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17 June 2025

Peter Kim, MD MS
Division Director, Anti-Infective Products
Office of Antimicrobial Products
FDA, CDER
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

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|---|---|
| **Product Name:** | NUZYRA® (Omadacycline) Immediate Release Film-Coated Tablets, 150mg |
| **NDA#:** | 209816 |
| **Sequence#:** | 0194 |
| **Supplement #:** | N/A |
| **Submission Type:** | **Product Correspondence: Pediatric PK Study (3487-1) - Response to PREA Noncompliance Letter** |

Dear Dr. Kim:

Reference is made to NDA(s) 209816 and NDA 209817 approvals for both oral and iv formulations, and community acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) indications on 02 October 2018.

Reference is also made to NUZYRA post marketing requirements (PMR)/post marketing commitments (PMC), including pediatric study 3487-1.

**Study 3487-1** requires Paratek to conduct a single dose pharmacokinetic and safety study in children ages 8 to 17 years who are receiving antibacterial drug therapy for an infectious disease.

Reference is further made to Parateks extension request for study 3487-1 submitted 07 April 2025 (NDA 209816, Sequence 0186), FDA PREA Non-Compliance Letter dated 06 May 2025, and FDA extension request denial letter for study 3487-1 dated 22 May 2025.

The purpose of this submission is to provide a formal response to FDAs PREA Non-Compliance Letter. The Sponsor is providing a full response in Section 1.17.2, which includes explanation for the delay of the study.

Paratek has had consistent and reliable communication with FDA by way of protocol submissions, extension requests, and meeting engagements regarding the omadacycline pediatric program.

While Paratek always anticipated that enrollment would be challenging in the study given the vulnerable population, the lack of any direct benefit for the patient, and the blood collection requirements, we have encountered more challenges than anticipated in site identification and a slower than anticipated enrollment rate.

In the approximately 36 months that the study has been enrolling, a total of (b) (4) potential patients have been identified and pre-screened for the study.

Additionally, sites have communicated that many potentially eligible patients are either not being admitted at all or are not being admitted for as long as required for protocol inclusion to ensure serial PK sample collection.

During the course of the study, Paratek has continuously evaluated options in order to increase enrollment and complete the study including alternative sites of care, home health care and ex-US enrollment. In addition, throughout the entirety of the study Paratek continued site identification efforts as well as ongoing engagement with the participating sites. Paratek has listened to site recommendations and tried to accommodate adjustments and suggestions that would improve enrollment without jeopardizing the study conduct and data.

Despite numerous challenges, Paratek has continued to make progress and generate critical data to advance the pediatric program. Data generated to date has (b) (4) Most recently, Paratek submitted (b) (4) an extension request that was denied, and a meeting request to discuss the pediatric program with FDA prior to receiving the non-compliance letter.

Paratek remains committed to completing study 3487-1, as well as all other pediatric assessments previously agreed to, and looks forward to the discussion at the meeting currently scheduled.

This submission contains:

**Module 1**

- Cover letter
  - FDA PREA Non-Compliance Letter dated 06 May 2025
  - FDA Pediatric extension request denial letter dated 22 May 2025
- FDA Form 356h
- 1.17.2 Correspondence regarding post marketing requirements

This information has also been submitted under separate cover to NDA 209817 (Sequence No. 0178) and cross referenced to IND 075928 (Sequence No. 0379) and IND 073431 (Sequence No. 0291).

This electronic application has been prepared by Paratek Pharmaceuticals, Inc. Paratek Pharmaceuticals, Inc. certifies that all submission files were checked and verified to be free of viruses. All documents were scanned for malicious content when processed/created within Veeva Vault using Carbon Black Defense (client version 3.4.0.1086). The technical point of contact for this submission is Debora Aleide and can be reached at (484) 751-4949 or deb.aleide@paratekpharma.com.

This submission contains trade secrets and confidential commercial information exempt from public disclosure pursuant to exemption 4 of the Freedom of Information Act and FDA regulations, and the disclosure of which is prohibited by the Federal Food, Drug, and Cosmetic Act, the Trade Secrets Act, and other applicable law. Pursuant to FDA regulations, Paratek is entitled to notice, an opportunity to object, and an opportunity to seek pre-release judicial review in the event that FDA determines that all or any part of this submission may be disclosed.

If you should have any questions or concerns regarding this submission, please do not hesitate to contact me at the contact information below or Stephen Viccica at 484-751-4909 or stephen.viccica@paratekpharma.com.

