Summary Basis for Regulatory Action

Date:	March 26, 2026
From:	Pankaj K. Mandal, PhD Review Committee Chair Office of Cellular Therapy and Human Tissue (OCTHT) Office of Therapeutic Products (OTP)
BLA STN:	125806/0
Applicant:	Rocket Pharmaceuticals Inc.
Submission Receipt Date:	August 1, 2023
Resubmission Receipt date	September 26, 2025
PDUFA* Action Due Date:	March 28, 2026
Proper Name:	marnetegragene autotemcel
Proprietary Name:	KRESLADI
Indication:	treatment of pediatric patients with severe leukocyte adhesion deficiency-I (LAD-I) due to biallelic variants in *ITGB2* without an available human leukocyte antigen (HLA)-matched sibling donor for allogeneic hematopoietic stem cell transplant

***** PDUFA=Prescription Drug User Fee Act

Recommended Action: The Review Committee recommends accelerated approval of marnetegragene autotemcel.

Director, Office of Clinical Evaluation, Office of Therapeutic Products

Director, Office of Compliance and Biologics Quality

Discipline Reviews	Reviewer / Consultant - Office/Division
Regulatory Project Manager	Jennifer Albert, RN, DCPM, OTP/ORMRR
CMC • CMC Product (Product Office and OCBQ/DBSQC) • Facilities review (OCBQ/DMPQ) • Establishment Inspection Report (OCBQ/DMPQ and Product Office) • QC, Test Methods, Product Quality (OCBQ/DBSQC and Product Office)	Pankaj Mandal, PhD, CBER/OTP/OCTHT Andrew Timmons, PhD, CBER/OTP/OGT Athena Russell, PhD, CBER/OTP/OGT Sukyoung Sohn, PhD, CBER/OTP/OGT Phillip Thai, CBER/OCBQ/DMPQ Jared Greenleaf, CBER/OCBQ/DMPQ Rabia Ballica, PhD, CBER/OCBQ/DMPQ Wei Tu, CBER/OCBQ/DBSQC Claire Wernly, PhD, CBER/OCBQ/DBSQC Kouassi Ayikoe, PhD, CBER/OCBQ/DBSQC
Clinical • Clinical (Product Office) • Postmarketing safety Pharmacovigilance review (OBPV/DE) • BIMO (OCBQ/DIS)	Erica Glancy, MD, CBER/OTP/OCE Shelby Elenburg, MD, CBER/OTP/OCE Phillip Blanc, MD, MPH, CBER/OBPV/DPV Haecin Chun, CBER/OCBQ/DIS
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Labeling • Clinical (OTP/OCE) • Promotional (OCBQ/APLB) • PNR (OCBQ/APLB)	Afsah Amin, CBER/OTP CAPT Teresa Vu, CBER/OCBQ/DCM/APLB Hanah Pham, PharmD, CBER/OCBQ/DCM/APLB
Other Review(s) not captured above categories: • Consult (Analytical assessment of leachables in final DP)	Andrey Sarafanov, CBER/OTP/OPPT
Advisory Committee Summary	NA

Table of Contents

1. Introduction

Rocket Pharmaceuticals Inc. (herein Applicant or Rocket) submitted Biologics License Application (BLA) 125806 for marnetegragene autotemcel with the proprietary name KRESLADI. KRESLADI is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of pediatric patients with severe leukocyte adhesion deficiency-I (LAD-I), due to biallelic variants in *ITGB2* without an available human leukocyte antigen (HLA)-matched sibling donor for allogeneic hematopoietic stem cell transplant (HSCT), a rare, and life-threatening pediatric immunodeficiency.

Following review of the initial BLA submitted on August 1, 2023, a Complete Response Letter was issued on June 14, 2024, due to outstanding Chemistry, Manufacturing, and Controls (CMC) issues that could not be resolved during the review cycle. In a Type A meeting with Rocket on July 8, 2024, four critical manufacturing and quality deficiencies were discussed, requiring resolution prior to BLA approval: (1) insufficient CD34+ Cell Identity Assay validation for dose determination, (2) insufficient drug product stability data to establish commercial shelf-life, (3) lentiviral vector mycoplasma test method validation performed on an inappropriate test sample , and (4) inadequate drug product sterility testing methodology. In response to FDA concerns, Rocket submitted a comprehensive resubmission on September 26, 2025, addressing the four critical manufacturing and quality deficiencies. This resubmission also contained additional safety and biomarker data over a longer follow-up duration. The resubmission sufficiently addressed each CMC issue with additional stability studies, assay revalidation, additional supportive data and commitments to resolve non-critical issues in a post-marketing setting.

The Applicant has provided substantial evidence of effectiveness based on a single adequate and well-controlled clinical investigation, Study RP-L201-0318 (Study 0318), with confirmatory evidence for KRESLADI for the treatment of pediatric patients with severe LAD-I with biallelic variants in *ITGB2* and without an available HLA-matched sibling donor for allogeneic HSCT. The clinical evidence from Study 0318 demonstrates substantially improved expression of both CD18 and CD11a on neutrophils indicating restoration of the CD18/CD11a heterodimer (leukocyte function-associated antigen-1; LFA-1) function post-KRESLADI administration. Functional restoration of LFA-1 serves as a surrogate endpoint that is reasonably likely to predict clinical benefit of improved survival in severe LAD-I for purposes of accelerated approval. The overall benefit-risk profile of KRESLADI is favorable in a disease associated with premature death in childhood due to life-threatening complications when untreated.

Study 0318 was a single-arm, open label, 24-month clinical trial assessing the safety and efficacy of a single dose of KRESLADI in 9 pediatric patients (median age 42 months; range: 9.8 to 117 months) with severe LAD-I and without an HLA-matched sibling donor for allogeneic HSCT. This study forms the basis of the efficacy evaluation and regulatory action. Interpretation of the Applicant-proposed clinical efficacy endpoints including allo-HSCT-free survival and incidence of serious infections was limited due to several design, conduct, and statistical limitations (see section 6). Given these limitations, only objective measures of treatment response, CD18 and CD11a expression on neutrophils (reflecting LFA-1 function), were evaluable and interpretable for purposes of efficacy assessment. Substantial improvement in both CD18 and CD11a surface expression was observed in all treated patients at months 12 and 24 which was sustained over at least 42 months of follow-up. These improvements reflect restoration of the CD18/CD11a heterodimer (LFA-1) function, whose deficiency is the root molecular cause of LAD-I and are expected to result in improved neutrophil endothelial cell adhesion and recruitment to sites of infections, thereby reducing the risk of serious and life-threatening infections and improving survival. Therefore, it is appropriate to consider the functional restoration of LFA-1 as reflected in CD18 and CD11a improved expression as a surrogate endpoint that is reasonably likely to predict clinical benefit in severe LAD-I.

