Ironshore Pharmaceuticals & Development, Inc.
10 Market Street, Suite 715
Camana Bay, Grand Cayman
Cayman Islands, KY1-9006

May 29, 2024

Tiffany R. Farchione, M.D.
Director, Division of Psychiatry Products
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Attn: *CDR Eugene Lee, Regulatory Project Manager*

Re: **RESPONSE TO PREA NON-COMPLIANCE LETTER**
NDA 209311; Serial# 0104
JORNAY PM® (methylphenidate hydrochloride) extended-release capsules (HLD200)

Cross Ref: **IND 118074 SN0064**

Dear Dr. Farchione:

Reference is made to Ironshore Pharmaceuticals & Development, Inc.'s (Ironshore's) New Drug Application (NDA) 209311 for JORNAY PM® (methylphenidate HCl) extended-release 20 mg, 40 mg, 60 mg, 80 mg, and 100 mg capsules for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older (SN0000). The drug was approved by FDA in August 2018, with the brand name JORNAY PM, and listed on May 20, 2019. JORNAY PM was launched in the United States in June 2019.

Reference is also made to the Notification of Non-Compliance with Pediatric Research Equity Act (PREA) dated April 23, 2024, for the PREA Postmarket Requirement (PMR) number 3465-1 and its timeline for completion, per the August 8, 2018, NDA approval letter.

The purpose of this submission is for Ironshore to provide a formal response to the above referenced PREA Non-Compliance letter. The deferred PMR including associated timelines per the August 8, 2018, NDA approval letter was as follows:

3465-1 *A Phase 3, 3-Week, Double-blind, Randomized, Placebo-controlled, Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of Evening-dosed Jornay PM (methylphenidate hydrochloride) extended-release in Children Aged 4 to 5 With Attention Deficit Hyperactivity Disorder (ADHD).*

Final Protocol Submission: 11/30/2018
Study/Trial Completion: 02/28/2020
Final Report Submission: 08/31/2020

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An extension to the deferred PMR milestone dates was requested by Ironshore on April 16, 2020 (SN0055 to IND 118074 and SN0072 to the NDA as a letter of cross-reference), citing ongoing discussion with the Agency related to protocol design and the potential impact of the COVID-19 public health emergency. The following proposed revised PMR milestone dates were accepted by FDA on June 3, 2020:

Final Protocol Submission: *July 2020*
Study/Trial Completion: *February 2023*
Final Report Submission: *August 2023*

Ironshore submitted a request for Release from the Postmarketing Requirement (PMR) 3465 1 (SN0094) on February 24, 2023, and a (PMR) Release Denied letter was issued by the Agency, on April 25, 2023. Ironshore submitted a second extension request (SN0098) to the PMR timeline on July 17, 2023 for the following clinical study:

HLD200-112 v3.0: A Phase 3, Multicenter, 3-Week Fixed-dose, Randomized, Double-blind, Placebo-controlled, Parallel-group Efficacy, Safety and Pharmacokinetic Study of Evening Dosed Methylphenidate Hydrochloride Extended-Release Capsules in Children Aged 4 to 5 Years with Attention Deficit Hyperactivity Disorder

Ironshore acknowledges the lack of study initiation once COVID-19 pandemic-related procedures and public safety measures restrictions were lifted. This was due to the financial constraints caused by insolvency leading up to NDA approval, and the higher costs post-pandemic. Ironshore was unable to execute, as stated in the formal response to the Agency submitted May 12, 2023 (SN0096) in response to the Postmarketing Requirement (PMR) Release Denied letter received on April 25, 2023. Ironshore has subsequently stabilized and rebuilt the organization, which included a financial restructuring and change in ownership/management/leadership, completed in April 2022. This restructuring was necessary following receipt of the Complete Response Letter (July 28, 2017) and delay in NDA approval and commercial product launch, which rendered the Company unable to service its extensive debt, and fund ongoing operations, including the post approval commitment study.

Ironshore is and has always been committed to conducting the study in accordance with PMR 3465-1 and fulfilling our PREA requirements, and now has the capital to do so. First patient first visit is on track for (b) (4), with completion of the study by (b) (4) and for the final clinical study report to be available by (b) (4) (NCT06431256). Clinical study plans have been finalized, the contractual agreements with the Clinical Research Organization (CRO) and Principal Investigators initiated, and ongoing identification of clinical sites is well underway. Data management and randomization and trial supply management systems have been developed. In addition, clinical trial material (drug product and placebo) has been manufactured. Ironshore is committed to fulfilling our PREA requirements and will continue to provide FDA with updates.

A letter of cross-reference regarding this response to the PREA Non-Compliance letter is also being submitted to IND 118074 (SN0064), on May 29, 2024.

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Please note that this submission does not include any of the changes described in 21 CFR 314.60(f)(1). As such, a patent certification/recertification is not included in this submission.

This submission is provided in electronic CTD (eCTD) format via the ESG. The information contained in this submission is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430. Should you have any questions regarding this submission, please contact me at 1-345-749-8174 or bev@ironshorepharma.com.

Sincerely,

DocuSigned by:
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Bev Incledon, PhD
Chief Scientific Officer/Executive VP R&D
Ironshore Pharmaceuticals & Development, Inc.
10 Market Street, Suite 715
Camana Bay, Grand Cayman
Cayman Islands KY1-9006
Mobile: 1-345-525-8174
Fax: 1-877-386-4343
email: bev@ironshorepharma.com

Electronic Submission Specifications

This submission is compliant with FDA's Guideline for Industry: *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (February 2020).

All files were checked and verified to be free of viruses.

Anti-Virus Program	Avast Business Antivirus
Program Version	24.4.2801
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The IT point of contact for this submission is:

Name	Katharine Manson
Phone Number	(905) 234-3472
Email Address	kmanson@intrinsik.com