Our STN: BL 125734/0

BLA APPROVAL
June 28, 2023

CellTrans Inc.
Attention: Jose Oberholzer, MD, MHCM, FACS
2201 W. Campbell Park Drive, Suite 23
Chicago, IL 60612

Dear Dr. Oberholzer:

Please refer to your Biologics License Application (BLA) received May 19, 2020, submitted under section 351(a) of the Public Health Service Act (PHS Act) for donislecel-jujn.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2213 to CellTrans Inc., 2201 W. Campbell Park Drive, Ste 23, Chicago, IL 60612, under the provisions of section 351(a) of the PHS 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 donislecel-jujn which is indicated for the treatment of adults with Type 1 diabetes who are unable to approach target HbA1c because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: 00566813, 00679042, and 03791567.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture donislecel-jujn at your facility located at 1740 West Taylor St., Building (b) (4) Ste C200, University of Illinois Health Hospital, Chicago, IL 60612. Release of donislecel-jujn is limited by the dating period to the manufacturing location. If you wish to manufacture at another location or change the dating period, please submit a supplement with supporting data.

You may label your product with the proprietary name LANTIDRA and market it in two individual infusion bags one containing LANTIDRA and one containing rinse solution. The LANTIDRA bag contains not more than 10 cc of estimated packed islet tissue and

not more than 1 x 10^6 Equivalent Islet number (EIN) in 400 ml supplied volume. The LANTIDRA bag is aseptically connected to a smaller Rinse Bag containing 200 mL of supplied volume of transplant media.

DATING PERIOD

The dating period for LANTIDRA and Rinse bags shall be six hours from the date and time of product manufacture, when stored in an insulated container at 15°C to 25°C. The date of manufacture shall be defined as the date and time of the final formulated drug product is filled into LANTIDRA infusion bag. The date of manufacture for the Rinse bag shall be defined as the date and time of the transplant media is filled into the Rinse bag.

FDA LOT RELEASE

You are not currently required to submit samples or protocols of future lots of LANTIDRA to the Center for Biologics Evaluation and Research (CBER) for release by the Director, CBER, under 21 CFR 610.2(a). 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.

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, 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 the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations :

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of LANTIDRA (donislecel-jujn) or in the manufacturing facilities.

LABELING

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft content of labeling including the Package Insert and Patient Package Insert submitted under amendment 64, dated June 28, 2023 and the draft carton labels submitted under amendment 55, dated June 7, 2023 and container labels submitted under amendment 52 dated May 08, 2023.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert and Patient Package Insert submitted on June 28, 2023. 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* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton labels submitted on June 7, 2023 and secondary container and carrier labels submitted on May 08, 2023, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125734/0 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports and FDA's Adverse Event reporting System website at https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at https://www.fda.gov/vaccines-blood-biologics/lot-release/lot-distribution-database-ldd.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because the biological product for this indication has an orphan drug designation, you are exempt from this requirement.

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

We acknowledge your written commitment as described in your letter of June 27, 2023 as outlined below:

1. CellTrans, Inc. commits to reassess the analytical levels of organic leachables from the container closure system (two units, 750- and 1000-mL bags) using a methodology with validated limit of quantification (LOQ) values that are reliably below the reporting limit of (b) (4) (monitoring level, calculated based on the toxicological concern threshold). Based on this analytical reassessment, for compounds found above the reporting limit, CellTrans, Inc. also commits to perform a toxicological assessment and will submit the final reassessment of the organic leachables analytical levels and their toxicological assessment as a Post Marketing Commitment – Final Study Report by February 29, 2024.

   Final Study Report Submission: February 29, 2024

We request that you submit information concerning Chemistry, Manufacturing, and Control Postmarketing Commitments and final reports to your BLA, STN BL 125734/0. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Commitment – Status Update**. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- describe what has been accomplished to fulfill the non-section 506B PMC; and,
- summarize any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment – Final Study Report**.

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, please contact the Regulatory Project Manager for this application.

Sincerely,

Melissa Mendoza, JD
Director
Office of Compliance and Biologics Quality
Center for Biologics
Evaluation and Research

for
Celia M. Witten, PhD, MD
Acting Director
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics
Evaluation and Research