Meitheal Pharmaceuticals
8700 W. Bryn Mawr, Suite 600S
Chicago, IL 60631

meitheal
Generics | Brands | Biologics

February 20, 2025

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

RE:

NDA 211672 Xenleta (lefamulin) Tablets; eCTD Sequence #0161

NDA 211673 Xenleta (lefamulin) Injection, eCTD Sequence #0163

Product Name: Xenleta (lefamulin) Tablets, 600 mg; Xenleta (lefamulin) Injection, 150 mg

Subject: RESPONSE TO "Notification of Non-Compliance with PREA"
DEFERRAL EXTENSION REQUESTED

Dear Dr. Kim,

Please refer to the New Drug Application (NDA) 211672 for Xenleta (lefamulin) Tablets and NDA 211673 for Xenleta (lefamulin) Injection, held by Hong Kong King-Friend Industrial Company Limited ("HKF").

Reference is also made to the "*Notification of Non-Compliance with PREA"* of 10th January 2025 and the "*Deferral Extension Denied*" letter of 10th January 2025, which pertains to PMR 3672-8.

3672-8 *Conduct a single-dose study to evaluate the pharmacokinetics and safety of intravenous XENLETA (lefamulin) in children from 2 months to less than 18 years of age with suspected or confirmed bacterial infections receiving standard of care.*

This submission provides HKF's response to the Notification of Non-Compliance with PREA. HKF's response includes a request for deferral extension of the required pediatric study and associated justification.

On 16 and 17 December 2024, ownership of NDAs 211672 and 211673 was transferred from Nabriva Therapeutics PLC ("Nabriva") to Hong Kong King-Friend Industrial Company Limited ("HKF").

Prior to this transfer, the following key activities are noted:

- 6 January 2023: Nabriva publicly announced its intention to wind-down operations (b) (4)
- (b) (4)
- 26 November 2024: Nabriva submitted to FDA a request for a deferral extension for PMR 3672-8, (b) (4)
- 16 & 17 December 2024: Transfer of ownership of NDAs 211672 and 211673 from Nabriva to HKF.
- 10 January 2025: FDA denied Nabriva's deferral extension request due to lack of justification around enrollment issues and deemed internal business issues and recent transfer of ownership as insufficient reasons not to fulfil the PMR. Notification of noncompliance with PREA letter issued to HKF.

HKF regrets the delay in the conduct of this study and recognizes the importance of pediatric evaluations in drug development and would like to re-start the work to fulfill the PMR as soon as possible. As described below, there are several challenges which will delay the ability to resume the pediatric study as per PMR 3572-8, and therefore the submission of the final report.

A. Resuming Xenleta Injection vial and diluent bag manufacturing

As stated in the Prescribing Information, Xenleta Injection must be diluted with *the diluent supplied with XENLETA Injection,* before administration by intravenous infusion. Each supplied diluent infusion bag contains 250 mL of 10 mM citrate buffered (pH 5) 0.9% sodium chloride.

(b) (4)

The diluent infusion bag is supplied along with Xenleta Injection vials, as described in Xenleta Injection Prescribing Information.

For conducting the clinical study as per PMR 3672-8, both Xenleta Injection (vial) and the specific citrate buffer diluent in a compatible bag would be needed, (b) (4)

(b) (4)

3 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page

C. Deferral Extension Request:

Due to the challenges and necessary transfer work as described above, it will take about (b) (4) (b) (4) to re-start the pediatric clinical study PMR 3672-8. Further, due to the challenges in recruiting subjects, particularly infants and children less than 6 years of age, the remaining clinical study is estimated to take 4 years, or 48 months to complete.

Hereby, a deferral extension is being requested for the required PMR 3672-8 pediatric study. The proposed timelines are provided below.

Study Completion: (b) (4)

Final Report Submission: (b) (4)

The proposed timelines are intended to allow for the extensive work that will be necessary to (b) (4) complete the remaining clinical study as per PMR 3672-8. We hope that the proposal above will be acceptable.

Lastly, as part of HKF's justification for deferral extension, HKF provided a detailed timeline which outlines the actions Nabriva took beginning from January 2023. With Nabriva's request for deferral extension submitted 26 November 2024, the ownership transfer date (17 December 2024) in close proximity to the PMR deadline (12/2024), it was not possible for HKF to adequately address and manage this PMR. With transfer of ownership, HKF fully accepts responsibility and oversight of the PMR with the intent to work responsively with FDA to complete the study.

This submission has been prepared in accordance with the Guidance for Industry on Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications and is being submitted to the FDA via the Agency's WebTrader. We certify that this submission is virus free as tested by SentinelOne endpoint protection Version 24.1.5.277

On behalf of HKF, Meitheal Pharmaceuticals Inc. (US Agent) submits this request.

If there are any questions, please do not hesitate to contact the undersigned,

or

Jinsong Liu, Ph.D., Executive Vice President of Regulatory and Strategic Alliances, Meitheal Pharmaceuticals, Inc, at 224-938-5331 or email me jliu@meithealpharma.com;

Sincerely,

rshah@meithealpharma.com

Digitally signed by rshah@meithealpharma.com
Date: 2025.02.20 15:26:56 -06'00'

Roopang Shah

Director, Regulatory Affairs

Meitheal Pharmaceuticals, Inc.

Tel: 224-545-0612

Fax: 847-789-8750

Email: rshah@meithealpharma.com