DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021743/S-014 and S-016 **SUPPLEMENT APPROVAL**

OSI Pharmaceuticals, Inc.
Attention: Christine Boisclair
Vice President, Global Regulatory Affairs
41 Pinelawn Road
Melville, NY 11747

Dear Ms. Boisclair:

Please refer to your supplemental new drug applications dated November 20, 2008, received November 20, 2008, and March 17, 2009, received March 18, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tarceva (erlotinib) Tablets.

We acknowledge receipt of your submissions dated March 31, April 8, 29, May 15, 20 and 27, July 17, August 14 and 19, October 6, 9 and 30, November 16, 19 and 25, December 7 and 17, 2009; January 6, 13 and 29, February 19, March, 22, 24(2), 25, 26, 30 and 31(2) and April 2, 2010.

S-016 provides for Tarceva (erlotinib) Tablets monotherapy for the maintenance treatment of patients with locally advanced or metastatic non-small cell lung cancer whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.

S-014 provides for updating the Drug Interactions and Clinical Pharmacology, Pharmacokinetics sections of the Package Insert.

We have completed our review of these applications, as amended. They are 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, please submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). For administrative purposes, please designate this submission, "SPL for approved NDA 021743/S014/S016."

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. This is because the disease/condition does not exist in children.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments in your correspondence dated March 31, 2010. These commitments are listed below.

1628-1 A randomized controlled trial in patients with histologically documented, advanced or recurrent (Stage IIIB and not amenable for combined modality treatment) or metastatic (Stage IV) non-small cell lung cancer (NSCLC) who have not experienced disease progression or unacceptable toxicity during chemotherapy with 4 cycles of platinum-based chemotherapy, comparing erlotinib as maintenance therapy with erlotinib at progression. The primary endpoint should be overall survival. This will be a trial to determine which is superior, erlotinib maintenance or erlotinib at progression. Regarding biomarkers, all eligible patients should have known EGFR by IHC status and EGFR mutation status.

Final protocol submission date: January 2011
Trial Completion date: June 2015
Final Report Submission date: December 2015

1628-2 A Phase 3, multicenter, open-label, randomized trial of erlotinib (Tarceva®) treatment versus chemotherapy in patients with advanced non-small-cell carcinoma of the lung who present with mutations in the tyrosine kinase (TK) domain of the epidermal growth factor receptor (EGFR).

The primary endpoint is progression-free survival in patients who present with mutations in the tyrosine kinase domain of the EGFR. Other endpoints include objective response, overall survival, location of progression, safety profile, gene mutation analysis of EGFR in serum and Quality of life (LCSS).

Eligible patients have a histologic diagnosis of non-small-cell lung cancer (NSCLC), stage IV or stage IIIB with malignant pleural effusion or N3 tumors that have not received prior chemotherapy and are not candidates for thoracic irradiation, who present with exon 19 deletions or exon 21 mutations in the tyrosine kinase domain of EGFR.

Final protocol submission date: January 2010
Trial Completion date: December 2012
Final Report Submission date: December 2013

1628-3 A randomized, double-blind, placebo-controlled, Phase 3b trial comparing bevacizumab therapy with or without erlotinib after completion of chemotherapy with bevacizumab for the first-line treatment of locally advanced, recurrent, or metastatic non–small cell lung cancer (NSCLC).

The primary endpoint is progression-free survival. Other endpoints include overall survival and safety.

Eligible patients have a histologic diagnosis of non-small-cell lung cancer (NSCLC), stage IV or stage IIIB not amenable for combined modality therapy and are eligible for bevacizumab therapy.

Final protocol submission date: October 2005
Trial Completion date: October 2009
Final Report Submission date: October 2010

1628-4 A multi-center randomized, double-blind, placebo-controlled, Phase 3 trial of single-agent Tarceva (erlotinib) following complete tumor resection with or without adjuvant chemotherapy in patients with stage IB-IIIA non-small cell lung carcinoma who have EGFR-positive tumors.

There are two co-primary endpoints: disease free survival in patients having EGFR positive tumors by IHC or FISH. Other endpoints include overall survival, safety and biomarker evaluation.

Eligible patients have completely resected stage IB – IIIA NSCLC. They may have received adjuvant chemotherapy but not adjuvant radiation. Eligible patients must have primary tumor tissue analyzed for and be positive for EGFR IHC and/or FISH.

Final protocol submission date: June 2006
Trial Completion date: December 2014
Final Report Submission date: June 2015

Submit clinical protocols to your IND 053728 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all 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**."

POSTMARKETING COMMITMENT—FULFILLED

We have received your submission dated November 20, 2008, which contains the final report for the following postmarketing commitment listed in the November 18, 2004 approval letter for this application:

81-1 A double-blind randomized Phase 3 study to evaluate the efficacy of Tarceva or placebo following 4 cycles of platinum-based chemotherapy in patients with histologically documented advanced or recurrent (stage IIIB and not amenable for combined modality treatment) or metastatic (Stage IV) non-small cell lung cancer (NSCLC) who have not experienced disease progression or unacceptable toxicity during chemotherapy. The primary endpoint will be PFS. The study will also be sized to detect a realistic difference in survival. For eligibility all patients must have EGFR expression status determined by Dako Kit prior to randomization. Analyses of results will include assessment of treatment effect in the subgroup with EGFR expression status positive and the subgroup with EGFR expression status negative.

Protocol submission date: March, 2005
Trial Start: June, 2005
Final Report Submission: December, 2008

We have reviewed your submission and conclude that the commitment was fulfilled.

POSTMARKETING COMMITMENT—OPEN

The following commitment acknowledged in our November 18, 2004, letter is open:

81-2 A randomized Phase 3 study to evaluate the efficacy of Tarceva or chemotherapy (Alimta or Taxotere) following 4 cycles of platinum-based chemotherapy in patients with histologically documented advanced or recurrent (stage IIIB and not amenable for combined modality treatment) or metastatic (Stage IV) non-small cell lung cancer (NSCLC) who have experienced disease progression or unacceptable toxicity during chemotherapy. The primary endpoint will be overall survival (subject to FDA agreement during SPA review). For eligibility all patients must have EGFR expression status determined by Dako Kit prior to randomization. Analyses of results will include assessment of treatment effect in the subgroup with EGFR expression status positive and the subgroup with EGFR expression status negative.

Protocol submission date: March, 2005
Trial Start: June, 2005
Final Report Submission: December, 2008

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 package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

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 Paul Zimmerman, Regulatory Project Manager, at 301-796-1489.

Sincerely,

{See appended electronic signature page}

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

Enclosure
Package Insert

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21743	SUPPL-16	OSI PHARMACEUTICALS INC	TARCEVA (ERLOTINIB HCL) 25/100/150MG TAB
NDA-21743	SUPPL-14	OSI PHARMACEUTICALS INC	TARCEVA (ERLOTINIB HCL) 25/100/150MG TAB
NDA-21743	PMR/PMC-1	OSI PHARMACEUTICALS INC	TARCEVA (ERLOTINIB HCL) 25/100/150MG TAB

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
04/16/2010