DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125294/S-045

SUPPLEMENT APPROVAL

Sicor Biotech UAB
c/o Teva Branded Pharmaceutical Products R&D
Attention: Arthur Merlin d'Estreuz, MSc, MTOPRA
Associate Director, Regulatory Affairs
41 Moores Road, PO Box 4011
Frazer, PA 19355

Dear Mr. d'Estreux:

Please refer to your Supplemental Biologics License Application (sBLA), dated January 31, 2018, received January 31, 2018, submitted under section 351(a) of the Public Health Service Act for GRANIX® (tbo-filgrastim) injection, 300 mcg/1 mL and 480 mcg/1.6 mL.

In addition to the new single-dose vial presentation, this Prior Approval supplemental biologics application provides for updates to the GRANIX United States Prescribing Information (USPI) regarding pediatric information to Sections 1 Indications and Usage, 6 Adverse Reactions, 8 Use in Specific Populations, and 12 Clinical Pharmacology based on results from Study XM02-ONC-201 which address PMR 2333-1.

APPROVAL & LABELING

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (prescribing information, patient information sheet, and vial IFU) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "*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.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on June 26, 2018, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3).* For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved BLA 125294/ S-045**." Approval of this submission by FDA is not required before the labeling is used.

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.

Because none of these criteria apply to your application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We have received your submission dated January 31, 2018, containing the final report for the following postmarketing requirement listed in the August 29, 2012 approval letter for BLA 125294.

PMR 2333-1 Phase 2 trial in 50 pediatric patients 1 month to 16 years of age to evaluate pharmacokinetics, pharmacodynamics, and safety data in patients with solid tumors without bone marrow involvement. Submit the protocol for Agency review and concurrence prior to beginning the trial and in advance of the "final protocol submission" date so that agreement on the essential trial elements can be reached.

Draft Protocol Submission:	02/2013
Final Protocol Submission:	06/2013
Trial Completion:	06/2016
Final Report Submission:	12/2016

We have reviewed your submission and conclude that the above requirement was fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our August 29, 2012, letter.

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

We remind you of your postmarketing commitments:

3458-1 Evaluate all potential leachables that are organic in nature (e.g., volatile, semi-volatile, and non-volatile compounds) by appropriate methods at the end of shelf-life for at least one vial drug product batch and at release for the next manufactured commercial drug product vial batch. The leachables analyzed should not be restricted just to the leachables that were identified in the extractable study. Provide data from these studies and data to support the suitability of the methods chosen for analysis.

The timetable you submitted on July 27, 2018, states that you will conduct this study according to the following schedule:

At Release Result Submission:	03/2019
End of Shelf Life Result Submission:	03/2021

3458-2 Provide shipping validation data for the vial drug product from real-time shipping studies or from studies that are sufficiently representative of the commercial shipping conditions. The data should include an assessment of product quality pre- and post-shipping. Include a detailed description of how the study was performed, and if performed using simulated studies, provide a justification for how the simulated studies are sufficiently representative of commercial shipping conditions.

The timetable you submitted on July 27, 2018, states that you will conduct this study according to the following schedule:

Final Report Submission:	12/2018

3458-3 Optimize the polysorbate 80 method to lower the variability observed during routine release and stability testing of vial drug product, and re-assess the current lots on release and stability to tighten the specifications appropriately. Submit data to support the appropriateness of the optimized polysorbate 80 method and data to support the re-evaluation of the acceptance criterion.

The timetable you submitted on July 27, 2018, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2018

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the prescribing information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Suria Yesmin, Regulatory Project Manager, at 301-348-1725.

Sincerely,

{See appended electronic signature page}

Albert Deisseroth, MD, PhD
Associate Supervisory Division Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of 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/

ALBERT B DEISSEROTH
07/31/2018