BLA 761240

BLA APPROVAL

Coherus BioSciences, Inc.
Attention: Nathalie Vandenkoornhuyse-Yanze, Ph.D.
Senior Vice President, Regulatory Affairs
333 Twin Dolphin Drive, Suite 600
Redwood City, CA 94065

Dear Dr. Vandenkoornhuyse-Yanze:

Please refer to your biologics license application (BLA) dated August 31, 2021, received August 31, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for Loqtorzi (toripalimab-tpzi) injection.

We acknowledge receipt of your resubmission dated June 23, 2022, which constituted a complete response to our April 29, 2022, action letter.

This BLA provides for the following indications for Loqtorzi (toripalimab-tpzi):

Loqtorzi, in combination with cisplatin and gemcitabine, for first-line treatment of adults with metastatic or with recurrent, locally advanced nasopharyngeal carcinoma (NPC); and

Loqtorzi, as a single agent, for the treatment of adults with recurrent unresectable or metastatic NPC with disease progression on or after a platinum-containing chemotherapy.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2023 to Coherus BioSciences, Inc., Redwood City, CA, 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 approved to manufacture toripalimab-tpzi at (b) (4) You may label your product with the proprietary name, Loqtorzi, and market it in 240 mg/6 mL single-dose vial, injection, for intravenous use.

DATING PERIOD

The dating period for Loqtorzi shall be 36 months from the date of manufacture when stored at 5 ± 3°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.

Results of ongoing stability should be submitted throughout the dating period, as they become available, including the results of stability studies from the first three production lots.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Loqtorzi 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 Loqtorzi, 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.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on November 17, 2022 (container) and December 21, 2022 (carton), 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 *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761240**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for toripalimab-tpzi was not referred to an FDA advisory committee because this biologic is not the first in its class; the clinical trial design is acceptable; the application did not raise significant safety or efficacy issues; and the application did not raise significant public health questions on the role of the biologic in the diagnosis, cure, mitigation, treatment, or prevention of a disease.

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 necessary studies are impossible or highly impracticable, since nasopharyngeal cancer (NPC) is rare in the pediatric population and the conduct of a clinical study of toripalimab-tpzi in pediatric NPC is not feasible.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

[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.

4471-1 Conduct a clinical trial enrolling a total sample size of 100 patients in the United States (U.S.) and Canada, that includes a sufficient representation of patients in racial and ethnic minority subgroups and is reflective of the U.S. population of patients with nasopharyngeal carcinoma (NPC), to further characterize the safety and efficacy of toripalimab in combination with cisplatin and gemcitabine in these patients. Include a sufficient number of patients with the keratinizing subtype reflecting the incidence of keratinizing NPC in the U.S. population. 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 toripalimab.

The timetable you submitted on July 14, 2023, states that you will conduct this study according to the following schedule:

Trial Completion:	12/2027
Final Report Submission:	06/2028

Submit the datasets with the final study report submission.

4471-2 Conduct an assessment to determine the presence of neutralizing anti-drug antibodies against toripalimab in all patient samples that tested positive for binding anti-drug antibodies in all completed studies with unexpired immunogenicity samples, as well as all ongoing and planned studies by using a validated neutralizing anti-drug antibody assay. Evaluate the potential clinical impact of the neutralizing anti-drug antibodies on pharmacokinetics, efficacy and safety of toripalimab in a final report.

The timetable you submitted on July 14, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission:	12/2023

Submit the datasets with the final study report submission.

Submit clinical protocols to your IND 162563 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 314.81(b)(3)(i)]. 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

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] 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 Raniya Ali Al-Matari, Ph.D., Regulatory Health Project Manager at Raniya.Al-Matari@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Paul Kluetz, M.D.
Deputy Director
Oncology Center of Excellence
Supervisory Associate Director (acting)
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- 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/

PAUL G KLUETZ
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