Sincerely,

Stephen Viccica

Digitally signed by Stephen Viccica
Date: 2025.06.16 15:55:54 -04'00'

Stephen Viccica, MS

Executive Director and Head, Regulatory Affairs
Paratek Pharmaceuticals, Inc.
1000 First Avenue
Suite 200
King of Prussia, PA 19406
Phone: (484) 751-4909
Fax: (484) 751-4995
Email: Stephen.viccica@paratekpharma.com

NDA 209816
NDA 209817

**NOTIFICATION OF**
**NON-COMPLIANCE WITH PREA**

Paratek Pharmaceuticals, Inc.
Attention: Stephen Viccica, MS
Executive Director and Head, Regulatory Affairs
1000 First Avenue, Suite 200
King of Prussia, PA 19406

Dear Stephen Viccica:

Please refer to your new drug applications (NDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (the Act) for the following drugs, which were approved on October 2, 2018.

NDA 209816 Nuzyra (omadacycline) tablet
NDA 209817 Nuzyra (omadacycline) injection

The Agency has determined that you have failed to meet the postmarketing requirement (PMR) of the Pediatric Research Equity Act (PREA) for these applications because you have not yet submitted your pediatric assessment for:

PMR 3487-1 which was deferred until February 28, 2025.

Under the provisions of section 505B(d)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) [21 U.S.C. 355c(d)(1)], you must respond in writing within 45 calendar days of the date of this letter. Your response should include the reason(s) for the delayed pediatric assessment and a date by which you expect to submit the assessment. You may also include a request for a deferral extension, if applicable, which should be identified as a "**DEFERRAL EXTENSION REQUESTED**" in your response.

While you are required to respond to this Non-Compliance letter as instructed above, you are not required to submit another deferral extension request, as we have received your April 7, 2025, deferral extension request, and it is currently under review.

In accordance with the FD&C Act, FDA will post this letter and your response to the website at https://www.fda.gov/drugs/development-resources/non-compliance-letters-under-505bd1-federal-food-drug-and-cosmetic-act with redactions for any trade secrets and confidential commercial information 60 calendar days from the date of this letter.

Please identify your response to this letter as a "**RESPONSE TO PREA NON-COMPLIANCE LETTER.**" To facilitate our review, submit this information to your NDA with a cross-reference letter to the investigational new drug application (IND) to which your protocol has been submitted.

If you have any questions, contact Eva Zuffova, Regulatory Project Manager, at 301-796-0697 or email eva.zuffova@fda.hhs.gov

Sincerely,

*{See appended electronic signature page}*

Peter Kim, MD, MS
Director
Division of Anti-Infectives
Office of Infectious Diseases
Office of New Drugs
Center for Drug Evaluation and Research

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**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.**

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/s/

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PETER W KIM
05/06/2025 03:06:32 PM

NDA 209816
NDA 209817

**DEFERRAL EXTENSION DENIED**

Paratek Pharmaceuticals, Inc.
Attention: Stephen Viccica, MS
Executive Director and Head, Regulatory Affairs
1000 First Avenue, Suite 200
King of Prussia, PA 19406

Dear Stephen Viccica:

Please refer to your new drug applications (NDAs) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Nuzyra (omadacycline) tablets (NDA 209816) and Nuzyra (omadacycline) for injection (NDA 209817), approved on October 2, 2018.

We also refer to your request for a deferral extension dated April 7, 2025, for the following Postmarketing Requirement (PMR) that was established under the Pediatric Research Equity Act (PREA):

3487-1 Conduct a single dose pharmacokinetic and safety study in children ages 8 to 17 years who are receiving antibacterial drug therapy for an infectious disease.

Draft Protocol Submission: 05/2019
Final Protocol Submission: 08/2019
Study Completion: 12/2020
Final Report Submission: 05/2021

We have completed our review of this request and have determined that we cannot extend the Final Report Submission date for this PMR because we need to first discuss your overall pediatric development program during the upcoming meeting scheduled on June 20, 2025.

If you do not submit your required pediatric postmarketing studies by the Final Report Submission date, your reporting status will be shown as delayed and you will be subject to the enforcement mechanism authorized under 505B(d) of the Act, including issuance of a noncompliance letter pursuant to 505B(d)(1). This letter and your response, if any, will be made publicly available on FDA's website 60 days after issuance of the former with redactions for any trade secrets and confidential commercial information.[1] Your

[1] http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm343203.htm

submission must be made as part of your NDAs or as a supplement to your approved NDAs 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.

If you have any questions, contact Eva Zuffova at 301-796-0697 or eva.zuffova@fda.hhs.gov.

Sincerely,

*{See appended electronic signature page}*

Peter Kim, MD, MS
Director
Division of Anti-Infectives
Office of Infectious Diseases
Office of New Drugs
Center for Drug Evaluation and Research

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**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.**

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/s/

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PETER W KIM
05/22/2025 09:13:31 AM