Pharmaceutical
PROJECT SOLUTIONS INC

17 April 2025

**DEFERRAL EXTENSION REQUESTED- RESPONSE TO A PREA NON-COMPLIANCE LETTER**

Nick Kozauer, MD
Division of Neurology 2
Office of Neuroscience
Office of New Drugs
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 213436
Trudhesa (dihydroergotamine mesylate) Nasal Spray
Sequence No.: 0063
DEFERRAL EXTENSION REQUESTED- RESPONSE TO A PREA NON-COMPLIANCE LETTER

Dear Dr. Kozauer:

Reference is made to the Agency's 05March 2025 notification of PREA non-compliance for Trudhesa (dihydroergotamine mesylate) Nasal Spray, NDA 213436. Please note, Impel Pharmaceutical purchased this application In February 2024 and has conducted a full regulatory evaluation of the PREA commitments associated with requirements. As such, the following update and deferral extensions are requested:

| Description | Current Commitment | Extension Date Requested | Update/Comments |
|---|---|---|---|
| **PMR 4136-1: Juvenile animal toxicology study of the in rat Final Report Submission** | 31-Dec-24 | (b) (4) | Impel has completed the in-life study of a 90-day Toxicology Dosing Study to support shelf0life extension. This study will also provide data to support the dosing of the juvenile tox study. We anticipate filing the report from this study (b) (4). Following the issuance of this data, protocol development will be initiated for the juvenile study. |
| **PMR #4136-2: INP104-202 Phase 2, open label, single ascending dose, safety, tolerability and PK study in 6 to < 12 yr**<br><br>**Study Completion** | Dec-24 | (b) (4) | Original protocol submitted and agreed upon in September 2021. A protocol amendment will be submitted to align with current PREA strategy. |

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| **PMR# 4136-3: INP104-201 A randomized, double-blind, placebo-controlled, single-dose, efficacy and safety study in 6 to <18yr, optional open-label extension** | | | |
| **Protocol Agreement** | May-23 | No Agreement | Agreement on the protocol has not been reached. A protocol amendment will be submitted to align with current PREA strategy. |
| **Study Completion** | Jul-26 | (b) (4) | |
| **Final report Submission** | Dec-26 | | |

It should also be noted, following the acquisition of Trudhesa, an evaluation of the PREA clinical program was conducted and determined a pediatric indication will not be considered within the PREA commitment. As such, Impel is preparing to submit revised protocols (b) (4) to satisfy the commitment of PREA. These revised protocols will be submitted for Agency review and agreement as soon as available.

If you have any questions concerning this submission, or need additional information, please contact me via email at mgoodhead@pharmaprojectsolutions.com or via telephone at (813) 927-9302.

Sincerely,

Melissa L. Goodhead

Digitally signed by Melissa L. Goodhead
Date: 2025.04.17 15:30:08 -04'00'

Melissa L. Goodhead, MSc, RAC
Regulatory Agent for
Impel Pharmaceuticals LLC

# Electronic Submission Specifications

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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| **Anti-Virus Program** | Windows Security<br>CrowdStrike Falcon Sensor |
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