Our STN: BL 125820

**ACCELERATED BLA APPROVAL**
February 14, 2025

Bavarian Nordic A/S
Attention: Todd Phillips, Pharm.D.
Bavarian Nordic, Inc.
1005 Slater Road, Suite 101
Durham, NC 27703

Dear Dr. Phillips:

Please refer to your Biologics License Application (BLA) received June 17, 2024, under section 351(a) of the Public Health Service Act (PHS Act) for Chikungunya Vaccine, Recombinant.

## LICENSING

Effective this date, we have approved your BLA for Chikungunya Vaccine, Recombinant, under accelerated approval pursuant to section 506(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) and the regulations for accelerated approval, 21 CFR 601.41. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Chikungunya Vaccine, Recombinant under your existing Department of Health and Human Services U.S. License No 2096. Chikungunya Vaccine, Recombinant is indicated for the prevention of disease caused by chikungunya virus in individuals 12 years of age and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT05349617, NCT05072080, NCT05065983, NCT03992872, NCT03483961.

## 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 clinical studies establishing that the biological product has an effect on a surrogate 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 an adequate and well-controlled study to verify and describe clinical

benefit attributable to this product. Clinical benefit is evidenced by effects such as prevention of disease caused by chikungunya virus.

**Accelerated Approval Required Studies**

We remind you of your postmarketing requirement (PMR) specified in your submission of January 30, 2025.

1. To conduct a randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, and immunogenicity of VIMKUNYA, an adjuvanted chikungunya virus virus-like particle (CHIKV VLP) vaccine for the prevention of chikungunya disease in adolescents (12 to <18 years) and adults (≥18 years).

   Final Protocol Submission: February 28, 2025

   Study Implementation Readiness Verification Submission and Study Initiation: September 30, 2025

   Study/Trial Completion: September 30, 2029

   Final Report Submission: August 31, 2030

We expect you to complete design, implementation readiness verification, initiation, accrual, completion, and reporting of this clinical trial within the framework described under amendment 134 to your IND 17998, dated October 29, 2024.

Please submit the protocol to your IND 17998, with a cross-reference letter to this BLA (STN BL 125820), explaining that this protocol was submitted for review to the IND. In your submission, refer to the sequential PMR number for this study (PMR #1) and the submission number as shown in this letter (STN BL 125820).

You must conduct this clinical trial with due diligence. If the required postmarketing study fails to verify that clinical benefit is conferred by Chikungunya Vaccine, Recombinant, or is not conducted with due diligence, including with respect to the conditions set forth below, we may withdraw this approval.

You must submit reports of the progress of the clinical trial, 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). 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 the final study report as a supplement to this BLA, STN BL 125820.** 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 Chikungunya Vaccine, Recombinant, drug substance and formulated bulk drug product at Bavarian Nordic (b) (4) . The drug product will be filled at (b) (4) labeled and packaged at (b) (4)

You may label your product with the proprietary name VIMKUNYA and market it in single dose presentation of 0.8 mL in 1-mL pre-filled syringes.

## ADVISORY COMMITTEE

We did not refer your application to the Vaccines and Related Biological 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 which would have benefitted from an advisory committee discussion.

## DATING PERIOD

The dating period for the Chikungunya Vaccine, Recombinant, shall be 36 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date when the (b) (4) Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency.

## FDA LOT RELEASE

Please submit samples of the product in labeled final containers and protocols showing results of all applicable tests. 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.

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 Chikungunya Vaccine, Recombinant, or in the manufacturing facilities.

**LABELING**

We hereby approve the draft content of labeling including: Package Insert, submitted under amendment 72, dated February 14, 2025, and the draft carton and container labels submitted under amendment 65, dated January 31, 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 February 14, 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 January 31, 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/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125820 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 (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 for Vaccines* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports-vaccines. 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.

For information on the postmarketing safety reporting requirements for combination products as described in 21 CFR 4, Subpart B, and the dates by which combination product applicants must comply with these requirements, please refer to the Postmarketing Safety Reporting for Combination Products webpage available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

**TROPICAL DISEASE PRIORITY REVIEW VOUCHER**

We also inform you that you have been granted a tropical disease priority review voucher (PRV), as provided under section 524 of the FDCA. This PRV has been assigned a tracking number, PRV BLA 125820. All correspondences related to this voucher should refer to this tracking number.

This voucher entitles you to designate a single human drug application submitted under section 505(b)(1) of the FDCA or a single biologic application submitted under section 351 of the Public Health Service Act as qualifying for a priority review. Such an application would not have to meet any other requirements for a priority review. The list below describes the sponsor responsibilities and the parameters for using and transferring a tropical disease PRV.

