RP-L201-0318 Clinical Study Report, data cut 24 Jul 2023

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Marne-cel Resulted in Durable Neutrophil CD18/CD11 Expression Throughout Follow-up



Neutrophil CD18 expression is reported utilizing CD18 monoclonal antibody (clone 6.7).
*Baseline dim/weak neutrophil CD18 expression in Patient 2 in ~63% of cells with neutrophil CD11a/CD11b expression <2%, likely indicating abnormal/unstable protein.
†Baseline neutrophil CD18 expression in Patient 3 in ~5.8% of cells with neutrophil CD11a/CD11b expression <2%, likely indicating abnormal/unstable protein.
PMNs=polymorphonuclear cells.

Data on file. Rocket Pharmaceuticals RP-L201-0318 and RP-L201-0121-LTFU, BLA 120d Efficacy Update Figure 17 (Source Listing 2.3.3.2); data cut 24 Jul 2023.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Marne-cel Efficacy Summary

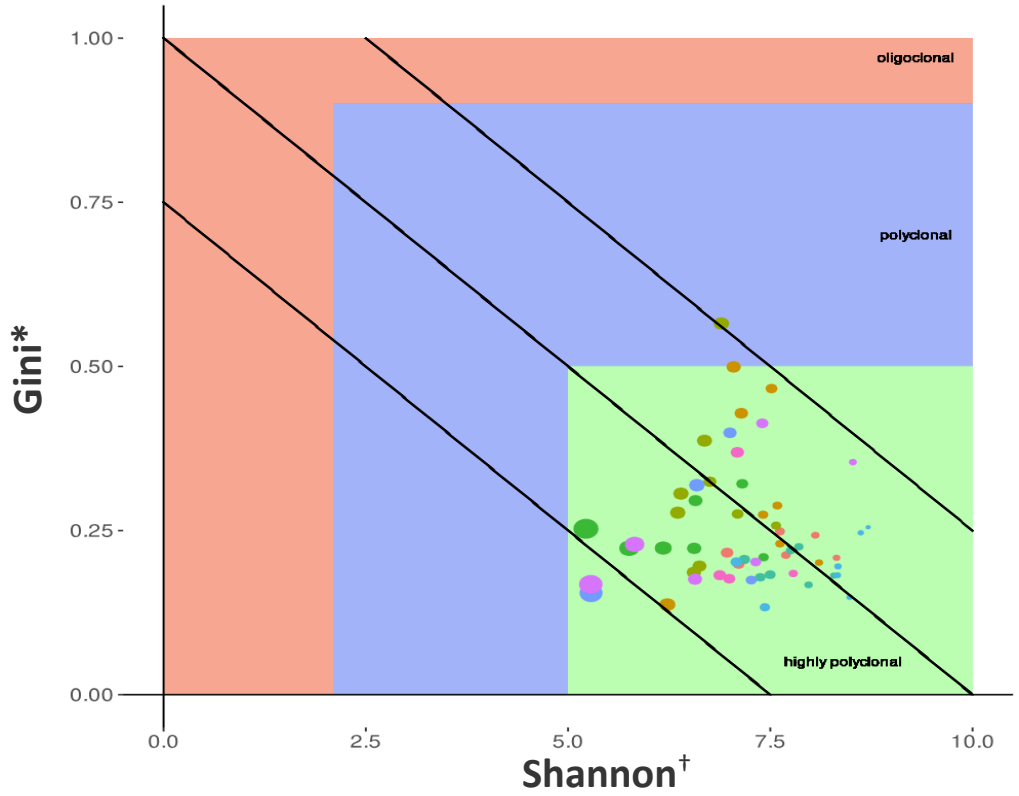
- All patients followed for at least 1.5 years; 8/9 patients followed for at least 2 years
- **Neutrophil engraftment** achieved in **9/9** patients (Range:13-34 days, Median: 19 days)
- **100% survival in the absence of allo-HSCT** at least 1.5 years post-infusion and all patients enrolled at <1 year of age have surpassed age 2 years without allo-HSCT
  - Evidence of spontaneous **resolution** of LAD-I-related **skin rash** and periodontal abnormalities and **restoration of wound repair** capabilities
  - **No typical LAD-I infections** since gene-modified cell engraftment
- Significant reduction in infection related hospitalizations following engraftment
- **Sustained** >10% **CD18 PMN expression** (Range: 16.2–87.4% with 18 to 42 months of follow-up), with concomitant sustained **CD11a/b expression,** in the setting of ≥0.1 **VCN** integration

