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25 August 2026

Emily Freilich, M.D., Director, Division of Neurology Products I (DNI)
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266

Attn: Melinda Bauerlien, M.S., Senior Regulatory Business Process Manager

BLA:	**103,846**
Sponsor:	**Solstice Neurosciences**
Product:	**MYOBLOC® (rimabotulinumtoxinB) Injection**
Submission Category:	**RESPONSE TO PREA NONCOMPLIANCE LETTER DEFERRAL EXTENSION REQUESTED**
Serial Sequence #:	**0189**

Dear Dr. Freilich,

This submission pertains to BLA 103846, MYOBLOC® (rimabotulinumtoxinB) Injection, for which marketing authorization was granted on 08 December 2000, under US License No. 1718 (STN 103846). MYOBLOC was granted Orphan Drug status for the approved indication: the treatment of adult patients to reduce the severity of abnormal head position and neck pain associated with cervical dystonia and for the treatment of chronic sialorrhea in adults.

Per approval of S-5190 for the treatment of chronic sialorrhea in adults, the sponsor is required to assess the safety and effectiveness of MYOBLOC for the claimed indication in pediatric patients under the Pediatric Research Equity Act (PREA). Cross reference is made to IND 100454, under which studies SN-SIAL-302 and SN-SIAL-352 were submitted to comply with the post-marketing requirements (PMRs).

Post Marketing Requirements (PMRs):

PMR 3687-1

A randomized, double-blind, placebo-controlled, dose-response study in pediatric subjects 3 to less than 17 years of age with chronic troublesome sialorrhea. Subjects will be randomized to receive a single injection session of low-dose MYOBLOC, high-dose MYOBLOC, or placebo. Children ages 6 to less than 17 years of age will be enrolled first. Study SN-SIAL-302: A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled, Single-treatment Efficacy and Safety Study of MYOBLOC for the Treatment of Chronic Sialorrhea in Pediatric Subjects was to be conducted to satisfy this PMR.

PMR 3687-2

"A long-term, open-label safety and efficacy study in pediatric subjects 3 to less than 17 years of age with chronic troublesome sialorrhea that will follow the randomized, double-blind, placebo-controlled study. The long-term safety study needs to include information from at least 100 patients treated with MYOBLOC for chronic sialorrhea for 4 consecutive treatments over approximately 1 year, with at least 50 of these patients treated with the highest dose of MYOBLOC recommended in the label. Submit an interim report for the long-term safety study, for safety information from pediatric patients ages 6 to < 17-years-old treated with MYOBLOC for sialorrhea for 4 consecutive treatments." Study SN-SIAL-352: A Phase 3, Multicenter, Long-term, Open-label Safety, Tolerability, and Efficacy Study of MYOBLOC for the Treatment of Chronic Sialorrhea in Pediatric Subjects was to be conducted to satisfy this PMR.

The Status of PMRs 3687-1 and 3687-2

Solstice received the FDA acknowledgment of the final protocols for SN-SIAL-302 and SN-SIAL-352 in December 2019, along with the agreed-upon PMR timelines. Planning and study start-up activities for both SN-SIAL-302 and SN-SIAL-352 have been suspended, and no subjects have been enrolled.

On July 21, 2023, Solstice received a communication from the FDA requesting further information regarding the suspension of activities for the PREA studies PMR 3687-1 and 3687-2, as referenced in the Annual Report, and our plans to address these PREA requirements. In our August 7, 2023, response, Solstice stated that the company had been focusing on the PMR/PMC related to spasticity (PMR 2324-9 and PMC 2324-10) as these are safety related (based on concerns about distal spread of the toxin) and were perceived to be more critical than the ones for pediatric extension that is the purpose of PMR 3687-1 and PMR 3687-2, and further that there was a shortage of product which made initiation of these studies impossible. The response concluded that Solstice would like to discuss alternative approaches with the FDA to address the PMRs in lieu of the studies described to satisfy the post-approval study requirements.

To address the FDA's concerns, Solstice submitted a Type C meeting request (Sequence 0163) on August 09, 2024, to discuss the status of these postmarketing requirements. On December 12, 2024, Solstice Neurosciences received notification of non-compliance for PMR 3687-1 of the PREA for pediatric assessment for this application. The written response to the questions for the meeting request was received by email on January 29, 2025. In the response, the agency stated (b) (4) would not satisfy the pediatric sialorrhea requirements of PMR 3687-1 and PMR 3687-2. The proposed study was insufficient for the agency to independently evaluate the efficacy and safety of the product in the treated population. In addition, these studies often lack sufficient rigor and clinical meaningfulness. Most recently, the FDA sent a Notification of Non-Compliance With PREA letter for PMR 3687-2 to Solstice on July 17, 2026.

Deferral Extension Request for PREA PMR 3687-1 and PMR 3687-2

We reported the drug shortage to the Agency on December 20, 2024, and drug product stock out on January 16, 2025. In addition, we reported drug shortage to the Agency on April 9, 2026, and drug product stock out on April 17, 2026. A temporary resolution of the stock-out situation has occurred. We released a supply of the 0.5 mL presentation to the market on July 28, 2026, which will supply the market for 6-8 weeks. (b) (4). There will still be a shortage of all presentations of the drug product for the foreseeable future. Our priority is the continuity of care for patients currently on MYOBLOC therapy, as well as maintaining this drug as an option for new patients in need. Therefore, due to the uncertain supply of this drug, we are unable to initiate clinical studies at this time; as a result, Solstice is requesting a deferral extension for PMR 3687-1, and PMR 3687-2.

PMR 3687-1

FDA Agreed Timeline from the August 20, 2019, Supplement Approval Letter:

Draft Protocol Submission: Submitted 11/2017
Final Protocol Submission: 12/2019
Study/Trial Completion: 06/2023
Final Report Submission: 12/2023

Proposed PMR 3687-1 Timeline:

Draft Protocol Submission: Submitted 11/2017
Final Protocol Submission: 12/2019
Trial Completion: 06/2033
Final Report Submission: 12/2033

PMR 3687-2

FDA Agreed Timeline from the August 20, 2019, Supplement Approval Letter:

Draft Protocol Submission: Submitted 11/2017
Final Protocol Submission: 12/2019
Interim Report: 12/2023
Study/Trial Completion: 06/2024
Final Report Submission: 12/2024

Proposed PMR 3687-2 Timeline:

Draft Protocol Submission: Submitted 11/2017
Final Protocol Submission: 12/2019
Interim Report: 12/2033
Trial Completion: 06/2034
Final Report Submission: 12/2034

This submission contains materials for one module:

Module 1: Administrative Information including:
Cover letter
Form FDA 356h

Solstice requests that all information in this file be treated as confidential to the extent possible in accordance with 21 CFR 20.61, and that no information from this file may be provided to any unauthorized people without our written consent.

Please contact Joseph Duran, Senior Manager, Regulatory Affairs, or Terri Valentine, Director, Regulatory Affairs, at (301) 838-2610 or regulatory@supernus.com with any questions regarding this submission.

Sincerely,

Joseph Duran

Digitally signed by Joseph Duran
Date: 2026.08.21 16:03:13 -04'00'

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