Confirmatory evidence includes mechanistic evidence from nonclinical studies demonstrating transduction of CD18-deficient hematopoietic stem cells with the lentiviral vector (LVV) in KRESLADI leading to CD18 and CD11a surface expression and functional correction of leukocyte adhesion defects. Because LAD-I pathogenesis is well-established and caused by dysfunction of a single molecular pathway and a single molecular defect, CD18/CD11a (LFA-1) heterodimer deficiency, the established natural history knowledge that heterodimer function is not restored in the absence of treatment serves as additional confirmatory evidence.

The safety database includes 9 patients followed for up to 42 months from product administration. The available safety database is limited as expected for a rare disease; however, it is considered sufficient for purposes of a safety evaluation. Treatment with KRESLADI involved not only administration of the product, but also administration of chemotherapeutic agents for myeloablative conditioning prior to product administration. These agents are associated with serious safety risks, such as cytopenias and serious infections, which were observed in the clinical study. Overall, the observed adverse events are attributable to the myeloablative conditioning and the underlying disease. The safety profile of KRESLADI administration is acceptable for this life-threatening disease with limited treatment options. There is a theoretical risk of insertional oncogenesis with

KRESLADI given it is based on an LVV that integrates into the genome. There were no cases of insertional oncogenesis or hematologic malignancy observed in the KRESLADI clinical program and this risk will be monitored during a post-marketing, long-term follow-up study.

Regulatory Flexibility

LAD-I is a very rare disease with only about 450 cases reported in the literature. Due to the serious clinical manifestations including life-limiting severe infections and other inflammatory sequelae, LAD-I causes substantial morbidity, especially in the severe form with early death in childhood without definitive treatment. The only available therapeutic option currently is supportive care and allogeneic HSCT which is associated with serious toxicities and life-threatening complications. In this therapeutic context, regulatory flexibility in the review and approval decision of this BLA is warranted and was exercised in the following ways:

1. Acceptance of a single adequate and well-controlled clinical investigation in a very small number of pediatric patients (N=9) with severe LAD-I along with confirmatory evidence.

2. Acceptance of objective measures of treatment effect that are central to the disease pathogenetic mechanism, CD18 and CD11a expression on neutrophils, as novel surrogate endpoints that are reasonably likely to predict clinical benefit on survival under the accelerated approval provisions. Verification of clinical benefit on survival will be assessed as a post-marketing requirement.

3. Acceptance of a safety database of 9 patients followed over a long duration (up to 42 months) as sufficient to support the product's safety assessment.

4. Acceptance of healthy donor materials for manufacturing two process performance qualification (PPQ) lots.

5. Use of long-term drug product stability data from representative small-format containers rather than requiring commercial container closures per 21 CFR 211.166(a)(4).

6. Acceptance of a 30-minute room temperature in-use hold time based on limited stability data and historical clinical use.

7. Acceptance of certain elements of assay validation data generated with an alternative, structurally similar vector (LV-RP-L301) for certain release assays performed on the LVV.

8. Acceptance of clinical assay validation studies for CD18 and CD11a biomarkers that partially adhered to the bioanalytical method guidance outlined in the 2022 FDA guidance entitled "M10 Bioanalytical Method Validation and Study Sample Analysis," (e.g., 2 independently-prepared dilution series instead of the recommended ≥3) but were of sufficient quality to enable data interpretation in the

setting of accelerated approval with a post-marketing requirement for bioanalytical assay optimization and further validation.

9. Observing manufacturing of another LVV at (b) (4) instead of the commercial vector based on high degree of similarity between LVV manufacturing processes.

10. Retrospective inclusion of final clinical lot (b) (4) manufactured using the proposed commercial manufacturing process for PPQ.

2. Background

LAD-I is a very rare (about 450 cases reported), autosomal recessive, genetic disease causing severe immune deficiency. It is caused by biallelic mutations in the *ITGB2* gene which encodes the protein CD18. CD18 forms a heterodimer with the CD11a protein (encoded by a different gene) and a functional heterodimer (called leukocyte function-associated antigen-1 (LFA-1)) is critical for neutrophil adhesion to endothelial cells. The absence or dysfunction of CD18 in leukocytes impairs its heterodimerization with alpha integrin subunits (e.g., CD11a) on the leukocyte surface which is essential for leukocyte endothelial adhesion and migration to sites of infection (Gu et al. 2004). Patients have increased propensity to serious and life-threatening infectious and inflammatory complications, which leads to reduced survival, especially in the severe form (defined as a neutrophil CD18 surface expression <2% with simultaneously reduced surface expression of CD11a to <2%). Allogeneic HSCT is the only therapeutic option for severe LAD-I and it is curative when performed in infancy/early childhood.

The severity of LAD-I, as defined by the level of reduction in CD18 surface expression, correlates with allo-HSCT free survival, with improved outcomes seen in moderate versus severe disease. Published literature documents normalization of both CD18 and CD11a surface expression in severe LAD-I patients following successful allo-HSCT. In these cases, patients showed concurrent improvement in clinical outcomes including reduced infections and related complications (Chakraborty et al. 2020). Allogeneic HSCT clinical experience shows that even with mixed chimerism, children with severe LAD-I can remain alive and free of significant symptoms following transplant (Thomas et al. 1995; Qasim et al. 2009; Al-wahadneh et al. 2006; Zhu et al. 2025). In canine models of LAD-I, treatment with gene-modified cells led to improved CD18 surface expression in the range of 5-10% with improved survival and long-term protection against infection for up to 7 years following treatment (Bauer et al. 2008; Bauer et al. 2013).

The following lines of evidence support the predictive ability of LFA-1 (the CD18/CD11a heterodimer) functional improvement (reflected in increases in both CD18 and CD11a surface expression) in severe LAD-I supporting its use as a surrogate endpoint that is reasonably likely to predict clinical benefit on survival:

1. there is strong biologic plausibility of improved neutrophil CD18 and CD11a surface expression leading to functional restoration of the LAD-I molecular pathway with resultant improved clinical symptoms and improved survival;

2. available scientific evidence reports improved survival and infectious complications in association with increased functional CD18/CD11a surface expression from genetic restoration of neutrophil function through allo-HSCT; and

3. mechanistic evidence in LAD-I animal models following treatment with genetically modified cells demonstrates improved survival and clinical outcomes.