HSCT=hematopoietic stem cell transplant; LAD-I=leukocyte adhesion deficiency type-I; PMN=polymorphonuclear neutrophil; VCN=vector copy number.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Cumulative Integration Site Analysis (ISA): Highly polyclonal LV integration

Clonality and diversity of gene-modified cells[1]



No **oligoclonality** or **clonal dominance**

No evidence of **prominent insertions in proximity to oncogenic *loci***

1/UC50‡ 0.005 0.010

Patient 1 Patient 4 Patient 7
Patient 2 Patient 5 Patient 8
Patient 3 Patient 6 Patient 9

*The Gini index runs from 0 to 1 and describes how equally clones contribute to the integration site pool (Gini C 1912).[2] A low index suggests a polyclonal integration pattern with an even sequence abundance distribution, whereas a high index describes an unequal contribution of more dominant sequences to the overall sequence pool.

†The Shannon index is used to describe the overall diversity of the integration site pool. The higher the Shannon index, the more polyclonal the integration site repertoire in the individual sample[3]. Low Shannon values (≤ 2.1) indicate an oligoclonal integration pattern with low complexity and more prominent clones; values > 2.1 and < 5.0 indicate polyclonality and values ≥ 5.0 indicate a highly polyclonal integration pattern. The cut-off values for oligoclonality, polyclonality, or highly polyclonal samples were derived from a meta-analysis of all Rocket gene therapy programs. The values were in place at the time the analysis was executed on October 30th, 2023, and are dependent on the number of samples.

‡The UC50 (unique cell progenitors contributing the most to the expanded 50% of progeny cell clones) value describes how many integrations in a sample contribute to 50% of all sequences. When the UC50 is < 10, few sequences dominate the overall integration site pool; the higher the UC50 value, the more polyclonal the integration site pool.[4]

1. Data on file. Rocket Pharmaceuticals. BLA 120d Safety Update, Figure 1 (CISA Report – Figure 1), data cut 24 Jul 2023. 2. Gini C. Variabilità e mutabilità: contributo allo studio delle distribuzioni e delle relazioni statistiche; 1912. 3. Chao & Shen. *Environ Ecol Stat*. 2010;10:429–443. 4. Berry et al. *Mol Ther Methods Clin Dev*. 2017(4):17–26.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Marne-cel Safety Summary

- *Marne-cel is* associated with a favorable safety profile, with **no investigational product-related AEs reported**
  - No deaths reported throughout follow-up
  - No respiratory or hepatic complications related to Marne-cel
  - No cases of replication-competent lentivirus
  - No oligoclonality was observed in any patients as measured by ISA
  - No patients experienced GF or aGVHD during follow-up
- Most recorded AEs were consistent with those associated with **busulfan conditioning** and other study procedures
  - AEs were consistent with the expected safety profiles of those agents and procedures, notably: **anemia**, **mucosal inflammation** and **decreased platelet count***

*Anemia (n = 9, 100%), all Grade 3; mucosal inflammation (n = 7, 77.8%, , 57.1% of which were Grade 3; decreased platelet count (n = 6, 66.7%), all Grade 4.
AE=adverse event; aGvHD=autologous graft versus host disease; GF=graft failure; HSCT=hematopoietic stem cell transplant; ISA=integration site analysis.
Rocket Pharmaceuticals. RP-L201 BLA 120d Safety Update Table 6 (Source Table 1.2.5.1), data cut 24 Jul 2023.

