U.S. FOOD & DRUG ADMINISTRATION

BLA 761126

BLA APPROVAL

Tanvex BioPharma USA, Inc.
Attention: Bonnie Mills, PhD
Vice-President, Clinical Development & Regulatory Affairs
10394 Pacific Center Court
San Diego, CA 92121

Dear Dr. Mills:

Please refer to your biologics license application (BLA) dated and received September 28, 2018, and your amendments, submitted under section 351(k) of the Public Health Service Act for Nypozi (filgrastim-txid) injection.

This BLA provides for licensure of:

- Nypozi (filgrastim-txid) 300 mcg/0.5 mL, injection, for subcutaneous (SC) use in a single-dose pre-filled syringe (PFS) as biosimilar to US-Neupogen 300 mcg/0.5 mL, injection, for SC use in a PFS,
- Nypozi (filgrastim-txid) 300 mcg/0.5 mL, injection, for intravenous (IV) use in a PFS as biosimilar to US-Neupogen 300 mcg/0.5 mL, injection, for IV use in a PFS,
- Nypozi (filgrastim-txid) 480 mcg/0.8 mL, injection, for SC use in a PFS as biosimilar to US-Neupogen 480 mcg/0.8 mL, injection, for SC use in a PFS, and
- Nypozi (filgrastim-txid) 480 mcg/0.8 mL, injection, for IV use in a PFS as biosimilar to US-Neupogen 480 mcg/0.8 mL, injection, for IV use in a PFS.

We acknowledge receipt of your resubmission dated April 24, 2023, which constituted a complete response to our February 14, 2023, action letter.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2259 to Tanvex BioPharma USA, Inc, San Diego, CA, under the provisions of section 351(k) 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 Nypozi (filgrastim-txid). Nypozi is indicated to:

- Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever

- Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
- Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)
- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
- Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia
- Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture filgrastim-txid drug substance at Tanvex BioPharma USA, Inc., (FEI:3013021112), in San Diego, California. The final formulated drug product will be manufactured and filled at (b) (4) . The drug product will be assembled, labeled, and packaged at (b) (4). You may label your product with the proprietary name, Nypozi, and market it in 300 mcg/0.5 mL PFS injection and 480 mcg/0.8 mL PFS injection.

DATING PERIOD

The dating period for Nypozi shall be 24 months from the date of manufacture when stored at 2°C to 8°C, protected from light. 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)

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Nypozi to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. 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.

Any changes in the manufacturing, testing, packaging, or labeling of Nypozi, 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 with minor editorial revisions listed below and reflected in the enclosed labeling.

- Updated US License No., Initial U.S. Approval date and Revised date in the Prescribing Information
- Updated Issued date in the Patient Package Insert and Instructions for Use

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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, Patient Package Insert, Instructions for Use). 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 761126**." Approval of this submission by FDA is not required before the labeling is used.

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[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.

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.

Deferred Pediatric Assessments

We are deferring the required pediatric assessment for patients who weigh less than 36 kg for this application because this product is ready for approval for use in adults and development of a presentation for use in pediatric patients has not been completed.

Your deferred assessment required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) is a postmarketing requirement. The status of this postmarketing requirement must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(B) of the FDCA. This requirement is listed below.

4399-1 To develop a vial presentation that can be used to directly and accurately administer Nypozi (filgrastim-txid) to pediatric patients who weigh less than 36 kg requiring doses that are less than 0.3 mL (180 mcg).

Final Report Submission: 02/2025

Submit the protocols to your IND 113556, with a cross-reference letter to this BLA. Reports of this postmarketing requirement must be submitted as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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

We remind you of your postmarketing commitment:

4399-2 To conduct a study evaluating the impact of the (b) (4) If the data support (b) (4) TX01 manufacturing process will be provided. The plan will include an evaluation of (b) (4) .

The final report and updates to the drug substance manufacturing process will be reported per 21 CFR 601.12.

The timetable you submitted on February 10, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission 02/2025

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.

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:

[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

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

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

If you have any questions, contact Rolanda Bailey, Regulatory Project Manager, at (240) 402-5631 or email at Rolanda.Bailey@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Ann Farrell, MD
Director
Division of Nonmalignant Hematology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - Instructions for Use
- 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/

ANN T FARRELL
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