BLA 761460

BLA APPROVAL

AbbVie Inc.
Attention: Xiaoran Xu
Senior Manager, Regulatory Affairs
1000 Gateway Boulevard
South San Francisco, CA 94080

Dear Xiaoran Xu:

Please refer to your biologics license application (BLA) received September 29, 2025, and your amendments, submitted under section 351(a) of the Public Health Service Act for DECNUPAZ (pivekimab sunirine-pvzy) for injection, for intravenous use.

LICENSING

We have approved your BLA for DECNUPAZ (pivekimab sunirine-pvzy) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, DECNUPAZ under your existing Department of Health and Human Services U.S. License No.1889. DECNUPAZ is indicated for the treatment of adult patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN).

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture pivekimab antibody drug substance (b) (4), (b) (4) and pivekimab sunirine-pvzy drug substance and drug product at (b) (4) (b) (4) The final formulated drug product will be labeled and packaged at AbbVie Inc. (FEI: 3009751352) in North Chicago, Illinois, US. You may label your product with the proprietary name, DECNUPAZ, and market it as a 2 mg of lyophilized powder in a single-dose vial.

DATING PERIOD

The dating period for DECNUPAZ shall be 24 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) C. The dating period for your pivekimab antibody drug substance (b) (4) shall be (b) (4) months from the date of manufacture when stored at (b) (4) C.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of DECNUPAZ to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of DECNUPAZ, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide). 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 (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton labeling submitted on March 27, 2026, and container labeling submitted on March 13, 2026, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761460**." Approval of this submission by FDA is not required before the labeling is used.

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

ADVISORY COMMITTEE

Your application for DECNUPAZ was not referred to an FDA advisory committee because outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

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.

We are waiving the pediatric study requirement for less than 6 months of age because necessary studies are impossible or highly impracticable. This is because BPDCN is extremely rare in this age group.

We are deferring submission of your pediatric study for ages 6 months to <17 years of age for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

4996-1 Conduct a molecularly targeted pediatric cancer investigation using age-appropriate pediatric formulations to evaluate dosing, pharmacokinetics, safety, and preliminary efficacy of pivekimab sunirine monotherapy in pediatric patients ≥6 months to <17 years of age with relapsed/refractory CD123-positive acute myeloid leukemia.

Final Protocol Submission:	06/2026
Study Completion:	09/2029
Final Report Submission:	03/2030

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial. See guidance for industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act.*

Submit the protocol to your IND 130889, with a cross-reference letter to this BLA.

Reports of this required pediatric postmarketing study must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from this study. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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 a known serious risk of post-hematopoietic stem cell transplant non-relapse mortality and hepatotoxicity including veno-occlusive disease of the liver.

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.

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

4996-2 Conduct an integrated analysis to characterize serious toxicity after hematopoietic stem cell transplantation in adult and pediatric patients who receive pivekimab sunirine using data from a HSCT transplant registry and ongoing or completed studies to evaluate safety at least through day 180 after transplantation, including known serious risks of hepatic veno-occlusive disease, transplant related mortality (non-relapse mortality), and non-transplant related mortality. The number of patients available in the database and clinical trials will determine the sample size. Include details of all prior malignancy directed therapies and pivekimab sunirine dosing. The minimum duration of the study is to be no less than five years.

The timetable you submitted on May 12, 2026, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	05/2027
Final Protocol Submission:	11/2027
Interim Report Submission:	12/2031
Study Completion:	02/2035
Final Report Submission:	08/2035

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess a known serious risk of infusion related reactions, capillary leak syndrome, and serious hepatotoxicity, including veno-occlusive disease of the liver; to assess a signal of a serious risk of increased severe adverse reactions in patients with moderate renal impairment and with administration of strong and moderate CYP3A inhibitors; and to identify an unexpected serious risk of QTc prolongation.

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

4996-3 Conduct a clinical trial to assess and further characterize the known and potential serious risks related to the use of pivekimab sunirine, including whether long-term use of pivekimab sunirine is associated with an increased risk of serious infusion related reactions, capillary leak syndrome, and serious hepatotoxicity, including veno-occlusive disease of the liver. Summarize the safety outcomes when all patients have completed at least five years of treatment with pivekimab sunirine or withdrew earlier.

