15 May 2024

RESPONSE TO PREA NON-COMPLIANCE LETTER
DEFERRAL EXTENSION REQUESTED

Paul R. Lee, MD, PhD
Director, Division of Neurology 2
Office of Neuroscience
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 212,157 / Serial No. 0098
Elyxyb® (celecoxib oral solution)
RESPONSE TO PREA NON-COMPLIANCE LETTER
DEFERRAL EXTENSION REQUESTED

Dear Dr. Lee,

Reference is made to NOTIFICATION OF NON-COMPLIANCE WITH PREA (Notification) received on April 3, 2024, for postmarketing requirement (PMR) 3838-1 pertaining to submission of a pediatric assessment to the new drug application (NDA) 212,157 for Elyxyb® Oral Solution (lab code SP-105). The Notification stated that the submission for the pediatric assessment was deferred until August 31, 2023. Reference is also made to NDA SN0041 submitted on Dec 21, 2020, by the previous sponsor (Dr Reddy Laboratories) notifying that the clinical study associated with the PMR 3831-1 was placed on indefinite hold due to the Coronavirus Disease 2019 (COVID-19) epidemic and associated hardship in conducting pediatric clinical studies. Reference is made to NDA SN0065 submitted on February 20, 2023, where ownership of the NDA was accepted by Scilex Pharmaceuticals Inc. (Scilex).

Upon transfer of the NDA, Scilex reviewed the indefinite hold pertaining to PMR 3838-1 and concluded that (1) the PMR needs to be satisfied, (2) COVID-19 is no longer a significant impediment to conducting pediatric clinical studies, and (3) considering subjects safety it would be prudent to conduct a preceding open-label, single-dose pediatric pharmacokinetic (PK) and safety study ((b) (4)) to assess modeling-based proposed dosing for the pediatric efficacy study identified in the PMR: A Randomized, Double-blind, Placebo-controlled, Efficacy and Safety Study to Evaluate Elyxyb Oral Solution Compared to Placebo in the Treatment of Acute Migraine in Pediatric Patients Ages 6 to Less Than 18 Years ((b) (4)).

Specifically, the proposed efficacy study identified the following weight-based doses:

- (b) (4)

While the rationale for the proposed dosing is sound, it is based on extrapolation from adult PK data without confirmatory assessment in pediatric subjects. In the absence of any pediatric PK data, the outcomes from an efficacy study may be uninterpretable. Also, the lack of safety data from a smaller preceding study does not allow for the identification of potential population-specific adverse events of special interest (AESIs) in the efficacy study. Otherwise, the efficacy study will have to assume that the adverse events (AEs) observed for adults will be the same for pediatric subjects.

Therefore, we propose that a pediatric PK and safety study (Study (b) (4)) is conducted first to determine and confirm the predicted population-specific PK and establish a safety and effectiveness profile in an open-label setting. The study will allow for the design of the efficacy study to better meet its endpoints and provide population-specific PK for the label.

Study (b) (4) is designed as a Phase 1, multicenter, open-label, study to determine the PK, safety, tolerability, and effectiveness of SP-105 in pediatric subjects previously diagnosed with migraine (with or without aura). Pediatric subjects would first enter into the PK portion of the study where single-dose PK and safety are evaluated and then enter into an open-label extension phase to evaluate effectiveness of the product in the pediatric population.

(b) (4)

The (b) (4) trial protocol is provided in Attachment 1.

Once completed, the design of the efficacy study (b) (4) will be revisited and updated based on outcomes from (b) (4) and submitted to the NDA for agreement relative to the PMR 3838-1 commitment.

Therefore, further deferment is requested to allow for the conduct of SP-105 pediatric drug development program. The revised timelines are as follows:

Protocol submission to IND 125585 (Study SP-105-01):	10/2024
Study completion (Study SP-105-01):	08/2027
Final report submission (Study SP-105-01):	02/2028

Protocol submission to IND 125585 (Study SP-105-02):	06/2028
Study completion (Study SP-105-02):	12/2032
Final report submission (Study SP-105-02):	06/2033

Please do not hesitate to contact me if you have any questions or require further information. I can be reached at the phone number and email address provided below. Alternatively, you may contact Fedra Molaie-Holagh, Regulatory Consultant to Scilex Pharmaceuticals Inc. at (510) 767-0054 or at fedra.molaie-holagh@premierconsulting.com

Sincerely,

DocuSigned by:
Dmitri Lissin
Signer Name: Dmitri Lissin
Signing Reason: I approve this document
Signing Time: 15-May-2024 | 10:41:00 PDT
[illegible]A2E12A7E

Dmitri Lissin MD
Chief Medical Officer
Scilex Pharmaceuticals Inc
Phone: (650) 430-3238
Fax: (650) 397-6759
E-mail: dlissin@scilexpharma.com

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Technical Point of Contact

Annette Arlinghaus or Daniel Quach
Premier Consulting
8000 Jarvis Avenue, Suite 100
Newark, CA 94560
Office Number: 408-263-6861 x222
Fax: 1-408-263-1231
Email: regops@premierconsulting.com