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**Department of Health and Human Services  
Food and Drug Administration  
Center for Biologics Evaluation and Research (CBER)  
Office of Biostatistics and Pharmacovigilance (OBPV)  
Division of Pharmacovigilance (DPV)**

**PHARMACOVIGILANCE BLA RESUBMISSION MEMORANDUM**

**From:** Phillip Blanc, MD, MPH  
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**To:** Pankaj Mandal, PhD  
Chair of the Review Committee  
Office of Therapeutic Products

**Through:** Jaspal Ahluwalia, MD, MPH  
Branch Chief (Acting), PB3

Craig Zinderman, MD, MPH  
Associate Director for Medical Policy  
OBPV, CBER, FDA

**Subject:** Review of Pharmacovigilance Plan

**Sponsor:** Rocket Pharmaceuticals, Inc.

**Product:** KRESLADI (marnetegrage autotemcel)

**Application Type / Number** BLA / STN 125806/0

**Proposed Indication** *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).*<sup>1</sup>

**Resubmission Date:** September 26, 2025

**Action Due Date:** March 26, 2026

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<sup>1</sup> Except for Reviewer Comments, italicized text in this memorandum generally indicates language found in the Sponsor's source document. Sponsor-derived text noted in Reviewer Comments is indicated by bold italicized text.

## 1. Objective

This memo is written to review and assess key changes to the Sponsor's Pharmacovigilance Plan (PVP) (submitted to 125806/0.102), following the Sponsor's resubmission to its original Biologics License Application (BLA) (STN 125806/0) after FDA issued a Complete Response Letter (CRL) for the original BLA. For DPV's review of the Sponsor's PVP submitted prior to FDA's CRL (under STN 125806/0.65), please refer to DPV's review memorandum for STN 125806/0. Please see Appendix A for materials reviewed in support of this assessment.

## 2. Background and Overview of Key Changes to the Sponsor's Pharmacovigilance Plan

On August 1, 2023, the Sponsor submitted its original Biologics License Application (BLA) for KRESLADI (marnetegrane autotemcel) to STN 125806/0 *for the treatment of severe Leukocyte Adhesion Deficiency-I (LAD-I)*, which is a rare genetic condition characterized by inadequate expression of neutrophil CD18 due to mutations within the *ITGB2* gene. [1] Inadequate CD18 compromises antimicrobial function due, in part, to leukocytes' impaired adherence to affected endothelium. [1,2] Clinical sequelae include recurrent infections and impaired healing from wounds. [3]

As described in the Sponsor's draft label, *KRESLADI (marnetegrane autotemcel) is an autologous... gene therapy prepared from the patient's* [hematopoietic stem cells (HSCs)], representing an alternative to allogeneic HSC transplantation (HSCT). While allogeneic HSCT is a potentially definitive therapy for LAD-I [4], it comes with the challenges of non-autologous transplantation, including finding a suitable donor in a timely manner (e.g., before the patient experiences life-threatening illness), as well as potential direct and indirect risks (e.g., graft-versus-host disease [GvHD], infection, and chemotherapy toxicity). [4,5] Although autologously-derived marnetegrane autotemcel may not carry the same risks as non-autologous transplantation, the integrating retroviral vector-based treatment carries the potential serious risk of secondary malignancy due to replication-competent retrovirus or insertional mutagenesis. In accordance with FDA guidance [6], at least 15 years of safety follow-up, including collection of clinical samples and laboratory testing, would be indicated for patients receiving marnetegrane autotemcel. Given the CBER Biologics Effectiveness and Safety (BEST) Program was considered insufficient to characterize the serious risk of secondary malignancy, FDA required the Sponsor under the Food and Drug Administration Amendments Act (FDAAA) (Section 901, Title IX) to perform its proposed postmarketing safety registry study as a postmarketing requirement (PMR). On February 8, 2024, OBPV obtained concurrence from the CBER Safety Working Group and, on May 17, 2024, issued the PMR notification to the Sponsor. In its review memorandum for the original BLA, the Office of Therapeutic Products (OTP) clinical review team noted "substantial evidence of effectiveness and reasonable assurance of safety based on a single adequate and well-controlled investigation with confirmatory evidence." However, FDA issued the Sponsor a CRL on June 14, 2024, given Chemistry, Manufacturing, and Controls (CMC)-related issues (e.g., concerns over sterility testing, product shelf life).

On September 26, 2025, the Sponsor resubmitted to its BLA under STN 125806/0.82 with CMC-related materials and a slightly revised indication: *treatment of **pediatric patients with severe Leukocyte Adhesion Deficiency-I (LAD-I)*** (emphasis added). OBPV defers to the Office of Therapeutic Products (OTP) on the adequacy of resubmitted CMC data, as well as the final language for the indication statement, should the product be approved.