Table 1. Regulatory History

Regulatory Events / Milestones	Date
1. Orphan Drug designation granted (OD #16-5430)	November 9, 2016
2. Pre-IND meeting	March 19, 2018
3. IND submission	October 18, 2018
4. Rare Pediatric Disease designation granted (RPD-2018-194)	November 30, 2018
5. Fast Track designation granted	December 12, 2018
6. Regenerative Medicine Advanced Therapy designation granted	March 4, 2021
7. BLA 125806/0 submission	August 1, 2023
8. BLA filed with Deficiencies	September 29, 2023
9. Mid-Cycle communication	December 1, 2023
10. Late-Cycle meeting	January 26, 2024
11. Major Amendment	February 12, 2024
12. Complete Response	June 14, 2024
13. Type A- post CR action in person meeting	July 8, 2024
14. Incomplete Response	October 15, 2024
15. Re-submission after Complete Response	September 26, 2025
16. Action Due Date	March 28, 2026

3. Chemistry, Manufacturing, and Controls (CMC)

This BLA includes an adequate description of the manufacturing process and testing of KRESLADI, and the FDA CMC review team concludes that the manufacturing process, along with associated test methods and control measures, are capable of yielding a product with consistent quality characteristics.

a. Product Quality

Manufacturing Summary

KRESLADI consists of autologous, enriched CD34+ hematopoietic stem cells (HSCs) that have been genetically modified with a non-replicating LVV, LV-RP-L201, containing an intact copy of the *ITGB2* gene. The manufacture of KRESLADI involves the transduction of enriched, autologous CD34+ cells with the LV-RP-L201 LVV. This LVV is an HIV-1 based 3rd generation, self-inactivating, VSV-G pseudotyped lentiviral vector encoding the *ITGB2* gene.

The LV-RP-L201 LVV is manufactured by a contract manufacturer ((b) (4) via the (b) (4)

The starting material for KRESLADI manufacture consists of autologous CD34+ cells isolated from G-CSF and Plerixafor mobilized peripheral blood apheresis material collected by leukapheresis at qualified treatment centers. Leukapheresis material is shipped to the site of KRESLADI manufacture (b) (4) . Here, leukapheresis material containing CD34+ cells are washed and (b) (4) at a concentration of 3.4×10^5 - 6.1×10^6 viable cells per mL (3.2×10^5 - 6.1×10^6 CD34+ cells/mL) to form the (b) (4) RP-L201 drug product (DP). The (b) (4) DP is then dispensed into (b) (4) 50 mL EVA bags at a nominal fill volume of 30 mL. The filled bags are then labeled, frozen in a (b) (4), and cryopreserved at ≤-150 °C to await shipment back to the treatment center. The shelf life of KRESLADI is 6 months under the intended storage conditions. The cryopreserved DP is shipped to the treatment center in a qualified cryogenic shipper. At the treatment center, the DP is thawed and administered via intravenous infusion following myeloablative therapy. The time for DP to thaw and complete infusion is estimated to be about 30 minutes.

Manufacturing Control Strategy

The KRESLADI manufacturing control strategy consists of (1) raw material, component, and reagent qualification programs; (2) in-process monitoring; (3) in-process control testing; (4) lot release and stability testing; (5) manufacturing process validation and continuous process verification; and (6) traceability through chain of identity and chain of custody (COI/COC). The raw material, component, and reagent qualification program consists of source material risk assessment, vendor qualification, confirmation of the certificate of analysis, and material testing. Raw materials derived from animals and human donors are controlled to ensure the absence of microbial contaminants and adventitious agents. Critical process parameters are established for unit operations based on process knowledge and risk assessment studies. In-process monitoring and controls are implemented throughout the process to support process consistency. Lot release test methods are suitably validated or verified. The suitability of the commercial KRESLADI manufacturing process was assessed at (b) (4) manufacturing facility using healthy donor-derived starting material. Process validation studies demonstrated control of

the manufacturing process. Additional validation studies, including aseptic process simulation and shipping validation studies, were also performed. The KRESLADI LV-RP-L201 LVV manufacturing process was also validated at the contract manufacturing organization (b) (4) . KRESLADI specifications are adequate to ensure product quality and consistency with DP used in the clinical study. COI/COC are established at the time of apheresis collection and maintained throughout the manufacturing process to administration to ensure that the patient receives the correct autologous lot.

Manufacturing Risks, Potential Safety Concerns, and Management

Product Mix-Up

KRESLADI is an autologous product manufactured in a multi-product manufacturing facility; as such, product mix-ups, either of autologous lots or with other stem cell products manufactured at the same facility, would result in risks to patient's safety and will require remanufacturing of KRESLADI. To minimize the risk of product mix-up, KRESLADI is manufactured on a campaign basis - (b) (4) product lot is manufactured in a production suite at any given time. COI/COC is established at the point of apheresis collection and checked throughout the manufacturing process to ensure that the patient receives the correct autologous lot. COI/COC is maintained through barcodes and human-readable identifiers present on labels. Additionally, patient identifiers are confirmed prior to administration. Lot release testing confirms product identity.

Replication Competent Lentivirus (RCL)

KRESLADI is manufactured by transducing autologous CD34+ cells with a non-replicating LVV (LV-RP-L201) containing an intact copy of the ITGB2 gene. RCL is a theoretical concern for the KRESLADI manufacturing process. The likelihood of RCL generation is reduced by the LV-RP-201 LVV design: (1) the genetic elements are separated across 4 plasmids requiring multiple recombination events to form RCL; (b) (4) In accordance with current FDA guidance, and the final LV-RP-L201 and production cells are tested by co-culture prior to LVV lot release and use in the KRESLADI manufacturing process. No cases of replication-competent lentivirus (RCL) were observed throughout the RP-L201 clinical development program. RCL testing in peripheral blood (PB) was performed (at least three assessments at different timepoints) as recommended by the FDA guidance on testing for RCL.

Insertional Oncogenesis

While LVV integration poses a risk for insertional mutagenesis, no risk-associated integration profiles have been observed to date for KRESLADI. The risk of insertional oncogenesis is theoretically reduced through KRESLADI lot release testing acceptance criteria, with a maximum upper limit for vector copy number (VCN) integrations. The upper VCN limit is supported by lots administered during clinical

trials. No cases of secondary malignancies associated with RP-L201 have been reported throughout the RP-L201 clinical development program. Integration site analyses (ISA) have demonstrated highly polyclonal lentiviral integration patterns without evidence of clonal dominance or dominant integrations in proximity to oncogenic loci.

