Nalpropion™
PHARMACEUTICALS

May 10, 2023

Lisa Yanoff, M.D., Acting Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
5901-B Ammendale Road
Beltsville, Maryland 20705-1266

Re: NDA 200063 Serial Number 0200
Naltrexone HCl and Bupropion HCl Extended-Release Tablets
Response to Notification of Non-Compliance with PREA, PMR 2778-2

Dear Dr. Yanoff:

Reference is made to Nalpropion Pharmaceuticals LLC's NDA 200063 for Contrave (naltrexone HCl and bupropion HCl) Extended-Release Tablets and the following postmarketing requirement (PMR) outlined in the September 10, 2014, approval letter for NDA 200063:

2778-2 A clinical pharmacology (Part A) followed by a 52-week randomized, double-blind and placebo-controlled pediatric study (Part B) under PREA to evaluate the pharmacokinetics, safety, and efficacy of Contrave (naltrexone/bupropion) for the treatment of obesity in pediatric patients ages 12-17 years (inclusive). Part B should not be initiated until after the data from the juvenile animal study (PMR 2778-1) have been submitted to and reviewed by the Agency.

Reference is also made to the November 23, 2022 (Seq 0195) deferral extension request and submission of the updated protocol NaltrexBuprop-3001, version 3.0 entitled, "A Phase 3, Double-Blind, Randomized, Placebo-Controlled, Multicenter, 52-Week Treatment Study to Evaluate the Efficacy and Safety of Naltrexone and Bupropion Extended Release Combination in Adolescents with Obesity". Additional reference is made to the December 23, 2023 FDA letter, denying the deferral extension and to the April 12, 2023 FDA Notification of Non-compliance with PREA letter.

Nalpropion recognizes the importance of the PREA program and remains committed to fulfilling this postmarketing requirement. Several challenges have caused delay in completing this study on time. (1) After Nalpropion's acquisition of Contrave, a contract research organization (CRO) selection was made in Q4 2020. Through the process of ensuring trial readiness and patient safety a comprehensive review of the protocol and selected CRO was performed before the study initiation. This process revealed a series of specific protocol items that required revision and clarity, and a series of quality concerns with the identified CRO. Thus, the CRO contract was terminated in Q4 2021. (2) Protocol, version 2.0, was submitted to the FDA in Q1 2022 to address FDA comments and provide clarity on the protocol safety measures: dose modifications, dose interruption periods, subject stratification, and the required PK assessment. (3) Based on the FDA comments received on protocol version 2.0, several additional modifications were needed. This was completed and the updated protocol, version 3.0, was submitted to the FDA in Q4 2022.

Nalpropion is currently in the process of negotiating an agreement with the new CRO selected to support this study. The protocol is also under revision to address the additional FDA comments received in Q1 2023. We plan to submit the revised protocol, version 4.0, to the FDA in Q3 2023. The trial will be initiated after the protocol is submitted.

If you have any questions about this submission, please feel free to contact the undersigned at (949) 463-5345 or via email at achesnut@curraxpharma.com.

Sincerely,

Aaron Chesnut

Digitally signed by Aaron Chesnut
Date: 2023.05.10 13:49:39 -05'00'

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This submission is compliant with FDA's Guideline for Industry and current eCTD specifications.

All files were checked and verified to be free of viruses prior to transmission through the Electronic Submission Gateway.

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