DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 210496

**NDA APPROVAL**

Array BioPharma Inc.
Attention: Margie Vargo
Vice President, Regulatory Affairs
100 Cambridge Park Drive, Suite 505
Cambridge, MA 02140

Dear Ms. Vargo:

Please refer to your New Drug Application (NDA) dated June 30, 2017, received June 30, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Braftovi (encorafenib) capsules, 50 mg and 75 mg.

This new drug application provides for the use of Braftovi (encorafenib) 50 mg and 75 mg capsules, in combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

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 text.

## 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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the prescribing information and text for the Medication Guide. 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*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels **and** carton and immediate container labels that were submitted to the NDA on **May 25, 2018**, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 210496."** Approval of this submission by FDA is not required before the labeling is used.

## DATING PERIOD

The dating period for encorafenib shall be 15 months from the date of manufacture when stored at 20-25°C (68-77°F) with excursions permitted between 15-30°C (59-86°F). The retest dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored at below (b) (4) C.

## ADVISORY COMMITTEE

Your application for encorafenib was not referred to an FDA advisory committee because this is not the first drug in its class and there were no novel issues identified that would benefit from the Advisory Committee's expertise.

## 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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

## POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

3440-1 Conduct a clinical pharmacokinetic trial to evaluate the effect of repeat doses of a moderate CYP3A4 inducer on the repeat dose pharmacokinetics of encorafenib to assess the magnitude of decreased encorafenib exposure and to determine appropriate dosing recommendations. Design and conduct the trial in accordance with the FDA Guidance for Industry entitled, *Clinical Drug Interaction Studies* –

*Study Design, Data Analysis, and Clinical Implications*
(https://www.fda.gov/downloads/drugs/guidances/ucm292362.pdf).

The timetable you submitted on May 17, 2018, states that you will conduct this study according to the following schedule:

| | |
|---|---|
| Final Protocol Submission: | 07/2018 |
| Trial Completion: | 12/2022 |
| Final Report Submission: | 12/2023 |

3440-2 Conduct a clinical trial to evaluate the effect of repeat doses of encorafenib on the single dose pharmacokinetics of sensitive substrates of CYP1A2, CYP2B6, CYP2C9, CYP2D6, and CYP3A4 to assess the magnitude of exposure change for sensitive substrates of the above CYP enzymes and to determine appropriate dosing recommendations. Design and conduct the trial in accordance with the FDA Guidance for Industry entitled *Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications* (https://www.fda.gov/downloads/drugs/guidances/ucm292362.pdf).

The timetable you submitted on May 17, 2018, states that you will conduct this study according to the following schedule:

| | |
|---|---|
| Final Protocol Submission: | 07/2018 |
| Trial Completion: | 12/2022 |
| Final Report Submission: | 12/2023 |

3440-3 Submit the final clinical study report at the time of the final analysis of Trial CMEK162B2301 entitled, "A 2-part phase III randomized, open label, multicenter study of LGX818 plus MEK162 versus vemurafenib and LGX818 monotherapy in patients with unresectable or metastatic BRAF V600 mutant melanoma," to update the label with mature overall survival data.

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| Trial Completion: | 3/2022 |
| Final Report Submission: | 3/2023 |

Submit clinical protocols to your IND 113850 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **"Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."**

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the prescribing information and Medication Guide to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

## METHODS VALIDATION

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

## REPORTING REQUIREMENTS

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

## MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

## POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application, within two weeks of receipt of this letter.

If you have any questions, call Anuja Patel, Lead Regulatory Project Manager, at (301) 922-6512.

Sincerely,

*{See appended electronic signature page}*

Richard Pazdur, M.D.
Director
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
Carton and Container Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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RICHARD PAZDUR
06/27/2018