- The sponsor who redeems the PRV must notify FDA of its intent to submit an application with a PRV at least 90 days before submission of the application and must include the date the sponsor intends to submit the application. This notification should be prominently marked, "**Notification of Intent to Submit an Application with a Tropical Disease Priority Review Voucher**."

- This PRV may be transferred, including by sale, by you to another sponsor of a human drug or biologic application. If the PRV is transferred, the sponsor to whom the PRV has been transferred should include a copy of this letter (which will be posted on our website as are all approval letters) and proof that the PRV was transferred. When redeeming this PRV, you should refer to this letter as an official record of the voucher.

For additional information regarding the PRV, see FDA's guidance, *Tropical Disease Priority Review Vouchers,* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM080599.pdf.

**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 deferring submission of your pediatric studies for ages 0 to <12 years of age for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing studies 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 postmarketing commitments or required studies or clinical trials.

Label your annual report as an "**Annual Status Report of Postmarketing 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. These required studies are listed below:

2. Deferred pediatric study under PREA (EBSI-CV-317-006) to evaluate the safety and immunogenicity of VIMKUNYA in children 2 to <12 years of age.

   Final Protocol Submission: February 28, 2025

   Study Completion Date: June 30, 2028

   Final Report Submission: January 31, 2029

3. Deferred pediatric study under PREA (EBSI-CV-317-009) to evaluate the safety and immunogenicity of VIMKUNYA in infants 0 to <2 years of age.

   Final Protocol Submission: April 30, 2028

   Study Completion Date: February 29, 2032

   Final Report Submission: November 30, 2032

Submit the protocols to your IND 17998, with a cross-reference letter to this BLA, STN BL 125820 explaining that these protocols were submitted to the IND. In your submission, please refer to the sequential PMR numbers for these studies (PMR #2, PMR #3) and the submission number as shown in this letter (STN 125820).

Submit final study reports to this BLA STN BL 125820. In order for your PREA PMRs to be considered fulfilled, you must submit and receive approval of either an efficacy or a labeling supplement. Please refer to the sequential PMR number for these studies (PMR #2, PMR #3) and the submission number as shown in this letter (STN BL 125820). For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

- **Required Pediatric Assessment(s)**

We note that you have fulfilled the pediatric study requirement for ages 12 to <18 years of age for this application.

**POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B**

We acknowledge your written postmarketing commitments (PMC) as described in your correspondence of January 30, 2025, as outlined below:

4. Study titled "VIMKUNYA Pregnancy Registry: An observational prospective study of the safety of VIMKUNYA vaccine exposure in pregnant individuals and their offspring." This prospective, observational registry study of pregnant individuals residing in the United States and European Union will evaluate maternal and infant outcomes (until one year of age) in at least 50 individuals exposed to VIMKUNYA up to 28 days prior to or at any time during pregnancy.

   Final Protocol Submission: May 30, 2025

   Study Completion Date: August 31, 2030

   Final Report Submission: February 28, 2031

Please submit clinical protocols to your IND 17998, and a cross-reference letter to this BLA (STN BL 125820) explaining that this protocol was submitted to the IND. In your submission, please refer to the sequential PMC number for this study (PMC #4) and the submission number as shown in this letter (STN BL 125820).

If the information in the final study report supports a change in the labeling, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment Final Study Report**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. 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 Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,

- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

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

We acknowledge your written commitments as described in your correspondence of January 30, 2025, as outlined below:

5. To submit leachable data for unlabeled CHIKV VLP Drug Product syringes.

   Final Report Submission: October 31, 2028

6. To conduct a study to quantify the residual (b) (4) plasmid DNA (pDNA) levels on the first (b) (4) consecutive CHIKV VLP (b) (4) lots, and to submit data from this study.

   Final Report Submission: June 30, 2026

7. To conduct Finished Drug Product transport validation studies (b) (4) ) as described in section 3.2.P.3.5 (2.5.3.3) of your BLA 125820/0.

   Final Report Submission: June 30, 2025

8. To perform Drug Product (DP) transportation validation using the DP product performance qualification (PPQ) lots.

   Final Report Submission: February 28, 2026

We request that you submit information concerning nonclinical and chemistry, manufacturing, and control postmarketing commitments and final reports to this BLA, STN BL 125820. In your submission, please refer to the sequential PMC numbers for these studies (PMC #5, PMC #6, PMC #7, PMC #8) and the submission number as shown in this letter (STN BL 125820).

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

- **Postmarketing Commitment – Correspondence 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 Study Commitment – Correspondence 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.

To fulfill your commitments, submit your final reports to the BLA 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,

David C. Kaslow, MD
Director
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research