BLA 761394

BLA APPROVAL

Daiichi Sankyo, Inc.
Attention: Pranav J. Patel, PharmD
Associate Director, Regulatory Affairs
211 Mt. Airy Road
Basking Ridge, NJ 07920

Dear Dr. Patel:

Please refer to your biologics license application (BLA) dated January 29, 2024, received January 29, 2024, and your amendments, submitted under section 351(a) of the Public Health Service Act for DATROWAY (datopotamab deruxtecan-dlnk) lyophilized powder for intravenous infusion.

LICENSING

We have approved your BLA for DATROWAY (datopotamab deruxtecan-dlnk) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, DATROWAY under your existing Department of Health and Human Services U.S. License No. 2128. DATROWAY is indicated for treatment of adults patients with unresectable or metastatic, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture datopotamab drug substance intermediate at (b) (4) and datopotamab deruxtecan-dlnk drug substance at Daiichi Sankyo Chemical Pharma Co., Ltd., Onahama Plant, in Fukushima, Japan. The final formulated drug product will be manufactured and filled at (b) (4), and labeled and packaged at Daiichi Sankyo Europe GmbH in Pfaffenhofen, Germany, (b) (4) You may label your product with the proprietary name, DATROWAY, and market it in 100 mg lyophilized powder in single-dose vials for reconstitution and further dilution for intravenous infusion.

DATING PERIOD

The dating period for DATROWAY shall be 36 months from the date of manufacture when stored at 5°C ± 3°C, protected from light. 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 datopotamab drug substance intermediate shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating 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 DATROWAY 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 DATROWAY, 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 enclosed carton and container labeling as soon as they are available [e.g., changes consistent with annual reportable changes under 21 CFR 6101.12(d)], 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 761394**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for DATROWAY was not referred to an FDA advisory committee because outside expertise was not necessary; and 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 studies requirement for this application because necessary studies are impossible or highly impracticable as breast cancer is rare in the pediatric population.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4776-1 Conduct an integrated analysis of data from clinical trials and observational studies (e.g., real world evidence), post-marketing reports, and other sources to further characterize the safety and

[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.

efficacy/effectiveness of datopotamab deruxtecan in patients of underrepresented racial and ethnic minority groups with unresectable or metastatic HR+HER2- breast cancer (especially Black patients given their underrepresentation in the TROPION-Breast01 trial). The analyses should support an evaluation of comparative efficacy/effectiveness and safety between the population primarily represented in the trial (TROPION-Breast01) and the aforementioned underrepresented racial and ethnic minority population(s). This should also include pharmacokinetic data, if available.

The timetable you submitted on December 19, 2024, states that you will conduct this study according to the following schedule:

Draft Protocol Submission (Analysis Plan):	03/2026
Final Protocol Submission (Analysis Plan):	09/2026
Study Completion:	01/2030
Final Report Submission:	07/2030

4776-2 Complete [redacted] (b) (4) anti-drug antibody (ADA) assay validation and include report addendums containing high resolution drug tolerance data and justification to support that the ADA assays are fit-for-purpose to characterize the effects of ADA on pharmacokinetics, pharmacodynamics, safety, and effectiveness of datopotamab deruxtecan.

The timetable you submitted on December 19, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/2025

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 155696 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

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

[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

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 Dana Kappel, Regulatory Project Manager, at (301) 796-8768 or at Dana.Kappel@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Paul G. Kluetz, MD
Supervisory Associate Director (Acting)
Office of Oncologic Diseases
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/

PAUL G KLUETZ
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