18 June 2021

Jessica J. Lee, MD, MMSc, Director
Division of Gastroenterology
Office of Immunology and Inflammation
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266

RE: NDA 202342, eCTD Sequence #0100
Product Name: Esomeprazole Strontium Delayed Release Capsules 24.65 mg and 49.3 mg
Subject: RESPONSE TO PREA NONCOMPLIANCE LETTER
DEFERRAL EXTENSION REQUESTED

Dear Dr. Lee:

Please refer to the New Drug Application (NDA 202342) for Esomeprazole Strontium Delayed Release Capsules held by Belcher Pharmatech, LLC, a wholly owned subsidiary of Belcher Pharmaceuticals, LLC ("Belcher"). Reference is also made to the Notification of Non-Compliance with PREA letter of 5 May 2021. This submission provides Belcher's response to the Notification of Non-Compliance with PREA letter. Belcher's response includes the explanation for the delayed pediatric assessment and a request for deferral of the required pediatric studies.

On 23 February 2020, ownership of NDA 202342 was transferred to Belcher. Prior to this, the following key activities related to conduct of pediatric postmarketing studies occurred:

At the time of approval of NDA 202342 on 6 August 2013, the following 4 postmarketing studies were required, with final report submission expected as indicated:

- 2054-1: Deferred pediatric study under PREA to evaluate the pharmacokinetics, pharmacodynamics, and safety of esomeprazole strontium for healing and maintenance of healing of erosive esophagitis (EE) in patients 1 month to 17 years, inclusive. The study must also assess the efficacy of esomeprazole strontium in maintenance of healing of EE, including determination of the dose and treatment duration required to maintain healing of EE in this pediatric population. The study must include an adequate number of patients in different age groups to inform dosing, and to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and post-treatment bone-related safety assessments must be included.
    - Original Required Final Report Submission Date: April 2018

- 2054-2: Deferred pediatric study under PREA to evaluate the safety of esomeprazole strontium for treating symptomatic gastroesophageal reflux disease (GERD) in patients 1

year to 17 years, inclusive. The study must include an adequate number of patients in different pediatric age groups to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and posttreatment bone-related safety assessments must be included. This study may not be needed if the data from PMR 2054-1 are adequate to fulfill the requirement.
    - Original Required Final Report Submission Date: April 2021

- 2054-3: Deferred pediatric study under PREA to evaluate the pharmacokinetics, pharmacodynamics, and safety of esomeprazole strontium for reducing the risk of NSAID-associated gastric ulcer in patients 2 years to 17 years, inclusive. The study must include an adequate number of patients in different age groups to inform dosing, and to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and post-treatment bone-related safety assessments must be included.
    - Original Required Final Report Submission Date: October 2018

- 2054-4: Deferred pediatric study under PREA to evaluate the safety and efficacy of esomeprazole strontium in combination with clarithromycin and amoxicillin for the eradication of Helicobacter pylori in symptomatic pediatric patients 2 to 17 years, inclusive, with or without duodenal ulcer disease.
    - Original Required Final Report Submission Date: April 2021

Following an earlier transfer of NDA ownership, the previous owner of the NDA submitted a request on 27 March 2017 (sequence 0072) to defer the conduct of the required postmarketing pediatric studies. In response, the FDA requested a proposal for the timing of study protocol submission and study completion. Accordingly, in a 14 May 2018 submission (sequence 0080), the NDA owner proposed timing for these activities. The FDA then denied the deferral extension on 16 May 2019. The previous owner subsequently decided to divest of the product and discontinue marketing, and on 26 June 2019 (sequence 0089) submitted a request to withdraw NDA 202342 effective 30 September 2019.

In the NDA Annual Report submitted on 26 September 2019 (sequence 0090), the NDA holder confirmed that they had no plans to complete the pediatric studies since they had requested withdrawal of the NDA and had discontinued marketing the product. Esomeprazole Strontium Delayed Release Capsules have not been marketed since before the effective NDA withdrawal date, and the application is listed in the Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book) as discontinued.

Ownership of NDA 202342 was transferred to Belcher on 23 February 2020. Before this time, no progress was made on the conduct of the pediatric postmarketing studies, including protocol development, nor did any development of pediatric dosage forms that will be needed to conduct the studies take place. Since acquiring ownership of NDA 202342, Belcher has been transferring the manufacturing of Esomeprazole Strontium Delayed Release Capsules and intends to proceed with pediatric formulation and protocol development followed by conduct of the required

pediatric postmarketing studies. [redacted]

In this submission, Belcher requests [redacted], and requests that the timelines for protocol submission, study completion, and final report submission for the postmarketing pediatric studies be updated to the following:

- 2054-1: Deferred pediatric study under PREA to evaluate the pharmacokinetics, pharmacodynamics, and safety of esomeprazole strontium for healing and maintenance of healing of erosive esophagitis (EE) in patients 1 month to 17 years, inclusive. The study must also assess the efficacy of esomeprazole strontium in maintenance of healing of EE, including determination of the dose and treatment duration required to maintain healing of EE in this pediatric population. The study must include an adequate number of patients in different age groups to inform dosing, and to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and post-treatment bone-related safety assessments must be included.
  - Protocol Submission Date: [redacted]
  - Study Completion Date: [redacted]
  - Final Report Submission: [redacted]

- 2054-2: Deferred pediatric study under PREA to evaluate the safety of esomeprazole strontium for treating symptomatic gastroesophageal reflux disease (GERD) in patients 1 year to 17 years, inclusive. The study must include an adequate number of patients in different pediatric age groups to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and posttreatment bone-related safety assessments must be included. This study may not be needed if the data from PMR 2054-1 are adequate to fulfill the requirement.
  - Protocol Submission Date: [redacted]
  - Study Completion Date: [redacted]
  - Final Report Submission: [redacted]

- 2054-3: Deferred pediatric study under PREA to evaluate the pharmacokinetics, pharmacodynamics, and safety of esomeprazole strontium for reducing the risk of NSAID-associated gastric ulcer in patients 2 years to 17 years, inclusive. The study must include an adequate number of patients in different age groups to inform dosing, and to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and post-treatment bone-related safety assessments must be included.
  - Protocol Submission Date: [redacted]
  - Study Completion Date: [redacted]
  - Final Report Submission: [redacted]

- 2054-4: Deferred pediatric study under PREA to evaluate the safety and efficacy of esomeprazole strontium in combination with clarithromycin and amoxicillin for the eradication of Helicobacter pylori in symptomatic pediatric patients 2 to 17 years, inclusive, with or without duodenal ulcer disease.
  - Protocol Submission Date: (b) (4)
  - Study Completion Date: (b) (4)
  - Final Report Submission: (b) (4)

The proposed timelines are intended to allow time for development of an appropriate pediatric formulation and study protocols. Belcher regrets the delay in the conduct of these studies and recognizes the importance of pediatric evaluations in drug development. We hope that the proposal above will be acceptable. If there are any questions please do not hesitate to contact me by phone 727-471-0850 Ext:250 or email me at mihirt@belcherpharma.com.

This submission is provided entirely in eCTD format; therefore, no Table of Contents is being provided. All electronic files included as the archival copy of this submission are provided via the FDA's electronic gateway. All files were checked and verified to be free of viruses using Symantec Endpoint Protection Version 14 (14.3) build 558 (14.3.558.0000).

Sincerely,

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