Acknowledgements

UCL GREAT ORMOND STREET INSTITUTE OF CHILD HEALTH

Claire Booth, MBBS, PhD, FRCPCH
Adrian J. Thrasher, MBBS, PhD, FMedSci
Kritika Chetty, MBBS
Grainne O'Toole, RN
Jinhua Xu-Bayford, RN

UCLA MATTEL Children's Hospital
Children's Discovery & Innovation Institute

Dayna Terrazas, RN
Augustine Fernandes, PhD
Caroline Y. Kuo, MD
Satiro De Oliveira, MD
Theodore Moore, MD

SaludMadrid Hospital Infantil Universitario Niño Jesús
ciber ER FIBio Hospital Infantil Universitario Niño Jesús


Julián Sevilla, MD, PhD
Josune Zubicaray, MD
Marta González-Vicent, MD, PhD

iiS FJD INSTITUTO DE INVESTIGACIÓN SANITARIA FUNDACIÓN JIMÉNEZ DÍAZ

Cristina Mesa-Núñez, PhD
Juan Bueren, PhD

ciber Centro de Investigación Biomédica en Red

CIRM CALIFORNIA'S STEM CELL AGENCY

Ciemat

Inquiries or questions, please email:
ladclinicaltrial@rocketpharma.com

rocket pharma

Maria Chitty Lopez, MD
Ilana Moscatelli, PhD
Elena Almarza, PhD
Eileen Nicoletti, MD
Gayatri R. Rao, MD, JD
Grace Choi, BS
Miriam Zeini, PhD
Jonathan Schwartz, MD
Kinnari Patel, PharmD, MBA
Gaurav Shah, MD

Supplemental Slides

Marne-cel - Clinical Safety: Serious Adverse Events

- **Data** are available from **9/9** patients with 18–42 months follow-up after receiving Marne-cel
- **No Marne-cel-related serious adverse events have been reported**

Preferred Term	Screening to Day before Infusion Total N=9	Infusion to Neutrophil Engraftment N=9	1 to 90 Days Post-engraftment N=9	91 Days Post-engraftment to EoS N=9	1 Day After EoS to EoS-LTFU N=6	Infusion to EoS-LTFU Total N=9
Subject with any SAE	**7 (77.8)**	**1 (11.1)**	**3 (33.3)**	**4 (44.4)**	**None**	**4 (44.4)**
Gastroenteritis	-	-	-	2 (22.2)	-	2 (22.2)
Blood disorder	-	-	-	1 (11.1)	-	1 (11.1)
Bronchiolitis	-	-	-	1 (11.1)	-	1 (11.1)
COVID-19	-	-	-	1 (11.1)	-	1 (11.1)
Deafness neurosensory	-	-	-	1 (11.1)	-	1 (11.1)
Device related bacteraemia	-	-	1 (11.1)	-	-	1 (11.1)
Pneumonia viral	-	-	-	1 (11.1)	-	1 (11.1)
Pulmonary arterial hypertension	-	-	1 (11.1)	-	-	1 (11.1)
Stridor	-	-	-	1 (11.1)	-	1 (11.1)
Tonsillitis	-	-	-	1 (11.1)	-	1 (11.1)
Upper respiratory tract infection	-	-	1 (11.1)	1 (11.1)	-	1 (11.1)
Vascular device infection	-	-	-	1 (11.1)	-	1 (11.1)
Venoocclusive disease	-	1 (11.1)	-	-	-	1 (11.1)
Abdominal infection	1 (11.1)	-	-	-	-	-
Cellulitis	1 (11.1)	-	-	-	-	-
Deep vein thrombosis	1 (11.1)	-	-	-	-	-
Folliculitis	1 (11.1)	-	-	-	-	-
Otitis media acute	1 (11.1)	-	-	-	-	-
Pneumonia	1 (11.1)	-	-	-	-	-
Pneumonia bacterial	1 (11.1)	-	-	-	-	-
Pulmonary mass	1 (11.1)	-	-	-	-	-
Pyoderma gangrenosum	1 (11.1)	-	-	-	-	-
Rash	1 (11.1)	-	-	-	-	-
Streptococcal sepsis	1 (11.1)	-	-	-	-	-
Viral upper respiratory tract infection	1 (11.1)	-	-	-	-	-

SAE=serious adverse event; Eos=end of study; LTFU=long term follow-up.
Data on file. Rocket Pharmaceuticals RP-L201-0318 and RP-L201-0121-LTFU, BLA 120d Safety Update Table 7 (Source Table 1.2.8.1), data cut 24 Jul 2023.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