CMC PMCs/PMR

The following issues were identified but could not be resolved during the BLA review cycle. To allow patient access, these issues will be resolved through a post marketing requirement (PMR) and postmarketing commitments (PMCs) by December 31, 2028.

Complete analysis of process-related impurities in the drug product (DP) was unresolved. The leachables analysis did not include the contribution of the major process components utilized in KRESLADI manufacturing, and did not adequately address the risk associated with the presence of leachables in the DP.

Although sufficient information was provided to determine an in-use time limit and product shelf life, there are outstanding issues related to product stability and LV-RP-L201 LVV shipping. These issues will be addressed by conducting additional studies with subsequent revision of hold duration, as applicable. An additional shipping validation study under worst-case conditions with container closure integrity (CCIT) testing of LV-RP-L201 (b) (4) post-shipping will be performed.

Several issues related to analytical assay validation and sample handling remain unresolved. Specifically, (b) (4) will be performed for (b) (4) assays, supplemental validation studies will be performed to incorporate revised DP potency, vector copy number, and LV-RP-L201 (b) (4) assay methods. Additionally, the LV-RP-L201 (b) (4) assay acceptance criterion will be reassessed with additional manufacturing experience. Lastly, sterility testing of fresh test samples will be implemented.

Rocket will also implement improvements to patient monitoring assays. Rocket will update the LAD-1 Flow Cytometry assay protocol, used to evaluate the expression of CD11a/CD11b/CD18 on neutrophils from treated patients, to describe bridging procedures when transitioning between different antibody lots, including evaluation of assay performance at different concentrations of CD11a/CD11b/CD18. Finally, Rocket Pharmaceuticals will submit the Insertion Site Analysis assay protocol and validation report.

b. Testing Specifications

The final KRESLADI lot release specification is shown in Table 2. The analytical methods and their validations and/or qualifications, along with proposed PMCs, reviewed for the KRESLADI (b) (4) drug product were found to be adequate for the intended use in conjunction with the assay-related commitments described above.

Table 2: Final Commercial KRESLADI Release Specification

Attribute Category	Test	Method	Acceptance Criteria
General	Appearance	(b) (4)	Colorless to white to red, including shades of pink, light yellow and brown suspension Turbidity: clear to slightly cloudy Particulate: Free of intrinsic and extrinsic particulates. May contain small proteinaceous particles and visible cell aggregates (inherent particulates).
General	Total viable cell count	(b) (4)	3.4×10^5 – 6.1×10^6 cells/mL
Identity / Purity	Immunophenotype ($CD34^+$)	(b) (4)	(b) (4)
Potency / Purity	Viability	(b) (4)	(b) (4)
Potency	Transduction efficiency	(b) (4)	(b) (4)
Potency	Neutrophil adhesion assay	(b) (4)	(b) (4)
Potency	(b) (4)	(b) (4)	(b) (4)
Potency	(b) (4)	(b) (4)	(b) (4)
Potency / Safety	(b) (4) Vector Copy Number (VCN)	(b) (4)	(b) (4)
Potency / Safety	(b) (4)-VCN	(b) (4)	(b) (4)
Safety	Bacterial Endotoxins	(b) (4)	(b) (4)
Safety	Sterility	(b) (4)	No growth
Safety	Mycoplasma	(b) (4)	Not detected

c. CBER Lot Release

CBER Lot Release, including the submission of product samples to CBER, is not required. The basis for this decision is that KRESLADI is an autologous product; as such each lot will treat a single patient. Failure of a single lot will have minimal potential impact on public health.

d. Facilities Review / Inspection

Facility information and data provided in the BLA were reviewed by CBER and found to be sufficient and acceptable. The facilities involved in the manufacture of KRESLADI are listed in the table below. The activities performed and inspectional histories are noted in the table.

Name/Address	FEI number	DUNS number	Inspection/ Waiver	Justification /Results
(b) (4) *LVV manufacturing*	(b) (4)	(b) (4)	PLI	CBER/DMPQ (b) (4) VAI
(b) (4) *DS manufacturing; DP manufacturing; primary packaging and labeling*	(b) (4)	(b) (4)	Surveillance	OII/OBI (b) (4) VAI
(b) (4) *DP release testing*	(b) (4)	(b) (4)	Waiver	OII/OBPO (b) (4) VAI

DMPQ – Division of Manufacturing and Product Quality; DS – drug substance; DP – drug product; LVV – lentiviral vector; NAI – No Action Indicated; OBPO – Office of Biological Products Operations; OPQO – Office of Pharmaceutical Quality Operations; OTP – Office of Therapeutic Products; OII – Office of Inspections and Investigations; OBI – Office of Biologics Inspectorate; PLI – pre-license inspection; VAI – Voluntary Action Indicated

(b) (4)

CBER/DMPQ conducted a PLI of (b) (4). A Form FDA 483 list of observations was issued at the end of the inspection. The inspection is classified as VAI.

(b) (4)
OII conducted a surveillance inspection of (b) (4) . A Form FDA 483 list of observations was issued at the end of the inspection. The inspection is classified as VAI.

(b) (4)
OII conducted a surveillance inspection of (b) (4) . A Form FDA 483 list of observations was issued at the end of the inspection. The inspection is classified as VAI.

e. Container/Closure System

KRESLADI DP is filled into a 50 mL ethylene vinyl acetate (b) (4) bag (manufactured by (b) (4)). The (b) (4) bags feature a connected tubing set, which includes three-way split luer-activated needle-free injection ports (two female and one male) and sterile-weldable tubing. The bag is 510(k) cleared. (b) (4) performed the container closure integrity testing (CCIT) at the (b) (4) facility, employing the (b) (4) method; all acceptance criteria were met.

f. Environmental Assessment

The BLA included a request for categorical exclusion from an Environmental Assessment under 21 CFR 25.31. The FDA concluded that this request is justified, and no extraordinary circumstances exist that would require an environmental assessment.

4. Nonclinical Pharmacology/Toxicology

In vitro pharmacology studies were conducted using an immortalized LAD-I patient-derived lymphoblastic cell line (LCL) as well as healthy donor (HD) cord blood-derived (CB) CD34+ HSCs transduced with short hairpin ribonucleic acid (shRNA) to knock down CD18 expression and evaluate the activity of the Chim-CD18-WPRE LV vector, LV-RP-L201. These studies demonstrated that vector-driven ITGB2 transgene expression led to hCD18:CD11a receptor dimerization, improved neutrophil aggregation, intercellular adhesion molecule-I (ICAM-I) binding, resistance to shear stress, and respiratory burst function.

