DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022334/S-016

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936-1080

Attention: Lincy Thomas, Pharm.D.
Senior Associate Director, Drug Regulatory Affairs

Dear Dr. Thomas:

Please refer to your Supplemental New Drug Application (sNDA) dated November 2, 2011, received November 3, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Afinitor® (everolimus) Tablets, 2.5 mg, 5 mg, 7.5 mg, and 10 mg.

We also refer to our approval letter dated July 20, 2012, which contained an error of two electronic signatures. The letter should only contain the signature of the Division Director, Robert L. Justice.

This replacement approval letter incorporates the correction of the error. The effective approval date will remain July 20, 2012, the date of the original approval letter.

We acknowledge receipt of your amendments dated December 2, 21, and 22, 2011; January 19 and 20, February 2 (2) and 8, March 21, April 17, May 9 and 18, June 15, and July 10, July 12, July 17, and July 19, 2012.

This "Prior Approval" supplemental new drug application provides for a new indication for the treatment of postmenopausal women with advanced hormone receptor-positive, HER-2 negative breast cancer in combination with exemestane, after failure of treatment with letrozole or anastrozole.

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.

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), 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 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.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable since this indication does not occur in children.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

1899-1: Submit a final report, including datasets, for the final overall survival results from trial CRAD001Y2301 (BOLERO-2).

The timetable you submitted on July 10, 2012, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	December 2011
Trial Completion:	June 2014
Final Report Submission:	June 2015

1899-2: Conduct a 3-arm randomized trial investigating the combination of everolimus with exemestane versus everolimus alone versus capecitabine in patients with estrogen-receptor positive metastatic breast cancer after recurrence or progression on letrozole or anastrazole.

The timetable you submitted on July 10, 2012, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	November 2012
Trial Completion:	August 2016
Final Report Submission:	August 2017

Submit clinical protocols to your IND 066279 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study 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 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.

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 Christy Cottrell, Regulatory Project Manager, at (301) 796-4256.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Oncology Products 1
Office of Hematology & Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
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 L JUSTICE
07/20/2012