BLA 761336

BLA APPROVAL

Altor BioScience, LLC, an indirect wholly-owned subsidiary of ImmunityBio, Inc.
c/o: Margaret Hurley, MD, FRAPS
Hurley Consulting Associates Ltd.
25 DeForest Avenue, Suite 202
Summit, NJ 07901

Dear Dr. Hurley:

Please refer to your biologics license application (BLA) dated May 23, 2022, received May 23, 2022, and your amendments, submitted under section 351(a) of the Public Health Service Act for Anktiva (nogapendekin alfa inbakicept-pmln) solution.

We acknowledge receipt of your resubmission dated October 23, 2023, which constituted a complete response to our May 9, 2023, action letter.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2302 to Altor BioScience, LLC, an indirect wholly-owned subsidiary of ImmunityBio, Inc., Culver City, California 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 Anktiva (nogapendekin alfa inbakicept-pmln). Anktiva is indicated with Bacillus Calmette-Guérin (BCG) for the treatment of adult patients with BCG-unresponsive nonmuscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture nogapendekin alfa inbakicept-pmln drug substance at (b) (4). The final formulated drug product will be manufactured and filled at (b) (4) and labeled and packaged at (b) (4). You may label your product with the proprietary name, Anktiva, and market it in 400 µg/0.4 mL (1 mg/mL) injection.

DATING PERIOD

The dating period for Anktiva shall be 24 months from the date of manufacture when stored at 2 to 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.

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.

Any changes in the manufacturing, testing, packaging, or labeling of Anktiva, 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). 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 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 761336**." Approval of this submission by the 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 Anktiva 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 this application because necessary studies are impossible or highly impracticable due to the rarity of pediatric bladder cancer.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

4417-1 Complete clinical trial "QUILT-3.032: A Multicenter Clinical Trial of Intravesical Bacillus Calmette-Guerin (BCG) in Combination With ALT-803 (N-803) in Patients With BCG Unresponsive High Grade Non-Muscle Invasive Bladder Cancer," and provide annual updates on enrollment, complete response rate, and duration of response for all patients enrolled in Cohort 1 (non-muscle invasive bladder cancer [NMIBC] carcinoma in situ [CIS]). Annual reports should continue until all patients have either experienced recurrence of high-grade non-muscle invasive bladder cancer, progression, death, or been lost to follow-up, for up to 4 years.

The timetable you submitted on February 5, 2024, states that you will conduct this study according to the following schedule:

Interim Report Submission #1:	05/2025
Interim Report Submission #2:	05/2026
Interim Report Submission #3:	05/2027
Interim Report Submission #4:	05/2028
Trial Completion:	05/2029
Final Report Submission:	12/2029

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

We remind you of your postmarketing commitments:

4417-2 Implement a two-tier reference material system with a working reference material consistent with principles described in *ICHQ6B, Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products*. Provide the qualification report(s) and requalification protocol for the working reference materials to the BLA.

The timetable you submitted on April 16, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission (Qualification Report and Requalification Protocol): 03/2025

4417-3 Continue to optimize the reduced CE-SDS method to improve precision and repeatability. Provide a final study report to the BLA which includes any updates to the analytical procedure and supplemental assay validation data to support any modifications.

The timetable you submitted on April 16, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 09/2025

4417-4 Continue to optimize the CTLL-2 bioassay method to improve precision. Include in your studies adjustments to the parallelism criteria, as appropriate. Provide a final study report to the BLA which includes any updates to the analytical procedure and supplemental assay validation data to support any modifications.

The timetable you submitted on April 16, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/2025

4417-5 Continue studies to re-validate the ADA and NAb immunogenicity assays using a more suitable positive control, such as an anti-N-803 affinity purified antibody. To support the use of this positive control, validation data should be provided to demonstrate that the positive control can sufficiently bind to all domains of N-803 (e.g., IL-15 variant, IL-15RαSu domain, and IgG1 Fc domain) with adequate sensitivity or additional positive controls (e.g., domain-specific N-803 positive controls) may be needed to supplement your validation approach. Submit the final assay

validation reports to the BLA. If the validation results in different cut points, it may be necessary to re-analyze the clinical samples with the new cut-points. If so, submit the updated ADA and NAb data and analyses in the next Interim Report for QUILT-3.032.

The timetable you submitted on April 16, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2025
Updated ADA and NAb Data Submission: 05/2025

Submit clinical protocols to your IND 121976 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.

[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

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.

If you have any questions, contact Christal Lee, Regulatory Project Manager, at 240-402-2711 or Christal.Lee@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Paul G. Kluetz, MD
Supervisory Associate Director (Acting)
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
- 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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