

## **Data from the Phase III SATURN Study Show Tarceva Improved Progression-Free Survival When Used as a First-Line Maintenance Therapy for Advanced Non-Small Cell Lung Cancer**

**-- Data Showed Tarceva Improved PFS in Patients with Both Non-Squamous Cell Carcinoma and Squamous Cell Carcinoma ---- Patients with an EGFR Mutation Achieved a 10 Fold Increase in the Time Patients Live Without Their Disease Worsening --- Biomarker Data Suggest K-ras Mutation Status is not a Predictor of Efficacy in NSCLC Patients Treated with Tarceva --**

MELVILLE, N.Y., May 14, 2009 (BUSINESS WIRE) -- OSI Pharmaceuticals, Inc. (NASDAQ: OSIP) announced detailed results from the Phase III SATURN study of Tarceva<sup>(R)</sup> (erlotinib) as a single agent, first-line maintenance therapy for patients with advanced non-small cell lung cancer (NSCLC) who did not progress following first-line treatment with platinum-based chemotherapy. The study met both of its co-primary endpoints by demonstrating a statistically significant 41% improvement in the time patients live without their disease worsening (as measured by progression free survival, or PFS) compared with placebo (Hazard Ratio = 0.71, p-value <0.00001; a hazard ratio of less than one indicates a decreased risk of disease progression and a p-value of less than 0.03 indicates statistical significance) and a 45% increase in the time patients live without their disease worsening compared with placebo in the sub-set of patients who were determined to have tumors expressing the EGFR gene by Immunohistochemistry (IHC) (Hazard Ratio for PFS = 0.69, p-value <0.0001). The study confirmed findings from prior studies in later stage NSCLC patients that Tarceva demonstrated benefit across a broad spectrum of NSCLC patients. Importantly, the study demonstrated a PFS benefit for Tarceva maintenance therapy in both squamous cell carcinoma patients (HR=0.76, p-value=0.0148, n=359); and non-squamous patients (HR=0.68, p-value < 0.0001, n=525).

"The results of the SATURN study offer a clinically meaningful benefit for patients with advanced lung cancer," said Professor Federico Cappuzzo, principal investigator on the SATURN study from the Istituto Clinico Humanitas IRCCS, Milan, Italy. "If we can offer patients a once-daily, oral therapy with a favorable safety profile right after chemotherapy to extend the time they live without their disease progressing, this is an important step forward in the treatment of lung cancer."

Pre-planned biomarker analyses of tissue samples collected as part of the SATURN protocol provided important information on the potential role of EGFR mutations and K-ras mutations in predicting possible outcomes of Tarceva therapy in NSCLC patients. The subgroup analysis of patients whose tumors possessed an activating EGFR mutation and were eligible for analysis (n=49) demonstrated a statistically significant ten-fold increase in the time patients live without their disease worsening (as measured by PFS) for patients treated with Tarceva compared with placebo. The hazard ratio was 0.10 (p-value <0.0001). In the sub-population of patients tested for their EGFR mutation or wild-type status, a statistically significant PFS benefit of Tarceva therapy was also evident in patients with wild-type EGFR status after excluding those patients whose tumors had an activating EGFR mutation (HR=0.78, p-value < 0.0185, n=388).

In addition, the sub-group analysis of patients whose tumors possessed a K-ras mutation and were eligible for analysis (n=90) suggested a similar treatment benefit in terms of PFS to that seen in the overall population (HR=0.77, p-value=0.679).

The EGFR IHC status of the tumor was not predictive of outcome for Tarceva therapy in the study as demonstrated by HR of 0.69 in EGFR IHC positive (n=618) and HR of 0.77 in EGFR IHC negative (n=121) patients.

"The biomarker analyses in the SATURN study have shed an important light on the appropriate use of EGFR and K-ras mutation status biomarkers in Tarceva therapy. The data suggest that, while NSCLC patients with wild-type EGFR clearly benefit from Tarceva therapy, those whose tumors contain an EGFR mutation derive pronounced benefit and that those patients whose tumors contain a K-ras mutation should *not* be excluded from treatment with Tarceva," stated Colin Goddard, Ph.D., Chief Executive Officer of OSI Pharmaceuticals. "Presuming successful regulatory approval, we believe Tarceva will be the therapy of choice for NSCLC patients in the maintenance setting whose tumors possess an EGFR mutation, are of squamous cell histology, or are chemo ineligible while continuing to offer a non-chemotherapy choice for all NSCLC patients in this setting."

Twenty-five percent of patients treated with Tarceva had not seen their disease progress after six months compared with 15% of patients treated with placebo. Measurements of median PFS in the overall population in the study were impacted by an unusual step-wise data distribution in the Kaplan-Meier analysis (12.3 weeks for the Tarceva arm versus 11.1 weeks for the placebo arm) which is not representative of the robust overall PFS benefit as evident by the Hazard Ratio of 0.71 and an associated p-value of <0.00001.

Overall survival data (a secondary end-point in the study) is immature and is not expected to be available until later in the year.

There were no new safety signals seen in the study and using Tarceva maintenance therapy immediately following first-line chemotherapy did not appear to exacerbate any residual chemotherapy related side-effects. Sixty-four percent of patients in the Tarceva arm and 55% of patients on placebo received subsequent therapy after progressing.