On October 17, 2025, FDA requested that the Sponsor confirm any changes to its PVP since the original BLA submission, to which the Sponsor confirmed in its response (submitted to STN 125806/0.84), that no additional changes had been made. At FDA's request, the Sponsor revised its protocol synopsis for its postmarketing requirement (PMR) registry study (*Registry-based study for Gene Therapy of Severe Leukocyte Adhesion Deficiency-I (LAD-I)*) under STN 125806/0.84 (version 0.5, dated October 22, 2025) and under STN 125806/0.93 (version 0.6, dated January 21, 2026), reflecting changes to study milestone dates (versions 0.5 and 0.6) and demonstration of clinical benefit added as a primary objective (version 0.6). The table below summarizes changes the Sponsor made to the PMR milestone dates in the original BLA and in the current resubmitted BLA.

**Table 1.** Proposed Milestone Dates for the Sponsor's Proposed Postmarketing Safety Registry Study (*Registry-based study for Gene Therapy of Severe Leukocyte Adhesion Deficiency-I (LAD-I)*)

	Original BLA STN 125806/0 (Pre-Complete Response)		Resubmitted BLA STN 125806/0.82 (Post-Complete Response)
	Protocol Synopsis, Version 0.2; Dated January 17, 2024	Electronic Mail Communication; Dated May 22, 2024	Protocol Synopsis, Version 0.6; Dated January 21, 2026
Final Protocol Submission	June 30, 2024	September 30, 2024	June 30, 2026
Study Completion (Safety PMR)	June 30, 2039	November 30, 2044*	June 30, 2047**

	Original BLA STN 125806/0 (Pre-Complete Response)		Resubmitted BLA STN 125806/0.82 (Post-Complete Response)
	Protocol Synopsis, Version 0.2; Dated January 17, 2024	Electronic Mail Communication; Dated May 22, 2024	Protocol Synopsis, Version 0.6; Dated January 21, 2026
Final Study Report	December 30, 2039	May 31, 2045	December 31, 2047

\*The revised study completion date for the safety component of the PMR accounts for approximately five years for patient accrual and at least 15 years for patient follow-up.

\*\*The study completion and report submission dates—June 30, 2047, and December 31, 2047, respectively—for the safety component of the PMR differ from dates proposed for the efficacy component (December 31, 2033 and June 30, 2034, respectively).

Although the Sponsor revised the protocol synopsis with the aforementioned changes, it did not include all changes in its PVP. To align the PVP with the protocol synopsis, FDA requested that the Sponsor update the PVP; in response, the Sponsor submitted its revised PVP (version 0.5, dated February 20, 2026 under STN 125806/0.102), reflecting relevant changes that were made to the protocol synopsis, including follow-up duration (e.g., revising *up to 15 years* to *at least 15 years* for the Sponsor’s proposed postmarketing safety studies) and revised PMR study milestone dates.

**Reviewer Comment:** *In addition to changes relevant to the registry study protocol synopsis, the Sponsor revised its PVP to include **Subsequent malignancies (including those related to insertional oncogenesis)** instead of **Insertional oncogenesis** as an Important Potential Risk. This change broadens the scope of potential malignancies that patients may experience following treatment with marnetegrane autotemcel. The Sponsor reflected this change in an updated protocol synopsis (version 0.7, dated February 20, 2026, submitted to STN 125806/0.102). At FDA’s request, the Sponsor further revised its PVP (updated to version 0.6, dated February 25, 2026, submitted to STN 125806/0.107) to state that it will conduct safety follow-up for participants enrolled in its prelicensure trial (Study RP-L201-0318) for “at least” 15 years (instead of “up to” 15 years) in its long-term follow-up study (RP-L201-0121-LTFU). DPV considers the above changes to the PVP acceptable.*

On February 12, 2026, the CBER Safety Working Group (SWG) granted concurrence to require the Sponsor to conduct its proposed postmarketing registry as a PMR, accepting the proposed revised milestone dates as summarized in Table 1. On February 18, 2026, FDA issued the Sponsor a PMR notification for the postmarketing safety registry study.

### 3. DPV Assessment and Recommendations

Generally, due to factors such as sample size, assessment of the of the Sponsor's Phase I/II clinical trial safety data submitted with the Sponsor's original BLA was limited. To elucidate if a favorable benefit-risk profile remains over a long-term period (e.g., 15 years after treatment with marnetegrane autotemcel), further safety monitoring is indicated. OBPV and CBER SWG have concurred on a postmarketing registry study described in the Sponsor's PVP (version 0.6, submitted to STN 125806/0.107) to be conducted as an FDAAA Title IX PMR to evaluate safety concerning the serious risk of secondary malignancy due to replication-competent retrovirus or insertional mutagenesis. Should marnetegrane autotemcel be approved, conducting the proposed postmarketing registry study as a PMR, in addition to performing routine and enhanced pharmacovigilance, is warranted. The Sponsor's revised PVP (version 0.6, submitted to STN 125806/0.107) is acceptable.