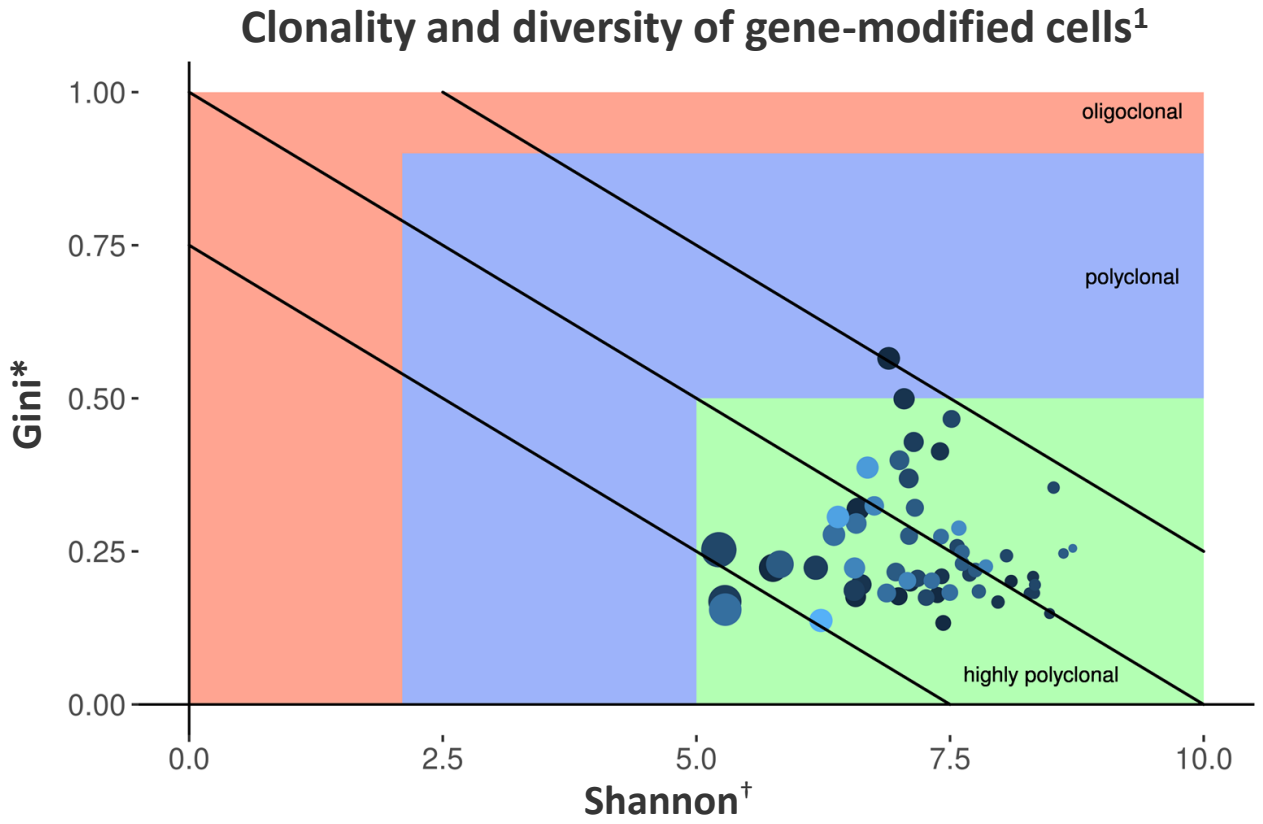
Marne-cel Clinical Safety: Severity Grade 3/4 AEs* Reported in >1 Patient