In vivo studies were conducted in either CD18 hypomorphic ($CD18^{HYP}$) or CD18 knockout ($CD18^{KO}$) mice to assess the safety and activity of lineage-negative (Lin-) murine hematopoietic stem and progenitor cells (mHSPCs) transduced with the LV-RP-L201. $CD18^{HYP}$ and $CD18^{KO}$ mice have deficient CD18 expression and impaired neutrophil migration and inflammatory responses similar to LAD-I patients. Successful engraftment of the LV-RP-L201 transduced Lin- cells was demonstrated in recipient $CD18^{HYP}$ or $CD18^{KO}$ mice with enhanced neutrophil extravasation to tissue-specific sites of inflammation. Likewise, bone marrow cells (BMCs) isolated from $CD18^{HYP}$ mice were re-transplanted into secondary recipients and showed stable vector copy number (VCN), multilineage reconstitution, and increased human CD18 (hCD18) expression. The transduction enhancers (TEs) (b) (4)

augmented hCD18 expression and improved neutrophil extravasation and function in both murine LAD-I models.

A 1-month in vivo toxicology and biodistribution (BD) study was also conducted using recipient (b) (4) and (b) (4) mice for safety evaluation of LV-RP-L201 transduced Lin- murine HSPCs. No premature mortality or unexpected deaths were observed over the course of the study period in recipient mice. Hematopoietic reconstitution was observed in the peripheral blood (PB) and BM and measurable VCN was detected in other hematopoietic organs, whereas undetectable or low VCN was observed in non-hematopoietic organs including the gonads.

In vivo studies using HD mobilized peripheral blood (mPB) or CB-derived CD34+ HSCs, with or without TEs, administered to immunodeficient NOD.Cg-(b) (4) *IL2rg*$^{(b)\ (4)}$/SzJ (NSG) mice demonstrated successful hematopoietic lineage reconstitution and hCD18 expression following transduction with the LV-RP-L201 as compared to the untransduced (UNT) and (b) (4) controls. Human CD45+ cells isolated from the BM of primary recipients were re-transplanted into secondary recipients and demonstrated multilineage hematopoietic reconstitution and sustained hCD18 expression.

Insertional analysis was conducted for Lin- murine HSPCs (pre-transplantation) as well as PB and BM of CD18^{HYP} mice transplanted with Lin- murine HSPCs transduced with the LV-RP-L201 from both primary and secondary recipients for different post-transplantation timepoints (1, 4, or 9 months). The insertion sites (ISs) of transduced cells and primary transplanted samples in mice showed an oligoclonal to polyclonal vector integration profile indicating no clonality. A decrease in clonal diversity from primary to secondary recipients with multiple identical clones contributing to hematopoietic repopulation was observed as expected for the secondary transplantation studies. There were no preferential integrations in or nearby genes previously associated with insertional mutagenesis. HD CB CD34+ cells (pre-transplantation) as well as PB of NSG mice transplanted with HD CB CD34+ cells transduced with the LV-RP-L201 after 3 months post-transplantation showed a similar polyclonal integration profile.

Carcinogenicity and developmental and reproductive toxicity studies were not conducted with KRESLADI. These studies are not warranted based on the drug product characteristics and safety profile.

5. Clinical Pharmacology

The clinical pharmacology assessment focused on the pharmacodynamic (PD) effects of KRESLADI and on assessment of the Applicant's proposed recommended dose. The nature of KRESLADI is such that conventional pharmacokinetic studies assessing absorption, distribution, metabolism, and elimination are not applicable. The data supporting the clinical pharmacology assessment of KRESLADI for the proposed indication was obtained from 9 patients treated with the product in clinical study RP-L201-0318. As part of the PD assessment, engraftment parameters for transduced cells (i.e., vector copy number, VCN) and expression of mechanistically relevant markers such as CD18 and CD11a were monitored longitudinally.

The VCN in peripheral blood mononuclear cells (PBMC) was variable among the 9 treated patients. Nonetheless, the median VCN appears to increase between Week 4 and Month 3 (range 0.14 to 2.4) and remain stable from Month 6 to 24 (range 0.49 to 3.6).

In Study RP-L201-0318, neutrophil CD18 and CD11a surface expression substantially improved after KRESLADI administration up to 42 months of follow-up post-product administration. Please refer to Section 6a for results details.

A dose-response assessment of available data did not identify KRESLADI dose as a factor affecting PD parameters.

Overall, the PD activity as measured by the CD18 and CD11a expression along with the observed consistent positive correlation between engraftment and PD parameters provide evidence of KRESLADI's pharmacodynamic effects in patients with LAD-I.

6. Clinical/Statistical

a. Clinical Program

The KRESLADI clinical development program includes 2 clinical studies: Study RP-L201-0318 (Study 0318) which serves as the pivotal study, and Study RP-L201-0121-LTFU (Study 0121-LTFU) which enrolled treated patients for long-term follow-up. Data from Study RP-L201-0318 form the basis of approval.

Study 0318 was a global, single-arm, open-label, 24-month study of KRESLADI in 9 pediatric patients aged 10 months-10 years (median age 3.5 years) with severe LAD-I based on clinical symptoms, biallelic mutations in *ITGB2,* and neutrophil CD18 surface expression <2%, and CD11a and/or CD11b surface expression <2% (if neutrophil CD18 surface expression ≥2%). Patients with an available HLA-matched sibling donor for allogeneic HSCT were excluded.

All patients underwent mobilization with G-CSF and plerixafor followed by apheresis. Busulfan was administered every 12 hours over 4 days and KRESLADI was administered 25 to 69 hours after the last busulfan dose.

Study 0318's primary endpoint was the proportion of patients alive and without allogeneic HSCT at least 1-year post-infusion and at age 2 years for patients <1 year old at study enrollment (allo-HSCT-free survival). Success on the primary endpoint was defined by the Applicant as improved HSCT-free survival over a historical rate of 39% at age 2 years (based on published literature review by Almarza Novoa et al.[1]). The authors of that literature review note that they were unable to calculate survival curves for severe LAD-I patients older than 2 years of age because precise survival duration was not noted for most cases in their study. Given this limitation and the limited support for the chosen historical comparator rate (based only on a single publication and on data

[1] Almarza Novoa E, S Kasbekar, AJ Thrasher, DB Kohn, J Sevilla, T Nguyen, JD Schwartz, and JA Bueren, 2018, Leukocyte adhesion deficiency-I: A comprehensive review of all published cases, J Allergy Clin Immunol Pract, 6(4):1418-1420.e10.

only to age 2 years), the comparison of HSCT-free survival is only applicable to patients enrolled at <1 year of age and who reached at least 2 years of age during the study. Of the 9 enrolled patients in Study 0318, only 3 were <1 year of age at study enrollment and were evaluable for the primary endpoint. HSCT-free survival in these 3 patients was 100% (95% CI: 29%,100%) at 24 months with the lower bound of the CI below the 39% survival benchmark selected by the Applicant as a success criterion. In the remaining 6 patients, the endpoint of HSCT-free survival at 24 months is not interpretable as it lacks an appropriate comparator threshold or control group. Across both studies, all 9 patients remained alive without allogeneic HSCT up to at least 42 months of follow up post-product administration.

