Our STN: BL 125738/0

BLA APPROVAL
April 17, 2023

Gamida Cell Ltd.
Attention: Priyanka Desai
116 Huntington Ave., 7th floor
Boston, MA 02116

Dear Ms. Desai:

Please refer to your Biologics License Application (BLA) received June 1, 2022, submitted under section 351(a) of the Public Health Service Act (PHS Act) for omidubicel-onlv.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2223 to Gamida Cell Ltd., Israel, 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 omidubicel-onlv, which is indicated for use in adults and pediatric patients 12 years and older with hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative conditioning to reduce the time to neutrophil recovery and the incidence of infection.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: 01221857; 01590628; 01816230; 02039557; 02504619; 02730299; and 04260698.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture omidubicel-onlv at your facility located at Gamida Cell Kiryat Gat Israel (KGI), (b) (4) (b) (4) You may label your product with the proprietary name OMISIRGE and market it in four individual infusion bags, one containing the Cultured Fraction, one containing Non-Cultured Fraction and two infusion bags containing the Infusion Solution. The Cultured Fraction infusion bag contains at least 8 x 10^8 total cells and at least 9.2 x 10^7 CD34+ cells with a minimum of 8.7% CD34+ cells frozen in

approximately 20 mL of solution. The Non-Cultured Fraction infusion bag contains at least 4 x 10^8 total cells and at least 2.4 x 10^7 CD3+ cells frozen in 10 mL of solution. The two infusion bags for the Infusion Solution contain (b) (4) of solution for the Cultured Fraction and (b) (4) of solution for the Non-Cultured Fraction.

ADVISORY COMMITTEE

We did not refer your application to the Cellular, Tissue, and Gene Therapies Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for omidubicel-onlv shall be 12 weeks from the date of manufacture when stored at ≤ -150°C for the Cultured Fraction and 15 weeks from the date of manufacture when stored at ≤ -150°C for the Non-Cultured Fraction. The date of manufacture shall be defined as the date of the final formulated drug product is filled into its final container closure for cryopreservation. The dating period for Infusion Solution supplied for the omidubicel-onlv final product shall be five months from the date of manufacture when stored at 2° to 8°C. The date of manufacture shall be defined as the date the Infusion Solution is filled in the final container closure.

FDA LOT RELEASE

You are not currently required to submit samples or protocols of future lots of omidubicel-onlv 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 omidubicel-onlv, or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including the Package Insert, submitted under amendment 67 (SN0068), dated April 17, 2023 and the draft carton and container labels submitted under amendment 61 (SN0062), dated March 30, 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, submitted on April 17, 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 and container labels submitted on March 30, 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 125738/0 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/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/vaccines/ucm458559.pdf and FDA's Adverse Event reporting System website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.

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 commitments as described in your letter of March 23, 2023 as outlined below:

1. Gamida Cell Ltd. commits to perform a residual (b) (4) impurities study on the omidubicel-onlv drug product to provide assurance that residual levels remain under the established limit of less than (b) (4) per batch, as informed by previous manufacturing experience. The study will include at least (b) (4) full scale batches, manufactured over the course of a year, that are representative of the commercial omidubicel-onlv drug product and include at least (b) (4) batches for each number of (b) (4) used in manufacturing (b) (4) (b) (4) Gamida Cell Ltd. also commits to submitting the (b) (4) impurities study protocol in a product correspondence supplement by June 30, 2023. Gamida Cell Ltd. will submit the final study report as a Postmarketing Commitment – Final Study Report by June 30, 2024.

   Final Study Report Submission: June 30, 2024

2. Gamida Cell Ltd. commits to execute a real process elemental leachables study of the final container closures for omidubicel-onlv to include the cultured fraction, non-cultured fraction, and infusion solution drug products over their manufacturing and storage periods. Given the complexity of the biological product, (b) (4) as Gamida Cell Ltd. performed for the assessment of organic leachables. Gamida Cell Ltd. will submit the final study report as a Postmarketing Commitment – Final Study Report by January 31, 2024.

   Final Study Report Submission: January 31, 2024

3. Gamida Cell Ltd. commits to notify the FDA when the master file (MF) (b) (4) holder has adequately resolved concerns with the MF. The notification will include a copy of a letter from the MF holder stating that they have received notification from the FDA that MF (b) (4) concerns have been adequately resolved. Gamida Cell Ltd. will submit this information as a Postmarketing Commitment – Status Update by February 29, 2024.

   Postmarketing Commitment - Status Update: February 29, 2024

We request that you submit information concerning chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA, STN BL 125738/0. 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

Tejashri Purohit-Sheth, MD
Acting Director
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics
Evaluation and Research