



NDA 212725/S-006

**SUPPLEMENT APPROVAL/  
FULFILLMENT OF POSTMARKETING  
COMMITMENTS**

Genentech, Inc.  
Attention: Sonia De Rubeis  
Regulatory Program Management  
1 DNA Way  
South San Francisco, CA 94080

Dear Ms. De Rubeis:<sup>1</sup>

Please refer to your supplemental new drug application (sNDA) dated and received June 17, 2022, and your amendments, submitted under section 505(b) the Federal Food, Drug, and Cosmetic Act (FDCA) for Rozlytrek (entrectinib).

This Prior Approval sNDA provides for updates to Section 1 INDICATIONS AND USAGE and Section 2 DOSAGE AND ADMINISTRATION of the Rozlytrek (entrectinib) US Prescribing Information (PI) making reference to an FDA-approved companion diagnostic which also supports the fulfillment of Postmarketing Commitments 3686-6 and 3689-8. This supplement also provides for changes in the storage conditions described in Section 16 HOW SUPPLIED/STORAGE AND HANDLING as well as other relevant sections of the Patient Information and carton and container label.

**APPROVAL & LABELING**

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

**WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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<sup>1</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.<sup>2</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Information), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>3</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

## **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

## **FULFILLMENT OF POSTMARKETING COMMITMENTS**

We have received your submission dated September 17, 2021, containing the final report for the following postmarketing commitments listed in the August 15, 2019, approval letters for NDA 212725 and NDA 212726.

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<sup>2</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>3</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

- 3686-6 Commit to providing adequate analytical and clinical validation results from clinical trial data to support labeling of the F1CDx test to detect ROS1 rearrangements for identifying patients who may benefit from entrectinib. The analytical validation should consist of precision, limit of detection, and accuracy studies for the ROS1 indication. The clinical validation should be supported by a clinical bridging study comparing F1CDx and the clinical trial enrollment assays.
- 3689-8 Commit to providing adequate analytical and clinical validation results from clinical trial data to support labeling of the F1CDx test to detect NTRK rearrangements for identifying patients who may benefit from entrectinib. The analytical validation should consist of precision, limit of detection, and accuracy studies for the NTRK indication. The clinical validation should be supported by a clinical bridging study comparing F1CDx and the clinical trial enrollment assays.

We have reviewed your submission and conclude that the above commitments were fulfilled.

We remind you that there are postmarketing requirements listed in the August 15, 2019, approval letters that are still open.

### **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Maryam Khazraee, Regulatory Health Project Manager, at 301-796-7119.

Sincerely,

*{See appended electronic signature page}*

Steven Lemery, M.D., M.H.S.  
Director  
Division of Oncology 3  
Office of Oncologic Diseases  
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Information

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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.**  
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/s/  
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STEVEN J LEMERY  
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