One of the secondary endpoints was the change in incidence of significant infections and hospitalizations pre- and post-infusion (using historical data for comparisons). For the infectious endpoint, the definition of infections and hospitalizations changed throughout different protocol versions and there was inconsistent data collection and missing data pre- and post-infusion with insufficient and incongruous documentation of infection incidences in the historical (pre-infusion) records. The clinical data review also revealed conflicting data among datasets, listings, reports/summaries, and caregiver testimonials (designed to fill data gaps) for infectious endpoints. As a result, the infectious endpoints were uninterpretable.

Study 0318 had several design and conduct limitations. The primary endpoint of HSCT-survival was compared to a pre-specified historical threshold which was based on a cohort of LAD-I patients followed up to 2 years of age. Therefore, the primary endpoint assumption for study success was only evaluable in 3 patients who were younger than 1 year of age at product administration. Even though all 3 patients survived to the end of study (24 months), the lower bound of the 95%CI for HSCT-free survival (29%) in this subgroup of 3 patients was below the Applicant's pre-specified historical threshold of 39%. This finding is not unexpected given that the study was likely underpowered to show an effect on HSCT-free survival in the 3-patient subgroup on which the comparison was based on. Furthermore, the secondary endpoint of incidence of infections was not interpretable due to significant limitations in the comparison between pre- and post-treatment data. Endpoint definitions changed during the course of the study and data collection was inconsistent with high rates of missing data.

Due to these limitations, only objective measures of neutrophil adhesion in the form of CD18 and CD11a expression on neutrophils (representing heterodimeric LFA-1 function), which were assessed as secondary endpoints, were interpretable and were the focus of the review. Treatment effects on these two objectively ascertained biomarkers were substantial and much less prone to bias compared to clinical measures. Seven of the 9 treated patients had baseline CD18 surface expression <2% and all 9 patients had baseline CD11a surface expression <2%. Substantial improvement in both CD18 and CD11a surface expression was observed in all treated patients at months 12 and 24 in Study 0318 and that was sustained over at least 42 months of follow-up across both Studies 0318 and 0121-LTFU. Median levels at months 12 and 24 for CD18 were 54% (range: 20% to 87%) and 50% (range: 16% to 82%) and for CD11a were 45% (range: 18% to 75%) and 39% (range: 17% to 65%). Post-treatment neutrophil CD18 surface expression showed a strong correlation with CD11a surface expression (based on data from the 7 evaluable patients with baseline CD18 surface expression <2%). The large

magnitude of improvement in post-treatment expression levels of CD18 and CD11a approximate the half normal expression expected in asymptomatic, *ITGB2* heterozygotes (healthy individuals). In summary, the large observed improvements in both CD18 and CD11a surface expression provide a strong scientific basis for concluding that LFA-1 function is restored after KRESLADI administration which is reasonably likely to predict clinical benefit on survival and infectious complications in pediatric patients with severe LAD-I.

b. Bioresearch Monitoring (BIMO) – Clinical/Statistical/Pharmacovigilance

BIMO inspection assignments were issued for the sponsor two clinical investigator sites (one foreign and one domestic), and a contract research organization that participated in the conduct of Protocol RP-L201-0318. The inspections did not reveal substantive issues that impact the data submitted in support of this original Biologics License Application (BLA).

Pediatrics KRESLADI has orphan drug designation and is, thus, exempt from PREA requirements. The safety and effectiveness of KRESLADI are established based on a single study in pediatric patients. Other Special Populations: N/A

7. Safety and Pharmacovigilance

The safety database includes 9 pediatric patients aged 10 months-10 years with severe LAD-I who received a single dose of KRESLADI at a median dose of 4.3×10^6 CD34+ cells/kg (range: 2.8×10^6 to 10×10^6 CD34+ cells/kg) in Studies RP-L201-0318 and 0121-LTFU. The median duration of follow up after KRESLADI administration was 4.2 years (range 3.6-5.7). The observed adverse events primarily reflect known adverse effects of myeloablative conditioning required prior to product administration in addition to effects of the underlying disease.

The majority of adverse events occurred between the start of myeloablative conditioning and the time of engraftment. Infection-related events were common throughout all study time points and were attributable to the conditioning regimen and the patients' underlying susceptibility to infections.

There were no deaths.

Serious adverse events included the following: pulmonary arterial hypertension in one patient with underlying congenital heart disease; veno-occlusive disease in one patient (resolved without sequelae) attributed to busulfan conditioning; bilateral sensorineural deafness (Grade 3) in one patient possibly related to busulfan and amikacin use; and a finding of abnormal clone (Grade 3) detected on routine bone marrow assessment which resolved approximately 2 months later with no evidence of hematologic malignancy (possibly related to myeloablative conditioning and a concurrent infection). There were no cases of malignancy.

The most common non-serious adverse events included mucositis, febrile neutropenia, infections (respiratory, gastrointestinal, urinary tract, candidiasis, vascular device-related), skin lesions (pyoderma gangrenosum, erythema, vesicles, hyperpigmentation),

pyrexia, nausea/vomiting, alopecia, and dermatitis. All 9 patients experienced Grade 3 or 4 cytopenias (anemia, thrombocytopenia, neutropenia) with the majority observed within the first 30 days after KRESLADI administration and likely related to myeloablative busulfan conditioning prior to product administration. Four of 9 patients experienced mild-moderate liver enzyme elevations.

Given the theoretical risk of insertional oncogenesis associated with the product being based on LVV, the Applicant is required to conduct a postmarketing observational study to assess long-term adverse reactions and the risk of malignancies among KRESLADI-treated patients for at least 15 years as a PMR. To determine if a favorable benefit-risk profile remains over a long-term period (e.g., 15 years after treatment with KRESLADI), conducting the proposed postmarketing study as a PMR, in addition to performing routine and enhanced pharmacovigilance (e.g., expedited reporting, periodic safety report summaries for all postmarketing malignancy reports), is warranted.

