NDA 212725 5 G

UPPLEMENT APPROVAL/
FULFILLMENT OF PO STMARKETING
REQUIREMENT/COMMITMENT

G e nentech, Inc.
Attention: onia De Rubeis G
Regulatory Program Management
1 DNA Way
outh an Francisco, CA 94 8

Dear Ms. De Rubeis:[1]

Please refer to your supplemental new drug application (sNDA) dated and received June 3 2 21, and your amendments, submitted under section 5 5(b) the Federal Food, Drug, and Cosmetic Act (FDCA) for Rozlytrek (entrectinib).

This Prior Approval sNDA provides for updates to ection 5 WARNIN AND PRECAUTION and ection 14 CLINICAL TUDIE of the U Prescribing Information (PI) based on the final study reports and datasets for Postmarketing Requirement 3689 1 and Postmarketing Commitment 3686 5 as well as other administrative updates to both the PI and the Patient Information.

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 HIGHLIGHT

Please note that we have previously granted a waiver of the requirements of 21 CFR 2 1.57(d)(8) regarding the length of Highlights of Prescribing Information.

[1] We update guidances periodically. For the most recent version of a guidance, check the FDA idance Documents Database https: www.fda.gov RegulatoryInformation idances 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 314.5 (l)] in structured product labeling (L) format using the FDA automated drug registration and listing system (eLI T), as described at FDA.gov.[2] Content of labeling must be identical to the enclosed labeling (text for the rescribing 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 L files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[3]

The L 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 314.5 (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 h ediatr c Resea h Eq ity Act (REA) (21 U. .C. 355), a l pplicati ns for new ctiv i gre ients (which includes new salts and new ixed combin tions), n w indi ations, n w dos ge forms, new dosing regimen , or n w rou of administration a requir to on ain an a se sment of the safe y and e f ctivene of the product for the claimed indication in pediatric patients nle s this requirement is waived, defe red, or in pplicabl .

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

FULFILLMENT OF POSTMARKETING REQUIREMENT/COMMITMENT

We have received your submission dated June 21, 2 21, containing the final report for the following postmarketing requirement and commitment listed in the August 15, 2 19, approval letters.

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[2] http: www.fda.gov ForIndustry Data tandards tructured roductLabeling default.htm

[3] 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.

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3689 1 S ubmit the final report, including datasets, from the first 54 patients with NTRK fusion solid tumors enrolled across the ALKA, TARTRK 1 [NCT 2 9781], and TARTRK 2 [NCT 2568267] studies to verify and describe the clinical benefit and further characterize the duration of response in patients who achieved a complete or partial response to entrectinib. All responding patients will be followed for at least 2 years from the onset of response or until disease progression, whichever comes first. Duration of response will be assessed by independent central review.

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3686 5 ubmit a report, including datasets, of clinical studies that further characterize the clinical benefit of entrectinib for the treatment of adult patients with RO S1 fusion positive metastatic N CLC by providing a more precise estimation of the BICR assessed overall response rate (ORR) and duration of response (DOR) in 92 RO S1 TKI naive patients with RO S1 positive N CLC and measurable disease enrolled across the ALKA, TARTRK 1 [NCT 2 9781] and TARTRK 2 [NCT 2568267] studies. rovide updated DOR results for the 4 responders in the efficacy evaluable population of 51 patients (primary analysis population) and for the additional 27 responders among the 41 additional patients with RO S1 positive N CLC with measurable disease as of the original data cut off date for the NDA. This report will be submitted after all responders have been followed for at least 18 months from the date of initial response.

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

We remind you that there are postmarketing requirements and or postmarketing commitments listed in the August 15, 2 19, approval letters that are still open.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.8 and 314.81).

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If you have any questions, call Maryam Khazraee, Regulatory Health roject Manager, at 3 1 796 7119.

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incerely,

{See appended electronic signature page}

Lola Fashoyin Aje, M.D., M. .H i
Deputy Director
Division of Oncology 3
Office of Oncologic Diseases
Center for Drug Evaluation and Research
Center for Drug Evaluation and Research i

ENCLO SURE :

- Content of Labeling

This is a r r s a i f a A l c r ic r c rd ha was sig d l c r ically. F ll wi g his ar ma if s a i s f a y a d all l c r ic sig a ur s f r his l c r ic r c rd.

/s/ A

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