DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202429/S-002 and S-003

SUPPLEMENT APPROVAL

Hoffmann-La Roche, Inc.
Attention: Irene Figari
Regulatory Program Management
1 DNA Way, MS #241B
South San Francisco, CA 94080

Dear Ms. Figari:

Please refer to your Supplemental New Drug Applications (sNDAs) dated October 17, 2012, and December 13, 2012, received October 18, 2012, and December 14, 2012, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zelboraf (vemurafenib) tablets; 960 mg.

We acknowledge receipt of your amendments dated May 8, 2013 and June 25, 2013 for each supplement.

S-002: The "Prior Approval" supplemental new drug application provides for the following changes to the package insert:

- DRUG INTERACTIONS: inclusion of drug-drug interaction study results
- WARNINGS AND PRECAUTIONS: Addition of new information under the subsection New Primary Malignancies regarding other malignancies, and addition of a new subsection Tumor Promotion in BRAF Wild-Type Melanoma
- Content and format revisions in accordance with the requirements of 21 CFR 201.56-57 and current labeling guidance and editorial changes; corresponding changes were also made in the Medication Guide.

S-003: The "Changes Being Effected" supplemental new drug application provides for the following changes:

- WARNINGS AND PRECAUTIONS: inclusion of information regarding non-cutaneous squamous cell carcinoma and toxic epidermal necrolysis, and inclusion of additional information under the Hepatotoxicity subsection regarding toxicity associated with concurrent ipilimumab administration.

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with the minor editorial revisions indicated in the enclosed labeling as follows:

- Inclusion of Recent Major Changes dates
- Deletion of the revision date at the end of the FPI section of the package insert
- Inclusion of the revision date at the end of Highlights and the Medication Guide

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 and 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.

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/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. 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.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 Norma Griffin, Regulatory Project Manager, at (301) 796-4255.

Sincerely,

{See appended electronic signature page}

Jeffrey Summers, M.D.
Deputy Director for Safety
Division of Oncology Products 2
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/

JEFFERY L SUMMERS
07/03/2013