The timetable you submitted on May 12, 2026, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission: 11/2026
Final Protocol Submission: 05/2027
Trial Completion: 08/2032
Final Report Submission: 02/2033

4996-4 Conduct an integrated analysis of ongoing and completed trials across the pivekimab sunirine development program to further characterize the known serious risk of pivekimab sunirine-related capillary leak syndrome (CLS), including incidence, appropriate diagnostic criteria, and effective treatment based on patient-level data and pooled analyses.

The timetable you submitted on May 12, 2026, states that you will conduct this trial according to the following schedule:

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Draft Protocol Submission (Analysis Plan):	05/2027
Final Protocol Submission (Analysis Plan):	11/2027
Trial Completion:	08/2032
Final Report Submission:	02/2033

4996-5 Conduct a clinical pharmacokinetic trial to evaluate the serious potential risk of increased severe adverse reactions in patients with moderate renal impairment receiving pivekimab sunirine. Assess the PK, serious adverse events, Grade 3/4 adverse events, and adverse events leading to dose modifications in patients with moderate renal impairment, as estimated by the Cockcroft-Gault equation. Develop and validate a more sensitive and reliable bioanalytical method for the ADC to adequately characterize the impact of moderate renal impairment on the PK of pivekimab sunirine (ADC). Implement adequate PK sampling procedures to allow for accurate PK analysis for the ADC and free payload. Design and conduct the study in accordance with the FDA Guidance for Industry entitled, "Pharmacokinetics in Patients with Impaired Renal Function — Study Design, Data Analysis, and Impact on Dosing."

The timetable you submitted on May 12, 2026, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	11/2026
Final Protocol Submission:	05/2027
Trial Completion:	08/2032
Final Report Submission:	02/2033

4996-6 Conduct a clinical pharmacokinetic trial to evaluate the serious potential risk of increased severe adverse reactions, Grade 3/4 adverse reactions, and adverse reactions leading to dose modifications, in patients on concomitant strong CYP3A inhibitors. Evaluate the potential impact of concomitant moderate CYP3A inhibitors on the pharmacokinetics of pivekimab sunirine and its free payload using a physiologically based pharmacokinetic (PBPK) modeling approach. Conduct further evaluation of moderate CYP3A inhibitors in a clinical trial if the PBPK results are insufficient to determine impact of moderate CYP3A inhibitors on PK of pivekimab sunirine and its free payload. Submit an interim report that includes the PK results and the PBPK report. Develop and validate a more sensitive and reliable bioanalytical method for the ADC to adequately characterize the impact of concomitant strong CYP3A inhibitors on the PK of pivekimab sunirine. Implement adequate PK sampling procedures to allow for accurate PK analysis for the ADC and free payload. Design and

conduct the study in accordance with the M12 Drug Interactions Studies Guidance.

The timetable you submitted on May 12, 2026, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission: 11/2026
Final Protocol Submission: 05/2027
Interim Report Submission:02/2031
Trial Completion: 08/2032
Final Report Submission: 02/2033

4996-7 Conduct a clinical trial to evaluate for serious QTc prolongation with FGN849 at the maximum approved dosing regimen of pivekimab sunirine as outlined in ICH E14 Q&A (R3) 6.1.

The timetable you submitted on May 12, 2026, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission: 05/2027
Final Protocol Submission: 11/2027
Trial Completion: 11/2030
Final Report Submission: 05/2031

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[4]

Submit clinical protocol(s) to your IND 130889 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.

[4] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4996-8 To perform a hold time study using a surrogate solution suitable to promote growth in relevant in-process containers in the actual production environment to simulate production conditions with a study design of N=3 for the number of experiments at (b) (4)

The timetable you submitted on February 13, 2026, states that you will conduct this study according to the following schedule:

Final report submission: 12/2028

4996-9 To implement the use of (b) (4)

The timetable you submitted on February 13, 2026, states that you will conduct this study according to the following schedule:

Final report submission: 12/2028

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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*.[5]

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.[6] Information and Instructions for completing the form can be found at FDA.gov.[7]

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements at 21 CFR 600.81.

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

[5] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[7] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, contact Sheila Ryan, PharmD, MPH, RAC, Senior Regulatory Health Project Manager, at (301) 796-2002 or sheila.ryan@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

R. Angelo de Claro, MD
Director
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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/

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