STN: BL 125816/0

BLA APPROVAL
December 3, 2025

Axogen Corporation
Attention: Jesse Bishop
13631 Progress Boulevard, Suite 400
Alachua, FL 32615

Dear Jesse Bishop:

Please refer to your Biologics License Application (BLA) received September 5, 2024, submitted under section 351(a) of the Public Health Service Act (PHS Act) for acellular nerve allograft-arwx.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2340 to Axogen Corporation, Alachua, Florida under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products and pursuant to section 506(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) and the regulations for accelerated approval, 21 CFR 601.41. 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 acellular nerve allograft-arwx, indicated for the treatment of adult and pediatric patients aged one month and older with:

- Traditional Approval for sensory nerve discontinuity ≤25mm and
- Accelerated Approval for sensory nerve discontinuity >25mm, as well as mixed and motor nerve discontinuity.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT01809002, NCT00948025, and NCT01526681.

ACCELERATED APPROVAL REQUIREMENTS

Under accelerated approval statutory provisions and regulations we may grant marketing approval for a biological product on the basis of adequate and well-controlled Study ANG-CP-007 (RECON) establishing that the biological product has an effect on an endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. This approval requires you to study the biological product further, to verify and describe its clinical

benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome.

Approval under these statutory provisions and regulations requires, among other things, that you conduct adequate and well-controlled study(ies) to verify and describe clinical benefit attributable to this product. Clinical benefit is evidenced by effects such as increased motor strength and improvement of sensation measured by Medical Research Council Classification (MRCC) motor and sensory at Month 24.

Accelerated Approval Required Studies

We remind you of your postmarketing requirement specified in your submission of Amendment 110, December 3, 2025.

1. Conduct a prospective, randomized, assessor-blinded, multicenter study (Protocol ANG-CP-013) to evaluate the clinical benefit of AVANCE (acellular nerve allograft-arwx) compared to sural nerve autograft for functional recovery following mixed and motor peripheral nerve injury. The study targets adults ≥18 years of age with mixed or motor nerve repairs in nerve gaps greater than 25 mm. The participants will be followed for 24 months post-surgical repair. The final study report will be submitted within 6 months of study completion, anticipated by 2031, including primary efficacy endpoints of Medical Research Council Classification (MRCC) motor and sensory recovery scores at Month 24.

   Final Protocol Submission: February 5, 2026

   Study Completion: December 5, 2030

   Final Report Submission: June 5, 2031

We expect you to complete design, initiation, accrual, completion, and reporting of these studies within the framework described in your letter of December 3, 2025.

Please submit the protocol to your IND 15419, with a cross-reference letter to this BLA, STN BL 125816 explaining that Protocol ANG-CP-013 was submitted to the IND. Please refer to the sequential number for each clinical trial and the submission number as shown in this letter.

You must conduct Study ANG-CP-013 with due diligence. If this required postmarketing study fails to verify that clinical benefit is conferred by acellular nerve allograft-arwx, or is not conducted with due diligence, including with respect to the conditions set forth below, we may withdraw this accelerated approval.

You must submit reports of the progress of Study ANG-CP-013 listed above as required under section 506(c) of the FDCA to this BLA 180 days after the date of approval of this

BLA and approximately every 180 days thereafter (see section 506B(a)(2) of the FDCA) (hereinafter "180-day reports").

You are required to submit two 180-day reports per year for each open study or clinical trial required under 506(c) of the FDCA. The initial report will be a standalone submission, and the subsequent report will be combined with your application's annual status report required under section 506B(a)(1) of the FDCA and 21 CFR 601.70. The standalone 180-day report will be due 180 days after the date of approval (with a 60-day grace period). Submit the subsequent 180-day report with your application's annual status report. Submit both of these 180-day reports each year until the final report for the corresponding study or clinical trial is submitted.

Your 180-day report must include the information listed in 21 CFR 601.70(b) and:

- Expected trial completion and final report submission dates;
- Any changes in plans since the last report, with rationale for any changes; and
- The current number of patients enrolled into each trial.

FDA recommends that you use form FDA 3989 PMR/PMC Annual Status Report for Drugs and Biologics, to submit your 180-day reports. Form FDA 3989, along with instructions for completing this form, is available on the FDA Forms web page at https://www.fda.gov/about-fda/reports-manuals-forms/forms.

Your 180-day reports, including both the standalone 180-day report submitted 180 days after the date of approval and the 180-day report submitted with your annual status report, must be clearly designated as **180-Day AA PMR Progress Report.**

FDA will consider the submission of your annual status report under section 506B(a)(1) of the FDCA and 21 CFR 601.70, in addition to the submission of reports 180 days after the date of approval each year (subject to a 60-day grace period), to satisfy the periodic reporting requirement under section 506B(a)(2) of the FDCA. You are also required to submit information related to your confirmatory trial as part of your annual reporting requirement under section 506B(a)(1) of the FDCA until the FDA notifies you, in writing, that the Agency concurs that the study requirement has been fulfilled or that the study either is no longer feasible or would no longer provide useful information.

Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Postmarketing Requirements and 506B Commitments are fulfilled or released.

Please submit final study report(s) as a supplement to this BLA, STN BL 125816. For administrative purposes, all submissions related to this postmarketing study requirement must be clearly designated as "**Subpart E Postmarketing Study Requirements**."

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture acellular nerve allograft-arwx at your facility located in (b) (4) facility in (b) (4) . You may label your product with the proprietary name AVANCE and market it in 16 size combinations (lengths of 15 mm to 70 mm and diameters of 1 to 5 mm).

Pursuant to 21 CFR 610.12(h)(2), an exception to sterility testing is approved under this license, because the data submitted in the BLA establish that the route of administration, the method of preparation, or any other aspect of the product precludes or does not necessitate a sterility test to assure the safety, purity, and potency of the product. If, at any time after approval, we obtain new information that indicates that a sterility test would be necessary to assure the safety, purity, and potency of acellular nerve allograft-arwx, we may provide written notice revoking approval of the exception to sterility testing.

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 which would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for acellular nerve allograft-arwx shall be 36 months from the date of manufacture when stored at ≤ -40°C. The date of manufacture shall be defined as the date of terminal sterilization.

FDA LOT RELEASE

Please submit protocols showing results of all applicable tests. You may not distribute any lots of nerve allograft-arwx 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 :

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 acellular nerve allograft-arwx, or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including the Package Insert, submitted under amendment 101, dated November 19, 2025, and the draft package and container labels submitted under amendment 99, dated November 19, 2025.

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 November 19, 2025. 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 November 19, 2025, 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 125816 at the time of use and include implementation information on Form FDA 356h.

PROMOTIONAL MATERIALS

Please note that the accelerated approval regulation concerning promotional materials (21 CFR 601.45) stipulates that all advertising and promotional labeling items that you wish to distribute in the first 120 days following approval, must have been received by FDA prior to the approval date. After approval, promotional items intended for dissemination after the first 120 days following approval must be submitted to the FDA at least 30 days prior to the anticipated distribution date. Please submit draft materials with a cover letter noting that the items are for accelerated approval, and an accompanying 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 advertisement and promotional labeling at the time of initial dissemination or publication, accompanied by FORM FDA 2253 (21 CFR 601.12(f)(4)).

Alternatively, you may submit promotional materials for accelerated approval products electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs* at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf.

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 in 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 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.

We are waiving the pediatric study requirement for neonates (birth to one month) because necessary studies are impossible or highly impracticable in this patient population. We note that you have fulfilled the pediatric study requirement for patients aged one month and older for this application.

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

Asha Das, MD
Acting Director
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics Evaluation and Research