NDA 209321/Original 1

CONVERSION to NDA TENTATIVE APPROVAL

Jacobus Pharmaceutical Company, Inc.
Attention: Laura R. Jacobus
Vice President & Director of Quality Assurance
37 Cleveland Lane, P.O. Box 5290
Princeton, NJ 08540

Dear Ms. Jacobus:

We refer to your new drug application (NDA) 209321 for Ruzurgi (amifampridine) 10 mg tablets, dated and received on June 15, 2018, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FFDCA). Your new drug application provided for the use of Ruzurgi (amifampridine) tablets for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adult patients (patients 17 years of age or older) and in pediatric patients (patients 6 to less than 17 years of age). For administrative purposes, we designated your NDA as follows:

- NDA 209321/Original 1 (Treatment of Lambert-Eaton myasthenic syndrome (LEMS) in patients 6 to less than 17 years of age)
- NDA 209321/Original 2 (Treatment of Lambert-Eaton myasthenic syndrome (LEMS) in patients 17 years of age or older)

The subject of this correspondence is NDA 209321/Original 1, which was approved for the treatment of LEMS in patients 6 to less than 17 years of age on May 6, 2019. We are writing to inform you that, consistent with the Court of Appeals for the Eleventh Circuit's September 30, 2021, decision in favor of Catalyst Pharmaceuticals, Inc. (hereafter referred to as Catalyst), FDA hereby converts the final approval of NDA 209321/Original 1 to a tentative approval.

Due to the 7-year orphan-drug exclusivity (ODE) for Catalyst's product, Firdapse (NDA 208078), your application for Ruzurgi for the treatment of LEMS in patients 6 to less than 17 years of age (NDA 209312/Original 1) may not be finally approved for marketing under section 505 of the FFDCA until the period of exclusivity has expired. This action conforms the NDA's status to the court's final judgment, as described in detail below.

Catalyst obtained orphan-drug designation for amifampridine phosphate on November 12, 2009, for "treatment of Lambert-Eaton myasthenic syndrome." Catalyst's NDA 208078 for Firdapse (amifampridine) tablets was approved on November 28, 2018, for

the treatment of LEMS in adults. It received 5-year new chemical entity (NCE) exclusivity. It was also eligible for ODE, which expires on November 28, 2025.

On May 6, 2019, your NDA for Ruzurgi (amifampridine) tablets, which had been administratively split, as described above, was approved for the treatment of LEMS in patients 6 to less than 17 years of age (NDA 209321/Original 1) and tentatively approved for the treatment of LEMS in adults, i.e., patients 17 years of age or older (NDA 209321/Original 2). NDA 209321/Original 2 was tentatively approved due to the ODE for Firdapse, which precludes final approval of that application, Original 2, for marketing under section 505 of the FFDCA until the period of exclusivity has expired.

FDA's regulations that implement the Orphan Drug Act specify, at 21 CFR 316.31(b), that orphan drug exclusive approval protects only the approved indication or use of an orphan designated drug. If such approval is limited to only particular indication(s) or use(s) within the rare disease for which the drug was designated, FDA may later approve the drug for additional use(s) or indication(s) within the rare disease or condition not protected by the exclusive approval.

In accordance with this regulation, FDA did not, therefore, consider the approval of NDA 209321/Original 1, for the treatment of LEMS in patients 6 to less than 17 years of age, to be blocked by Firdapse's ODE, because the scope of ODE for Firdapse was limited to the use of amifampridine for the approved indication for Firdapse, i.e., for the treatment of LEMS in adults.

On June 12, 2019, Catalyst brought suit against the FDA, challenging FDA's approval of Ruzurgi for the treatment of LEMS in patients 6 to less than 17 years of age on grounds that, among other things, the plain language of the Orphan Drug Act prohibited FDA from approving Ruzurgi, because it is the same drug as Firdapse and treats the same disease or condition as Firdapse.

The US District Court for the Southern District of Florida ruled in FDA's favor, but the Court of Appeals for the Eleventh Circuit reversed the district court's decision and directed the district court to enter judgment for Catalyst. The court concluded that the statutory phrase "same disease or condition" contained in the Orphan Drug Act is not ambiguous, and that FDA's approval of Ruzurgi was contrary to that unambiguous language.

On January 7, 2022, the Eleventh Circuit Court denied a petition for rehearing *en banc*.

On January 18, 2022, and January 20, 2022, the United States Supreme Court and the Eleventh Circuit Court, respectively, denied motions to stay issuance of the mandate. The mandate was issued on January 28, 2022, and the district court entered judgment for Catalyst on January 31, 2022. Accordingly, FDA is converting your final approval NDA 209321/Original 1 to a tentative approval.

Final Approval

To obtain final approval of this application, submit an amendment two or six months prior to the: (1) expiration of the exclusivity protection or (2) date you believe that your NDA will be eligible for final approval, as appropriate. In your cover letter, clearly identify your amendment as **"REQUEST FOR FINAL APPROVAL"**. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of any relevant court order or judgment settlement, or licensing agreement, as appropriate. In addition to a safety update, the amendment should also identify changes, if any, in the conditions under which your product was tentatively approved, i.e., updated labeling; chemistry, manufacturing, and controls data; and risk evaluation and mitigation strategy (REMS). If there are no changes, clearly state so in your cover letter. Any changes require our review before final approval and the goal date for our review will be set accordingly.

Until we issue a final approval letter, this NDA is not approved.

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

If you have any questions, contact Michelle Mathers, Regulatory Project Manager, at michelle.mathers@fda.hhs.gov or at (240) 402-2645.

Sincerely,

{See appended electronic signature page}

Teresa Buracchio, MD
Director
Division of Neurology 1
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use

19 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

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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/

TERESA J BURACCHIO
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