8. Labeling

The proposed proprietary name, KRESLADI, was initially reviewed by the Advertising and Promotional Labeling Branch (APLB) on October 17, 2023, and was found acceptable. CBER communicated the acceptability of the proprietary name to the Applicant on October 30, 2023. The proposed proprietary name, KRESLADI, was re-reviewed by APLB and found acceptable on December 3, 2025.

APLB, the Office of Gene Therapy (OGT), and the Office of Review Management and Regulatory Review (ORMRR) reviewed the proposed package and container labels on December 15, 2025, and asked the Applicant to make significant changes to the package and container labels. Following FDA guidelines, the Applicant revised the package and container labels. APLB, OGT, and ORMRR found revised version acceptable from a comprehension, readability, and promotional perspective and determined they meet regulatory/statutory requirements.

The Office of Clinical Evaluation (OCE) labeling review team, together with the relevant discipline review teams, reviewed and revised the proposed prescribing information to ensure that it meets regulatory/statutory requirements, is consistent with current labeling practice, conveys clinically meaningful and scientifically accurate information needed for the safe and effective use of the product, and provides clear and concise information for the healthcare providers. With the agreed revisions, the prescribing information is acceptable.

Several significant changes were made to the proposed prescribing information to enhance clarity and completeness of prescribing information. The indication was revised to specify that KRESLADI is indicated for pediatric patients with severe LAD-I due to biallelic variants in *ITGB2* without an available human leukocyte antigen (HLA)-matched sibling donor for allogeneic hematopoietic stem cell transplant. Limiting the indication to patients without an available HLA-matched sibling donor appropriately positions KRESLADI as a treatment option when the established standard of care is not available, rather than as a replacement for HSCT. The Warning and Precautions section was expanded to include warning about serious infections, and veno-occlusive disease. The adverse reactions section was revised to comprehensively capture safety events

occurring during the myeloablative conditioning period and throughout the two years following KRESLADI administration. Additionally, the Clinical Studies section was restructured to provide a comprehensive description of the pivotal study, population characteristics, and efficacy endpoints that served as the substantial evidence for KRESLADI's accelerated approval.

9. Advisory Committee Meeting

The submitted information, including clinical study design and trial results, did not raise unresolved scientific or regulatory questions that would benefit from advisory committee discussion. Therefore, this BLA was not referred to an Advisory Committee.

10. Other Relevant Regulatory Issues

KRESLADI received Orphan Drug, Rare Pediatric Disease, Fast Track, and Regenerative Medicine Advanced Therapy designations. The BLA received priority review designation. The Applicant also requested a rare pediatric disease priority review voucher (RPD PRV) under Section 529 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) upon approval. KRESLADI was granted RPD PRV upon approval.

11. Recommendations and Benefit/Risk Assessment

a. Recommended Regulatory Action

The Applicant has provided substantial evidence of effectiveness to support accelerated approval of KRESLADI for the treatment of pediatric patients with severe LAD-I with biallelic *ITGB2* variants and without an HLA-matched sibling donor for allo-HSCT. In addition, the Applicant has provided sufficient information, in conjunction with the requirements and commitments listed below, that the manufacturing process, along with associated test methods and control measures, can yield a product with consistent quality characteristics to support accelerated approval.

b. Benefit/Risk Assessment

The submitted data provide substantial evidence of effectiveness for KRESLADI based on a substantial treatment effect on a surrogate endpoint, restoration of LFA-1 (CD18/CD11a heterodimer) function reflected in improvements in neutrophil CD18 and CD11a surface expression, that is reasonably likely to predict clinical benefit on improved survival in severe LAD-I. CD18 and CD11a expression on neutrophils increased in all treated patients with median levels of both reaching those expected in asymptomatic (healthy) *ITGB2* heterozygotes with half normal expression expected. Several lines of confirmatory evidence support these findings including mechanistic evidence from *in vivo* nonclinical studies demonstrating CD34+ cell transduction with KRESLADI leading to CD18 and CD11a surface expression resulting in the functional correction of leukocyte adhesion defects and evidence from the natural history of the disease showing that CD18 and CD11a levels remain unchanged (low/absent) if not treated.

The serious risks observed in the studies are mostly secondary to the toxicities associated with myeloablative conditioning with busulfan required prior to product administration. No cases of insertional oncogenesis or hematologic malignancy were observed but that remains a theoretical risk given the LVV use in the product. The risk of hematologic malignancy will be assessed over longer term treatment as a PMR study.

Overall, LAD-I is a serious and life-threatening, rare disease of childhood with limited therapeutic options which include allogeneic HSCT with associated serious risks and high risk of mortality. There is a high unmet need for disease-modifying therapies that improve morbidity and mortality and avoid the life-threatening toxicities of allogeneic HSCT. In this therapeutic context, regulatory flexibility in applying the statutory requirements for approval is warranted and approval under the accelerated approval provisions based on restoration of LFA-1 (CD18/CD11a heterodimer) function is scientifically supported.

The observed restoration of LFA-1 (CD18/CD11a heterodimer) function, reflected in the substantial increases in CD18 and CD11a post-product administration, outweighs the observed and potential risks of the product considering the therapeutic context. To satisfy the accelerated approval requirements, clinical benefit on overall survival and HSCT-free survival will be assessed in the post-marketing setting through a PMR which will continue to follow the 9 treated LAD-I patients and enroll additional patients to characterize the clinical benefit over a long duration of follow-up.

c. Recommendation for Postmarketing Activities

Accelerated approval regulations require that the Applicant conduct adequate and well-controlled trials to verify and describe the clinical benefit of KRESLADI. The Applicant agreed to the following PMR:

1. Submit analyses of clinical outcomes including, at a minimum, overall survival, allogeneic HSCT-free survival, and infectious outcomes, as well as biomarker changes (e.g., neutrophil CD18 expression, CD11a expression) in: 1) all treated patients with severe LAD-I currently enrolled in Study RP-L201-0121-LTFU with each patient followed to at least 10 years of age; and 2) at least 4 newly treated pediatric patients with *ITGB2*-associated, severe LAD-I who are ≤1 year of age at the time of marnetegragene autotemcel administration with each patient followed to at least 2 years of age. All endpoints should be well defined, and data should be collected systematically and consistently considering potential confounding variables to enable data interpretation, e.g., antibiotic use in relation to incidence of serious infections, etc. Biomarker assessments should be based on appropriately validated bioanalytical assays (as assessed in PMR 2). All analyses should include comparisons to a suitable comparator for purposes of verifying and describing the clinical benefit of marnetegragene autotemcel in *ITGB2*-associated severe LAD-I.

