Our STN: BL 125743/0

BLA APPROVAL
December 15, 2023

GC Biopharma Corp.
Attention: (b) (4)

Dear (b) (4):

Please refer to your Biologics License Application (BLA) received July 14, 2023, submitted under section 351(a) of the Public Health Service Act (PHS Act) for immune globulin intravenous, human-stwk.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2033 to GC Biopharma Corp., Republic of Korea, 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, 10% solution of ALYGLO (immune globulin intravenous, human-stwk), which is indicated for treatment of primary humoral immunodeficiency (PI) in adults.

The review of this product was associated with the following National Clinical Trial (NCT) number(s): 02783482 and 04565015.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture the product, 10% solution of immune globulin intravenous human-stwk, at your facility located at (b) (4) You may label your product with the proprietary name, ALYGLO, and market it in three fill sizes: 50 mL, 100 mL, and 200 mL.

ADVISORY COMMITTEE

We did not refer your application to the Blood Products 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 10% solution of ALYGLO (immune globulin intravenous, human-stwk) shall be 36 months when stored at 2-8°C and 24 months when stored at 8-25°C from the date of manufacture. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your Drug Substance shall be (b) (4) days when stored at (b) (4).

FDA LOT RELEASE

Please submit final container samples of the product You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

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 :

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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 the 10% solution of ALYGLO (immune globulin intravenous, human-stwk), 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 Package Insert, the draft package, and container labels submitted under amendment 95 (SQ0099), dated December 13, 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 December 13, 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.

PACKAGE AND CONTAINER LABELS

Please electronically submit final printed package and container labels identical to the package and container labels submitted on December 13, 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 125743 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:

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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.

Also, in accordance with 21 CFR 606.170(b), you must notify the Director, Office of Compliance and Biologics Quality, CBER, of blood collection or transfusion related fatalities by telephone, facsimile, express mail, or secure email as soon as possible. A written report of the investigation must be submitted to the Director, Office of Compliance and Biologics Quality, CBER, by mail, facsimile, or electronically transmitted mail within 7 days after the fatality. The mailing address for fatality reports is:

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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.

We are waiving the pediatric study requirement for ages 0 to < 2 years because the necessary studies are impossible or highly impracticable due to the rarity of the diagnosis of primary PI in this age group.

We are deferring submission of your pediatric study for ages >= 2 years to < 17 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) is a required post-marketing study. The status of this post-marketing study must be reported according to 21 CFR 601.28 and section 505B(a)(4)(C) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any post-marketing commitments or required studies or clinical trials.

Label your annual report as an "**Annual Status Report of Post-marketing Study Requirement/Commitments**" and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. This required study is listed below:

1. GC5107D: An Open-Label, Single-Arm, Historically Controlled, Prospective, Multicenter Phase III Study to Evaluate the Pharmacokinetics and Safety of Immuno- Globulin Intravenous (Human) 10% GC5107 in Pediatric Subjects 2 years to <17 Years of Age with Primary Humoral Immunodeficiency

   Study Completion Date: May 30, 2026

   Final Report Submission: November 30, 2026

Submit the protocol(s) to your IND 16897, with a cross-reference letter to this BLA, STN BL 125743 explaining that this protocol was submitted to the IND.

Submit final study reports to this BLA, STN BL 125743. In order for your PREA PMR(s) to be considered fulfilled, you must submit and receive approval of either an efficacy or a labeling supplement.

For administrative purposes, all submissions related to this required pediatric post-marketing study must be clearly designated as:

- **Required Pediatric Assessment(s)**

POST-MARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitment(s) as described in your letter(s) of December 8, 2023, as outlined below:

2. GC BioPharma Corp. (GCBP) commits to characterize (b) (4) consecutive lots of Alyglo at release and at 6, 9, 12, and 24 months at both storage temperatures (2°C to 8°C and 25°C) using a method such as (b) (4) to measure (b) (4). GCBP also commits to include visual inspection and (b) (4) testing at each timepoint. GCBP also commits to submitting an interim study report by December 31, 2025, and a Post-marketing Commitment - Final Study Report by December 31, 2026.

3. GCBP commits to submitting the final report of the lifetime validation studies to support the proposed maximum (b) (4) of the (b) (4) as outlined in Protocol GC-PROT-00708, and (b) (4) as outlined in Protocol GC-PROT-00711, as Changes Being Effected (CBE) by December 31, 2025.

4. GCBP commits to submitting the final report of the lifetime validation studies to support the proposed maximum (b) (4) of the (b) (4) as outlined in Protocol GC-PROT-03857 as Changes Being Effected (CBE) by December 31, 2025.

5. GCBP commits to submitting the final report of the lifetime validation studies to support the proposed maximum (b) (4) of the (b) (4) as outlined in Protocol GC-PROT-00714 as Changes Being Effected (CBE) by December 31, 2025.

6. GCBP commits to analyzing the (b) (4) content starting from the (b) (4) manufactured during Pre-License Inspection (PLI) batches until obtaining at least (b) (4) lots of (b) (4). The final report will be submitted as Post-marketing Commitment - Final Study Report by December 31, 2024.

7. GCBP commits to submit the levels of Parvovirus B19 DNA from the (b) (4) ALYGLO manufacturing (b) (4) tested by the (b) (4) test on the (b) (4). Please also include the corresponding (b) (4) and turnaround times of B19 NAT results of the (b) (4) manufacturing (b) (4) tested. The testing data will be submitted as a Post-marketing Commitment - Final Study Report by December 31, 2024.

8. GCBP commits to submit data from leachables study/ies for the (b) (4) used for the storage of (b) (4) and a toxicological risk assessment demonstrating the ability of the process to remove potential impurities to safe levels. GCBP also commits to submitting an interim study report by July 31, 2024, and a Post-marketing Commitment - Final Study Report by December 31, 2026.

We request that you submit information concerning Chemistry, Manufacturing, and Control post-marketing commitments and final reports to your BLA, STN BL 125743. Please refer to the sequential number for each commitment.

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

- **Post-marketing Commitment – Status Update**
- **Post-marketing Commitment – Final Study Report**
- **Supplement contains Post-marketing Commitment – Final Study Report**

For each post-marketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Post-marketing 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 **Post-marketing Commitment – Final Study Report** or **Supplement contains Post-marketing 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

Nicole Verdun, MD
Director
Office of Therapeutic Products
Center for Biologics
Evaluation and Research