DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203469/S-009

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

ARIAD Pharmaceuticals
Attention: Andrew Slugg
Executive Director, Regulatory Affairs
26 Landsdowne Street
Cambridge, MA 02139-4234

Dear Mr. Slugg:

Please refer to your Supplemental New Drug Application (sNDA) dated January 24, 2014, received January 24, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Iclusig® (ponatinib) 15 mg and 45 mg tablets for oral use.

We acknowledge receipt of your amendments dated February 3, 2014, March 25, 2014, and July 21, 2014.

This "Prior Approval" supplemental new drug application proposes revisions to include information from the clinical pharmacology studies in the label.

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.

We note that your July 21, 2014, submission includes final printed labeling (FPL) for your package insert, and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

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 package insert, text for the patient package insert, Medication Guide), 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 includes 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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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, 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(s) 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 REQUIREMENTS

We have received your submission dated December 30, 2013, containing the final reports for the following postmarketing requirements listed in the December 14, 2012, approval letter for NDA 203469.

PMR 1984-2

Conduct a dedicated drug interaction trial in humans to determine the effect of co-administration of the strong CYP3A4 inducer, rifampin, on the pharmacokinetics of Iclusig™ (ponatinib) in healthy subjects.

Final Protocol Submission:	06/2012
Trial Completion:	06/2013
Final Report Submission:	12/2013

PMR1984-3

Conduct a dedicated clinical trial in humans to determine the effect of multiple doses of lansoprazole on the pharmacokinetics of Iclusig™ (ponatinib) in healthy subjects.

Final Protocol Submission:	06/2012
Trial Completion:	06/2013
Final Report Submission:	12/2013

PMR 1984-5

Characterize the effect of Iclusig™ (ponatinib) on platelet function by evaluating the effect of Iclusig™ (ponatinib) on platelet aggregation *in vitro*.

Final Protocol Submission:	02/2013
Trial Completion:	09/2013
Final Report Submission:	12/2013

PMR 1984-6

Evaluate the in vitro potential for the displacement of Iclusig™ (ponatinib), at a therapeutic concentration, from its protein binding sites in human plasma following addition of frequently used, highly protein-bound co-medications. Positive findings from this in vitro study may require additional trials in vivo.

Draft Protocol Submission:	02/2013
Final Protocol Submission:	04/2013
Study Completion:	01/2014
Final Report Submission:	03/2014

PMR 1984-7

Conduct a dedicated hepatic impairment trial, since drug clearance may be reduced with hepatic impairment (i.e., Child-Pugh classes A, B and C) on the pharmacokinetics of ponatinib when compared to healthy subjects.

Final Protocol Submission:	06/2012
Trial Completion:	06/2013
Final Report Submission:	12/2013

We have reviewed your submissions and conclude that the above requirements were fulfilled.

We remind you that there are postmarketing requirements listed in the December 14, 2012, and December 20, 2013, approval letters 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 package insert(s) to:

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

You must submit final promotional materials and package insert(s), 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 CAPT Diane Hanner, Regulatory Project Manager, at (301) 796-4058.

Sincerely,

{See appended electronic signature page}

Robert Kane, M.D.
Deputy Director for Safety
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling

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

/s/

ROBERT C KANE
07/24/2014