NDA 216190

COMPLETE RESPONSE

Fidelity BioPharma Co.
Attention: Song Lin, Chief Executive Officer
157 Church Street, Suite 1915
New Haven, CT 06510

Dear Song Lin:

Please refer to your new drug application (NDA) dated May 31, 2023, received May 31, 2023, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Ontralfy (tizanidine) oral solution, 2 mg/5 mL.

We also acknowledge receipt of your amendment dated March 7, 2024, which was not reviewed for this action. You may incorporate applicable sections of the amendment by specific reference as part of your response to the deficiencies cited in this letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

PRODUCT QUALITY

Drug Substance

1. We acknowledge the response that you provided on February 8, 2024, for the Agency's (b) (4) information request dated November 29, 2023. While we have not performed an in-depth review, in the response, you stated that there is no potential for the formation of (b) (4) (b) (4) per Sun Pharma's overall review of the synthetic scheme and manufacturing process for the drug substance. However, your conclusion was not made based on a proper application of the (b) (4) guidance.

   You determined that the (b) (4) score is not applicable because the (b) (4) is bonded to a (b) (4) and is thus out of scope of (b) (4) Therefore, the determination requires the use of alternative methods for establishing an acceptable intake (AI) limit. We recommend that you work with the drug master file (DMF) holder to establish an appropriate AI limit for

control of (b) (4) that may be found in the active pharmaceutical ingredient (API).

Process

(b) (4)

NONCLINICAL

The information provided is not adequate to support the proposed specification of NMT (b) (4)% for (b) (4) which would result in a maximum daily intake (b) (4)mg) of (b) (4) that exceeds the qualification threshold, as recommended in guidance (ICH Q3B(R2), August 2006). The OECD SIDS Initial Assessment Report on (b) (4) upon which you rely, contains only a summary of the available information on (b) (4) To address this deficiency, you would need to lower the specification consistent with guidance or provide additional data to support the specification of NMT (b) (4)%.

PRESCRIBING INFORMATION

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources and Pregnancy and Lactation Labeling Final Rule[1] websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.

CARTON AND CONTAINER LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate.

PROPRIETARY NAME

Please refer to correspondence dated, August 24, 2023, which addresses the proposed proprietary name, Ontralfy. This name was found conditionally acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to all of the application deficiencies that have been identified in this letter.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(*b*). The safety update should include data from all nonclinical and clinical studies/trials of the drug/product under consideration regardless of indication, dosage form, or dose level.

(1) Describe in detail any significant changes or findings in the safety profile.

(2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

- Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
- Present tabulations of the new safety data combined with the original/supplemental application data.

- Include tables that compare frequencies of adverse events in the original supplemental application with the retabulated frequencies described in the bullet above.

- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

(3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

(4) Provide case report forms and narrative summaries for each subject who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.

(5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original/supplemental application data.

(6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

(7) Provide a summary of worldwide experience on the safety of this drug/product. Include an updated estimate of use for drug/product marketed in other countries.

(8) Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting,

submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, contact Amy Bolger, Regulatory Project Manager, at Amy.Bolger@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Laura Jawidzik, MD
Deputy Director
Division of Neurology 1
Office of Neuroscience
Office of New Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LAURA A JAWIDZIK
03/29/2024 12:50:44 PM