BLA 761228

BLA APPROVAL

Immunocore Limited
Attention: Sheetal Thakur, Ph.D.
Associate Director, Regulatory Affairs, Immunocore LLC
Six Tower Bridge
181 Washington Street
Conshohocken, PA 19428-2068

Dear Dr. Thakur:

Please refer to your biologics license application (BLA) received June 23, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for KIMMTRAK (tebentafusp-tebn) injection.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2239 to Immunocore Limited, 92 Park Drive, Milton Park, Abingdon, Oxfordshire, United Kingdom, OX144RY, 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 KIMMTRAK (tebentafusp-tebn). KIMMTRAK (tebentafusp-tebn) is indicated for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture tebentafusp-tebn drug substance at AGC Biologics A/S in Soeborg, Copenhagen, Denmark. The final formulated drug product will be manufactured, filled, labeled, and packaged at Baxter Oncology GmbH, Halle/Westfalen, Germany. You may label your product with the proprietary name, KIMMTRAK, and market it in 100 mcg/0.5 mL solution for injection single-dose vials.

DATING PERIOD

The dating period for KIMMTRAK shall be 18 months from the date of manufacture when stored at 2°C - 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).

FDA LOT RELEASE

You are not currently required to submit samples of future lots of KIMMTRAK 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 KIMMTRAK, 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 Patient Information). 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 enclosed carton and container labeling and carton and container labeling submitted on December 1, 2021, 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*

[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.

Specifications. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761228.** Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for tebentafusp-tebn was not referred to an FDA advisory committee because

(1) the application did not raise significant safety or efficacy issues that were unexpected for a biologic of this class or in the intended population, and

(2) 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 this application because the necessary studies are impossible or highly impracticable as uveal melanoma is rare in pediatric populations and the molecular target gp100 is not known to be relevant for growth or progression of pediatric cancers.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4180-1 Conduct an assay validation study to demonstrate that the assay can accurately differentiate HLA-A*02:01 from other HLA A alleles for identification of patients with uveal melanoma who may benefit from treatment with Kimmtrak (tebentafusp-tebn) and use the data to support an FDA approved companion diagnostic HLA typing assay patient selection test.

The timetable you submitted on December 3, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/2022

4180-2 Conduct an assessment to determine the presence of neutralizing anti-drug antibodies against Kimmtrak (tebentafusp-tebn) in all patient samples that tested positive for binding anti-drug antibodies in studies IMCgp100-202 and IMCgp100-102 by using the validated neutralizing anti-drug antibody assay. Include an assessment of the clinical impact of the neutralizing anti-drug antibodies on pharmacokinetics, efficacy and safety of Kimmtrak (tebentafusp-tebn) in the study report.

The timetable you submitted on December 3, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 02/2022

Provide the datasets and analyses in the final study report.

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

We remind you of your postmarketing commitments:

4180-3 Monitor [redacted] (b) (4) the next three commercial batches of tebentafusp drug substance [redacted] (b) (4) cultures and submit the finalized report after evaluation of these results, along with potential updates of the control strategy [redacted] (b) (4) to FDA.

The timetable you submitted on November 3, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/2024

4180-4 Develop methods for extraction and quantitation of extractables/ leachables from the primary container closure system (CCS) in the presence of tebentafusp drug substance. Once methods have been developed and validated, incorporate the methods into the long-term stability study program [redacted] (b) (4) for monitoring of the level of extractables/ leachables in the process performance qualification (PPQ) batches over the duration of shelf-life. Submit the study results to FDA as part of the annual update.

The timetable you submitted on November 3, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 02/2023

4180-5 Implement [redacted] monitoring [redacted] of tebentafusp-tebn drug product and update Sections 3.2.P.3.3 and 3.2.P.3.4 of the BLA with [redacted] as a Critical Process Parameter.

The timetable you submitted on November 10, 2021, states that you will conduct this study according to the following schedule:

Implementation date: 06/2022

Submit clinical protocols to your IND 114314 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 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 for licensed biological products (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 for licensed biological products (21 CFR 600.81).

[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

---

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/

MARC R THEORET
01/25/2022 07:31:55 PM