    Milestone dates:
    Final protocol submission: June 30, 2026
    Interim study report submission: October 31, 2030
    Study completion: December 31, 2033
    Final study report submission: June 30, 2034

2. Submit data from supplemental validation studies performed on the LAD-1 Flow Cytometry assay described in SOP-778817. This validation is needed to enable data interpretation of your confirmatory study and specifically evaluate the performance of the CD18 (6p7) and CD11a assays throughout the complete analytical range, including low cell surface expression levels, and should include assessments of repeatability, linearity, accuracy, intermediate precision, and specificity.
Milestone dates:

    Final Protocol Submission: July 31, 2026
    Study Completion: December 31, 2026
    Final Study Report Submission: February 27, 2027

The Applicant will conduct routine and enhanced pharmacovigilance activities (with adverse event reporting as required under 21 CFR 600.80), and the following safety study as a PMR under section 505(o) of the FDCA:

3. Submit analyses of safety data from a postmarketing, prospective, longitudinal, observational study assessing and characterizing the long-term safety risks of marnetegragene autotemcel in patients with severe LAD-I including the risk of secondary malignancies. The study will enroll a minimum of 10 patients with severe LAD-I who receive marnetegragene autotemcel and safety data will be collected for each patient for at least 15 years after product administration

    Final Protocol Submission: June 30, 2026
    Study Completion Date: June 30, 2047
    Final Report Submission: December 31, 2047

3. An adequate leachables safety assessment for the KRESLADI drug product (DP) through its manufacturing process, storage, and in-use conditions. This assessment must include the following:

    a. Assessment of both organic and elemental extractables from the high-risk for leachables manufacturing/storage components of final DP (i. e. cumulative leachables in DP).

    b. The leachables study can be conducted by simulating the DP manufacturing process from the step with high-risk for leachables components (b) (4) , performed using maximal hold times and temperatures through the process, product freezing, shelf-life storage, thawing, and in-use processing.

    c. A full toxicological risk assessment for the identified leachables. Since the drug product is specifically intended for pediatric use, the permitted daily exposure (PDE) or comparator values should be calculated using the worst-case body weight assumption (e.g., 5-kg) for pediatric subjects administered

the LV-RP-L201 drug product for your leachables toxicological risk assessment.

Study milestone dates:
Final Protocol Submission: June 30, 2026
Study Completion Date: December 31, 2026
Final Study Report Submission: May 31, 2027

The Applicant agreed to the following CMC PMCs:

5. Rocket Pharmaceuticals, Inc. commits to conducting an additional in-use stability study to support in-use conditions for KRESLADI from the start of thaw to completion of infusion as described in the approved USPI. The final study report will be submitted as a "Postmarketing Commitment – In-use Stability Final Study Report" by September 30, 2026, and revise the hold duration in the USPI as supported by the in-use stability data.

   Final Study Report Submission: September 30, 2026

6. Rocket Pharmaceuticals, Inc. commits to provide a risk assessment and perform additional studies to evaluate the impact of changes to (b) (4) . The final study report will be submitted as a "Postmarketing Commitment – Final Study Report" by March 31, 2027.

   Final Study Report Submission: March 31, 2027

7. Rocket Pharmaceuticals, Inc. commits to (b) (4) The final report will be submitted as a "Postmarketing Commitment – Final Study Report" by March 31, 2027.

   Final Study Report Submission: March 31, 2027

8. Rocket Pharmaceuticals, Inc. commits to perform a prospective revalidation of the KRESLADI drug product potency assay by (b) (4) . The final validation study report will be submitted as a "Postmarketing Commitment – Final Study Report" by March 31, 2027.

   Final Study Report Submission: March 31, 2027

9. Rocket Pharmaceuticals, Inc. commits to conduct (b) (4) . The final study report will be submitted as a “Postmarketing Commitment – Final Study Report” by September 30, 2026.

   Final Study Report Submission: September 30, 2026

10. Rocket Pharmaceuticals, Inc. commits to perform supplemental validation of the (b) (4) . The final validation study report will be submitted as a “Postmarketing Commitment – Final Study Report” by March 31, 2027.

    Final Study Report Submission: March 31, 2027

11. Rocket Pharmaceuticals, Inc. commits to conduct additional studies to define the (b) (4) . The final study report will be submitted as a “Postmarketing Commitment – Final Study Report” by September 30, 2026.

    Final Study Report Submission: September 30, 2026

12. Rocket Pharmaceuticals, Inc. commits to conduct additional studies to evaluate whether assay (b) (4) . The final study report will be submitted as a “Postmarketing Commitment – Final Study Report” by March 31, 2027.

    Final Study Report Submission: March 31, 2027

13. Rocket Pharmaceuticals, Inc. commits to submit the Insertion Site Analysis (ISA) assay protocol and validation report. The final study report will be submitted as a “Postmarketing Commitment – Final Study Report” by March 31, 2027.

    Final Study Report Submission: March 31, 2027

14. Rocket Pharmaceuticals Inc. commits to updating Section 14.4 of SOP-778817, which describes the “LAD-1 Flow Cytometry” assay used throughout the RP-L201-0318 clinical study to evaluate the expression of CD18, CD11a, and CD11b on neutrophils from treated patients. The updated Section 14.4 will describe (b) (4)

(b) (4) similar to experiments performed as part of the method validation. The final study protocol will be submitted as a “Postmarketing Commitment – Final Study Protocol” by August 31, 2026.

Final Study Protocol Submission: August 31, 2026

15. Rocket Pharmaceuticals, Inc. commits to reassessing the acceptance criterion for the (b) (4) assay performed as part of release of the LV-RP-L201 lentiviral vector after (b) (4) additional LV-RP-L201 lots are manufactured and used to generate commercial KRESLADI DP. The final study report will be submitted as a “Postmarketing Commitment – Final Study Report” by December 31, 2028.

    Final Study Report Submission: December 31, 2028

16. Rocket Pharmaceuticals, Inc. commits to implement storage and shipping of KRESLADI sterility samples at (b) (4), conduct a (b) (4) hold time study for DP lot release and provide data to support (b) (4) sample testing with current validated sterility test method. The final study report will be submitted as a “Postmarketing Commitment” by March 31, 2027.

    Final Study Report Submission: March 31, 2027

17. Rocket Pharmaceuticals, Inc. commits to conduct an additional shipping validation study, under worst-case conditions, with container closure integrity testing (CCIT) of the (b) (4) performed post-shipping. CCIT will be performed via the (b) (4) method. The validation study report will be submitted as a “Postmarketing Commitment – Final Study Report” by August 30, 2026.

    Final Study Report Submission: August 30, 2026