BLA 761183/S-013

SUPPLEMENT APPROVAL
RELEASE FROM POSTMARKETING REQUIREMENT

Provention Bio, Inc.
Attention: Gargi Lakhwani
Regulatory Strategist - Associate Director, Global Regulatory Affairs
100 Morris Street
Morristown, NJ 07960

Dear Gargi Lakhwani:

Please refer to your supplemental biologics license application (sBLA) received October 29, 2025, and your amendments, submitted under section 351(a) of the Public Health Service Act for Tzield (teplizumab-mzwv) injection.

This Prior Approval sBLA provides for updates to the Prescribing Information and Medication Guide based on data from Part A of trial PRV-031-005/SFY18116 entitled, *Single Arm, Open-label Study to Assess the Safety and Pharmacokinetics of a 14-day Regimen of Teplizumab in Pediatric Stage 2 Diabetes (Participants With at Least Two Autoantibodies and Dysglycemia),* including expansion of the indication to delay the onset of Stage 3 type 1 diabetes (T1D) to pediatric patients between 1 to 8 years of age with Stage 2 T1D.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your supplement application, you are exempt from this requirement.

RELEASE FROM POSTMARKETING REQUIREMENT

We refer to following postmarketing requirement listed in our November 17, 2022, approval letter:

4359-1 Conduct a 12-month single-arm, open-label study to assess the safety and pharmacokinetics (PK) of teplizumab-mzwv in pediatric patients 0 to less than 8 years of age with two type-1 diabetes (T1D)-related autoantibodies and dysglycemia (Stage 2 T1D) [Part A], followed by a 12-month open-label extension [Part B].

Draft Protocol (Part A and Part B) Submission:	November 2022
Final Protocol (Part A and Part B) Submission:	May 2023
Interim Report Submission (Part A data):	April 2026
Study Completion (Part B):	October 2026
Final Report Submission (Parts A and B):	April 2027

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

We have determined that you are released from the above postmarketing requirement because the original approved indication for Tzield is within the scope of the orphan-drug designation (ODD) for the treatment of recent-onset T1D, which includes the distinction of Stage 2 T1D. As such, the original approval action was exempt from PREA requirements, and PMR 4359-1 should not have been issued under PREA.

We remind you that there are postmarketing requirements and postmarketing commitments listed in the November 17, 2022, approval letter that are still open.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the signal of a serious risk of Epstein-Barr Virus-associated lymphoproliferative disorders or to identify an unexpected serious risk of other potential malignancies due to immunosuppression.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess the signal of a serious risk of Epstein-Barr Virus-associated lymphoproliferative disorders or to identify an unexpected serious risk of other potential malignancies due to immunosuppression.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following trial:

4359-9 Complete the 12-month single-arm, open-label extension study PRV-031-005/SFY18116 to assess the long-term safety of teplizumab-mzwv in pediatric patients 0 to less than 8 years of age with at least two type-1 diabetes (T1D)-related autoantibodies and dysglycemia (Stage 2 T1D).

The timetable you submitted on April 6, 2026, states that you will conduct this trial according to the following schedule:

Study Completion:	October 2026
Final Report Submission:	April 2027

Submit clinical protocol(s) to your IND 102629 with a cross-reference letter to this BLA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your BLA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **REQUIRED POSTMARKETING PROTOCOL UNDER 505(o), REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o), REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o).**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as 21 CFR 601.70 requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 601.70. We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 601.12(f)(4)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety-related information [21 CFR 601.12(f)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(f)(4).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, contact Supendeep Dosanjh, Regulatory Project Manager, at Supendeep.Dosanjh@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Lisa Yanoff, M.D.
Deputy Director
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LISA B YANOFF
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