## APPENDIX A

### Materials Reviewed

**Table A1:** Materials Reviewed in Support of this Assessment

Date	Source	Document Information	Document(s) Reviewed
8/1/2023	Rocket Pharmaceuticals	STN 125806/0.0	Module 1.2, Cover Letter
1/19/2024	Rocket Pharmaceuticals	STN 125806/0.31	Module 5.3.5.2, Protocol Synopsis (Postmarketing Registry Study, v0.2)
5/14/2024	Rocket Pharmaceuticals	STN 125806/0.65	Module 1.16.1, Pharmacovigilance Plan (PVP), v0.4 Module 5.3.5.2, Protocol Synopsis (Postmarketing Registry Study, v0.4)

Date	Source	Document Information	Document(s) Reviewed
5/22/2024	Rocket Pharmaceuticals	Electronic Mail Communication	Postmarketing Requirement (PMR) Acknowledgement with Revised Study Milestone Dates
9/26/2025	Rocket Pharmaceuticals	STN 125806/0.82	Module 1.2, Cover Letter
10/24/2025	Rocket Pharmaceuticals	STN 125806/0.84	Module 1.11.3, Clinical Information Amendment, Information Request Response (Revised Study Milestone Dates)  Module 5.3.6, Protocol Synopsis (Postmarketing Registry Study, v0.5)
1/22/2026	Rocket Pharmaceuticals	STN 125806/0.93	Module 1.11.3, Protocol Synopsis (Postmarketing Registry Study, v0.6)
2/23/2026	Rocket Pharmaceuticals	STN 125806/0.102	Module 1.2, Cover Letter  Module 1.11.3, Clinical Information Amendment, Information Request Response (Commitment to Postmarketing Requirement [PMR], Revised Pharmacovigilance Plan [PVP] and Postmarketing Registry Study Protocol Synopsis)  Module 1.16.1, Pharmacovigilance Plan (PVP), v0.5  Module 5.3.6, Protocol Synopsis (Postmarketing Registry Study, v0.7; Postmarketing Registry Study v0.6 [Tracked Changes])
2/26/2026	Rocket Pharmaceuticals	STN 125806/0.107	Module 1.11.3, Clinical Information Amendment, Information Request Response (Revised Pharmacovigilance Plan [PVP])  Module 1.16.1, Pharmacovigilance Plan (PVP), v0.6

Date	Source	Document Information	Document(s) Reviewed
5/31/2024	FDA	STN 125806/0	Postmarketing Requirement (PMR) Notification
6/13/2024	FDA	STN 125806/0	Biologics License Application (BLA) Clinical Review Memorandum
6/14/2024	FDA	STN 125806/0	Complete Response Letter
6/28/2024	FDA	STN 125806/0	Pharmacovigilance Original Biologics License Application (BLA) Memorandum

## REFERENCES

<sup>1</sup> Novoa EA, Kasbekar S, Thrasher AJ, Kohn DB, Sevilla J, Nguyen T, et al. Leukocyte adhesion deficiency-I: a comprehensive review of all published cases. *J Allergy Clin Immunol Pract.* 2018;6(4):1418-20.

<sup>2</sup> Etzioni A. Leukocyte-adhesion deficiency [Internet]. In: Notarangelo LD, Feldweg AM, editors. UpToDate [cited 2026 Feb 26]. Available from: [https://www.uptodate.com/contents/leukocyte-adhesion-deficiency?search=leukocyte%20adhesion%20deficiency&source=search\\_result&selectedTitle=1%7E24&usage\\_type=default&display\\_rank=1](https://www.uptodate.com/contents/leukocyte-adhesion-deficiency?search=leukocyte%20adhesion%20deficiency&source=search_result&selectedTitle=1%7E24&usage_type=default&display_rank=1)

<sup>3</sup> Hanna S, Etzioni A. Leukocyte adhesion deficiencies. *Ann N Y Acad Sci.* 2012;1250:50-55. doi:10.1111/j.1749-6632.2011.06389.x

<sup>4</sup> Qasim W, Cavazzana-Calvo M, Davies EG, Slatter M, et al. Allogeneic hematopoietic stem-cell transplantation for leukocyte adhesion deficiency. *Pediatrics.* 2009;123(3):836-40. Correction published 2009;123(5):1436. doi:10.1542/peds.2008-1191

<sup>5</sup> Acevedo MJ, Wilder JS, Adams S, et al. Outcomes of related and unrelated donor searches among patients with primary immunodeficiency diseases referred for allogeneic hematopoietic cell transplantation. *Biol Blood Marrow Transplant.* 2019;25(8):1666-73. doi:10.1016/j.bbmt.2019.04.008

<sup>6</sup> U.S. Food and Drug Administration, Center for Biologics Evaluation and Research. Long term follow-up after administration of human gene therapy products [Internet]. FDA; 2020 [cited 2026 Feb 26]. Available from: <https://www.fda.gov/media/113768/download>