August 26, 2026

Peter Kim, MD, MS Director Division of Anti-Infectives Office of Infectious Diseases Office of New Drugs Center for Drug Evaluation and Research Central Document Room 5901-B Ammendale Road Beltsville, MD 20705-1266	**RESPONSE TO** **PREA NON-COMPLIANCE LETTER** **DEFERRAL EXTENSION REQUESTED**

NDA 216165 (Sequence: 0068)
EXBLIFEP® (cefepime and enmetazobactam) for injection
Re: Response to PREA Non-compliance Letter
Deferral Extension Requested for Pediatric Study AT-202 (PMR 4582-1)

Dear Dr. Kim:

This letter provides further information to support Orchid Pharma Limited's ("Orchid") request for an extension of the deferral of pediatric studies [AT-202 (PMR 4582-1)] for NDA 216165 [EXBLIFEP® (cefepime and enmetazobactam) for injection] and responds to the FDA's *PREA Non-Compliance letter* dated August 10, 2026 and the *letter of denial of our request* for an extension of the deferral for completing pediatric studies. By this letter, we both request reconsideration of our previous request for a deferral extension and provide the reasons for the delayed pediatric assessment.

Due to circumstances beyond the company's control, the pediatric assessment would not be completed by the due date mentioned in the original NDA approval letter dated February 22, 2024 specifically, PMR 4582-1:

4582-1 Conduct an open-label, single arm, non-comparative study to evaluate the pharmacokinetics, safety and tolerability of multiple doses of cefepime/enmetazobactam in pediatric patients from birth to less than 18 years of age with complicated urinary tract infections, including pyelonephritis.

Herewith Orchid provides the current status and progress of the study AT-202 trial, EU CT Number 2024-518003-22-00 cross referenced to IND 122269.

Current status and progress on ongoing studies:

- A total of 50 participants is planned to be enrolled in five age groups
- The trial was conducted in the Czech Republic, France, Hungary, Poland, Slovakia, and Spain for a total of 10 sites initiated.
- The trial has enrolled subjects from 2 to less than 18 years of age (cohorts 1, 2 and 3) up to the decision of temporary halt taken on 11 April 2025 due to the insolvency situation of Allecra Therapeutics, the trial sponsor. The first subject entered the trial on 11-Sep-2023. A total of 10 subjects were included and treated with study medication in 4 participating sites.
- No important emerging efficacy or safety findings were raised during the conduct of study so far.
- Orchid acquired the relevant assets, and transfer of NDA 216165 ownership from Allecra Therapeutics to Orchid Pharma Limited became effective on November 30, 2025 and was notified to FDA on December 17, 2025, eCTD sequence 0061.
- In parallel the change of sponsorship of AT-202 from Allecra Therapeutics to Orchid Pharma Europe GmbH was validated in EU CTIS platform by the Reference Member State and the Concerned Members States on 19 January 2026.

Office Address: Suite 337, 110 Fieldcrest Ave, 3rd Floor, Edison, NJ 08837
Phone Number: +1-732-427-6078 • Fax Number: +1-732-694-7007 • Email ID: contact@isazi.biz

- The trial is currently in the restart preparation phase with the resuming of patient enrollment planned in September 2026. It includes measures to boost the patient enrollment:
  - Change of CRO
  - Replacing inactive sites by sites with high subject recruitment potential in new countries
  - Relaxing some exclusion criteria not impacting PK and safety data (trial primary endpoints)
  - Facilitating the ICF process with optional electronic consent form

Updated trial timelines:

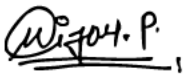
- Completion cohort 1,2,3: (b) (4)
- CSR: cohort 1, 2, 3: (b) (4)
- PK/PTA modelling to define cohorts 4, 5 cefepime-enmetazobactam doses: (b) (4)
- Protocol amendment submission for cohorts 4,5 in CTIS: (b) (4)
- Subject enrollment starts for cohorts 4, 5: (b) (4)
- Completion cohorts 4, 5: (b) (4)
- Final CSR: (b) (4)

Orchid has every intention of completing the pediatric assessment. The company has submitted a final protocol in May 2024 (sequence # 0052) and willing to complete the study as per updated timeline mentioned above.

We are fully committed to fulfilling the post-marketing obligations under PREA and to timely completion of the studies. We appreciate your consideration of this request and would be pleased to provide any additional information that you need, including documentation of any of the information provided in this letter.

Should you have any questions regarding this response, please contact me.

Sincerely,



Mr. Vijaykumar Satapara
US Agent for Orchid Pharma Limited
President and CEO – Isazi USA, Inc.
Suite 337, 110 Fieldcrest Ave,
Edison, NJ 08837
Tel: +1-732-427-6078
Email: Vijay.satapara@isazi.biz

Office Address: Suite 337, 110 Fieldcrest Ave, 3rd Floor, Edison, NJ 08837
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