Preferred Term	Screening to Day before Infusion Total N=9	Infusion to Neutrophil Engraftment N=9	1 to 90 Days Post-engraftment N=9	91 Days Post-engraftment to EoS N=9	1 Day After EoS to EoS-LTFU N=6	Infusion to EoS-LTFU Total N=9
Subject with any grade AE	**9 (100)**	**9 (100)**	**9 (100)**	**9 (100)**	**None**	**9 (100)**
Grade 3	7 (77.8)	0	1 (11.1)	4 (44.4)	-	0
Grade 4	-	9 (100)	4 (44.4)	-	-	9 (100)
Platelet count decreased	3 (33.3)	6 (66.7)	6 (66.7)	2 (22.2)	-	6 (66.7)
Grade 3	-	0	1 (11.1)	-	-	0
Grade 4	-	6 (66.7)	2 (22.2)	-	-	6 (66.7)
Neutrophil count decreased	-	5 (55.6)	2 (22.2)	-	-	5 (55.6)
Grade 3	-	0	1 (11.1)	-	-	0
Grade 4	-	5 (55.6)	-		-	5 (55.6)
White blood cell count decreased	-	5 (55.6)	1 (11.1)	-	-	5 (55.6)
Grade 3	-	3 (33.3)	-	-	-	3 (33.3)
Grade 4	-	2 (22.2)	-	-	-	2 (22.2)
Thrombocytopenia	2 (22.2)	3 (33.3)	2 (22.2)	1 (11.1)	-	3 (33.3)
Grade 3	1 (11.1)	0	1 (11.1)	-	-	0
Grade 4	-	3 (33.3)	1 (11.1)	-	-	3 (33.3)
Neutropenia	-	3 (33.3)	2 (22.2)	-	-	3 (33.3)
Grade 3	-	1 (11.1)	1 (11.1)	-	-	1 (11.1)
Grade 4	-	2 (22.2)	-	-	-	2 (22.2)
Anaemia	7 (77.8)	8 (88.9)	8 (88.9)	3 (33.3)	-	9 (100)
Grade 3	4 (44.4)	8 (88.9)	3 (33.3)	1 (11.1)	-	9 (100)
Febrile neutropenia	-	4 (44.4)	-	-	-	4 (44.4)
Grade 3	-	4 (44.4)	-	-	-	4 (44.4)
Mucosal inflammation	-	7 (77.8)	-	-	-	7 (77.8)
Grade 3	-	4 (44.4)	-	-	-	4 (44.4)

*Per the United States National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), v5.0, Grade ≥2.
AEs=adverse events.
Data on file. Rocket Pharmaceuticals RP-L201-0318 and RP-L201-0121-LTFU, BLA 120d Safety Update Table 6 (Source Table 1.2.5.1).023, data cut 24 Jul 2023.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.

Cumulative Integration Site Analysis (ISA): Highly polyclonal LV integration



No **oligoclonality** or **clonal dominance**

No evidence of **prominent insertions in proximity to oncogenic *loci***

1/UC50‡

0.005

0.010

Month

10 20 30 40

*The Gini index runs from 0 to 1 and describes how equally clones contribute to the integration site pool (Gini C 1912).[2] A low index suggests a polyclonal integration pattern with an even sequence abundance distribution, whereas a high index describes an unequal contribution of more dominant sequences to the overall sequence pool.

†The Shannon index is used to describe the overall diversity of the integration site pool. The higher the Shannon index, the more polyclonal the integration site repertoire in the individual sample[3]. Low Shannon values (≤ 2.1) indicate an oligoclonal integration pattern with low complexity and more prominent clones; values > 2.1 and < 5.0 indicate polyclonality and values ≥ 5.0 indicate a highly polyclonal integration pattern. The cut-off values for oligoclonality, polyclonality, or highly polyclonal samples were derived from a meta-analysis of all Rocket gene therapy programs. The values were in place at the time the analysis was executed on October 30th, 2023, and are dependent on the number of samples.

‡The UC50 (unique cell progenitors contributing the most to the expanded 50% of progeny cell clones) value describes how many integrations in a sample contribute to 50% of all sequences. When the UC50 is < 10, few sequences dominate the overall integration site pool; the higher the UC50 value, the more polyclonal the integration site pool.[4]

1. Data on file. Rocket Pharmaceuticals. BLA 120d Safety Update, Figure 1 (CISA Report – Figure 1), data cut 24 Jul 2023. 2. Gini C. Variabilità e mutabilità: contributo allo studio delle distribuzioni e delle relazioni statistiche; 1912. 3. Chao & Shen. *Environ Ecol Stat*. 2010;10:429–443. 4. Berry et al. *Mol Ther Methods Clin Dev*. 2017(4):17–26.

Data cutoff July 24, 2023; Results are presented from the on-going clinical trial and interim data from long term follow-up study.