CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761258Orig1s000

Trade Name:	**PENPULIMAB-KCQX injection, for intravenous use**
Generic or Proper Name:	
Sponsor:	**Akeso Biopharma Co., Ltd**
Approval Date:	**April 23, 2025**
Indication:	Penpulimab-kcqx is a programmed death receptor-1 (PD-1)-blocking antibody indicated: • in combination with either cisplatin or carboplatin and gemcitabine for the first-line treatment of adults with recurrent or metastatic non-keratinizing nasopharyngeal carcinoma (NPC) • as a single agent for the treatment of adults with metastatic non-keratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.

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APPROVAL LETTER

BLA 761258

CORRECTED BLA APPROVAL

Akeso Biopharma Co., Ltd.
c/o Akesobio, Inc.
Attention: Liang Liu, U.S. Agent
81 Belhaven Avenue
Daly City, CA 94015

Dear Liang Liu:

Please refer to your biologics license application (BLA) received July 16, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for penpulimab-kcqx injection for intravenous use.

We also refer to our approval letter dated April 23, 2025, which contained the following error: line numbers appeared in the Highlights section of the United States Prescribing Information labeling.

This corrected action letter incorporates the correction of the error. The effective action date will remain April 23, 2025, the date of the original letter.

We acknowledge receipt of your resubmission dated October 2, 2024, which constituted a complete response to our January 19, 2024, action letter.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2253 to Akeso Biopharma Co., Ltd., Zhongshan, Guangdong, China, under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product penpulimab-kcqx. Penpulimab-kcqx is indicated:

- in combination with either cisplatin or carboplatin and gemcitabine, for the first-line treatment of adults with recurrent or metastatic non-keratinizing nasopharyngeal carcinoma (NPC)
- as a single agent, for the treatment of adults with metastatic non-keratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture penpulimab-kcqx drug substance and drug product at Akeso Biopharma Co., Ltd., Zhongshan, Guangdong, China (FEI: 3017057933). You may label your product with the proper name, penpulimab-kcqx, and market it as a 100 mg/10 mL solution in a single dose vial.

DATING PERIOD

The dating period for penpulimab-kcqx shall be 36 months from the date of manufacture when stored at 5°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)

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of penpulimab-kcqx 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 penpulimab-kcqx, 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

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

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

We acknowledge your April 23, 2025, submission containing final printed carton and container labeling.

ADVISORY COMMITTEE

Your application for penpulimab-kcqx was not referred to an FDA advisory committee because evaluation of the safety data when used in the treatment of adults with recurrent or metastatic non-keratinizing nasopharyngeal carcinoma (NPC) in combination with either cisplatin or carboplatin and gemcitabine for first-line treatment and as a single agent for the treatment of adults with metastatic non-keratinizing NPC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy did not raise significant safety or efficacy issues that were unexpected for a biologic of this class.

PROPRIETARY NAME

If you intend to have a proprietary name for this product, the name and its use in the labeling must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry *Contents of a Complete Submission for the Evaluation of Proprietary Names* and *PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 through 2027*.)

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 this application because the product fails to represent a meaningful therapeutic benefit over existing therapies for pediatric

[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.

patients and is unlikely to be used in a substantial number of pediatric patients across all age groups.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4815-1 Complete the ongoing clinical trial AK105-304 (NCT04974398) titled "A Randomized, Double-blind, Multi-center Phase III Study of Penpulimab (AK105) combined with Chemotherapy versus Placebo Combined with Chemotherapy as First-Line Treatment for Recurrent or Metastatic Nasopharyngeal Carcinoma," to obtain mature overall survival (OS) data in accordance with the pre-specified statistical analysis plan to formally test OS at 80% information fraction and at the final OS analysis when 172 OS events are observed.

The timetable you submitted on March 25, 2025, states that you will conduct this study according to the following schedule:

Trial Completion:	05/2026
Final Report Submission:	10/2026

4815-2 Conduct a clinical trial enrolling an adequate number of patients in the United States (U.S.), that includes a sufficient representation of patients in demographic subgroups that are reflective of the U.S. patient population with nasopharyngeal carcinoma (NPC), to further characterize the efficacy and safety of penpulimab in combination with gemcitabine and either cisplatin or carboplatin in these patients. Conduct sparse sampling for supportive population pharmacokinetic and Exposure-Response (E-R) analyses. The E-R analyses may be used as supportive evidence for the efficacy and safety in the intended patient population. In the E-R analyses report, include an analysis of the presence and clinical impact of the neutralizing anti-drug antibodies on pharmacokinetics, efficacy, and safety of penpulimab.

The timetable you submitted on March 25, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	04/2025
Final Protocol Submission:	08/2025
Trial Completion:	06/2029
Final Report Submission:	12/2029

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

We remind you of your postmarketing commitments:

4815-3 Develop, validate, and implement an alternative biological activity assay for an improved control of potency for penpulimab-kcqx drug substance and drug product lot release and stability testing. Submit the analytical procedure, method validation report, proposed acceptance criterion, and justification for the proposed acceptance criterion, to support the implementation of alternative potency assay in a PAS to the BLA.

The timetable you submitted on March 28, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 09/2025

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 138576 for this product. 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*.[3]

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

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

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]

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

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.

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

If you have any questions, contact Ashley Lane, Senior Regulatory Health Project Manager, at Ashley.Lane@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, MD
Director
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

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/

RICHARD PAZDUR
04/29/2025 12:22:57 PM