DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 208772/S-004

SUPPLEMENT APPROVAL
FULLFILLMENT OF POSTMARKETING
REQUIREMENT AND COMMITMENT

ARIAD Pharmaceuticals Inc.
Attention: Guilin Huang, M.B.A., R.A.C.
Director, Regulatory Affairs
40 Landsdowne St.
Cambridge, MA 02139

Dear Ms. Huang:

Please refer to your Supplemental New Drug Application (sNDA) dated and received February 23, 2018, received and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ALUNBRIG (brigatinib) tablets, 30, 90 or 180 mg.

We also refer to our June 13, 2018 and October 1, 2018, correspondences, wherein we provided notification that postmarketing requirements (PMR) 3190-2 and 3190-4, and commitment (PMC) 3190-6, were fulfilled, and that the proposed changes to the brigatinib prescribing information based on studies to support these postmarketing requirements and commitment would be determined under this supplement (S-004).

This Prior Approval supplemental new drug application provides for the following changes to the U.S. prescribing information:

- To revise the Dosage and Administration, Dosage Modification for Strong or Moderate CYP3A Inhibitors (2.3) subsection, the Drug Interactions, Effect of Other Drugs on ALUNBRIG (7.1) subsection and the Clinical Pharmacology, Pharmacokinetics (12.3) subsection to recommend that patients avoid co-administration with a moderate CYP3A inhibitor during treatment with ALUNBRIG;

- To add a new subsection, Dosage Modifications for Moderate CYP3A Inducers (2.4) to the Dosage and Administration section; and to revise the Drug Interactions, Effect of Other Drugs on ALUNBRIG (7.1) subsection and the Clinical Pharmacology, Pharmacokinetics (12.3) subsection to recommend that patients avoid co-administration with a moderate CYP3A inducer during treatment with ALUNBRIG;

- To add a new subsection, Dosage Modifications for Patients with Hepatic Impairment (2.5) to the Dosage and Administration subsection, and to revise the Use in Specific

Populations, Hepatic Impairment (8.6) subsection and the Clinical Pharmacology, Pharmacokinetics (12.3) subsection to describe dosage modifications for patients with severe hepatic impairment;

- To add a new subsection, Dosage Modifications for Patients with Renal Impairment (2.6) to the Dosage and Administration section, and to revise the Use in Specific Populations, Renal Impairment (8.7) subsection and the Clinical Pharmacology, Pharmacokinetics (12.3) subsection to describe dosage modifications for patients with severe renal impairment; and,

- To update the Clinical Studies (14) section with updated duration of intracranial response data.

In addition, this supplement updates the corresponding portions of the Highlights section and Patient Information based on the above changes.

APPROVAL & LABELING

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

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 Patient Package Insert), 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

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 REQUIREMENT(S)/COMMITMENT(S)

Approval of this supplement fulfills the following postmarketing requirement and commitment listed in the April 28, 2017, approval letter for NDA 208772:

3190-3 Complete a clinical pharmacokinetic trial to determine an appropriate dose of brigatinib to minimize toxicity in patients with renal impairment.

Trial Completion:	September 2017
Final Report Submission:	June 2018

3190-5 Submit the final analysis of intracranial response duration based upon independent radiology reviewer assessment of imaging data collected for two years following the date of enrollment of the last patient in Study AP26113-13-201.

Trial Completion:	September 2017
Final Report Submission:	March 2018

We have reviewed your submission and conclude that the above requirement was fulfilled. You are no longer required to report on this requirement (PMR 3190-3) and on this commitment (PMC 3190-5).

We remind you that there are additional postmarketing requirement (PMR 3190-1) and commitment (PMC 3190-7) listed in the April 28, 2017, original NDA approval letter, that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the Prescribing Information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
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).

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. 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.

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 Leah Her, Senior Regulatory Health Project Manager, at (240) 402-6611.

Sincerely,

{See appended electronic signature page}

Jeffrey Summers, M.D.
Deputy Director of Safety
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Prescribing Information
Patient Package Insert

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/

JEFFERY L SUMMERS
12/21/2018