### **SATURN Safety Data**

There were no new or unexpected safety signals observed in the SATURN study. Adverse events were consistent with those observed in previous Tarceva studies in NSCLC, and included rash (49.2% with Tarceva versus 5.8% with placebo) and diarrhea (20.3% with Tarceva versus 4.5% with placebo). Dose reductions were necessary in 11% of the patients treated with Tarceva versus 1% of those treated with placebo. Discontinuations due to adverse events were necessary for 4.6% of the patients in the Tarceva arm versus 1.6% in the placebo arm. No exacerbation of residual chemotherapy related side-effects was evident when Tarceva was used in the maintenance setting immediately following the completion of a first-line chemotherapy regimen.

### **SATURN Regulatory Authority Filings**

In March, OSI submitted a supplemental New Drug Application (sNDA) for the use of Tarceva as a first-line maintenance treatment for patients with advanced non-small cell lung cancer (NSCLC) who have not progressed following first-line treatment with platinum-based chemotherapy. Additionally, Roche, OSI's international partner for Tarceva, filed an application in Europe with the European Medicines Agency (EMA). Both the U.S. and EU submissions are based on the Phase III SATURN data.

### **ASCO Presentations**

Data are being released co-incident with the publication of on-line abstracts by the American Society of Clinical Oncology (ASCO) in advance of their Annual Meeting in Orlando, May 29-June 2, 2009. The data will be presented in an oral presentation by F. Cappuzzo, M.D., medical oncologist and principal investigator of the SATURN study (Abstract #8001) on May 31, 2009 at 9:15a.m. EDT. Biomarker analyses from the SATURN study will be presented in a poster session by Dr. W. Brugger (Abstract #8020) on June 1, 2009 between 8a.m. and noon EDT.

### **Additional First-line Maintenance Study: ATLAS**

Results will also be presented from ATLAS, a second positive Phase III study evaluating Tarceva in the first-line maintenance setting, at ASCO. ATLAS showed that people lived longer without their cancer getting worse when taking the daily pill Tarceva in combination with Avastin compared with Avastin plus placebo, following initial treatment with Avastin plus chemotherapy. The ATLAS data will be presented in a late-breaking session by Vincent A. Miller, M.D., associate attending physician, Memorial Sloan-Kettering (Abstract #LBA8002) on Sunday, May 31, 2009 at 9:30a.m EDT.

### **About SATURN**

SATURN is an international, placebo-controlled, randomized, double-blind, Phase III study conducted by Roche that enrolled 889 patients with advanced NSCLC at approximately 160 sites worldwide. Patients were treated with four cycles of standard first-line platinum-based chemotherapy and were then randomized to Tarceva (150 mg) or placebo if their cancer did not progress. The primary endpoint of the study was progression-free survival in the overall population, as determined by investigators, and was defined as the length of time from randomization to disease progression or death from any cause. The co-primary endpoint was PFS in patients with EGFR positive tumors by IHC. Secondary endpoints included overall survival, safety and an evaluation of exploratory biomarkers, including EGFR mutations and K-ras mutations.

### **About Lung Cancer**

According to the American Cancer Society (ACS), lung cancer is the single largest cause of cancer death among men and women in the U.S. and nearly 159,390 Americans are expected to die from the disease in 2009. Most people with lung cancer are diagnosed with advanced stage disease that cannot be surgically removed or has spread to other parts of the body. The majority of people with advanced lung cancer survive less than one year. NSCLC is the most common type of lung cancer.

### **About Tarceva**

Tarceva is a once-a-day pill that targets the EGFR pathway. Tarceva is designed to inhibit the tyrosine kinase activity of the EGFR signaling pathway inside the cell, one of the critical growth factors in NSCLC and pancreatic cancers. Tarceva is indicated as a monotherapy for patients with locally advanced or metastatic NSCLC whose disease has progressed after one or more courses of chemotherapy. Results from two multicenter, placebo-controlled, randomized Phase III trials conducted in first-line patients with locally advanced or metastatic NSCLC showed no clinical benefit with the concurrent administration of Tarceva with platinum-based chemotherapy (carboplatin and paclitaxel or gemcitabine and cisplatin) and its use is not recommended in that setting.

In pancreatic cancer, Tarceva is indicated in combination with gemcitabine for the first-line treatment of patients with locally advanced pancreatic cancer, pancreatic cancer that cannot be surgically removed or pancreatic cancer that has spread to distant body organs.

### **Tarceva Safety**

There have been infrequent reports of serious Interstitial Lung Disease (ILD)-like events including deaths in patients taking Tarceva. Serious side effects (including deaths) in patients taking Tarceva include liver and/or kidney problems; gastrointestinal (GI) perforations (the development of a hole in the stomach, small intestine, or large intestine); and severe blistering skin reactions including cases similar to Stevens-Johnson syndrome. Patients taking Tarceva plus gemcitabine were more likely to experience bleeding and clotting problems such as heart attack or stroke. Eye irritation and damage to the cornea have been reported in patients taking Tarceva. Women should avoid becoming pregnant and avoid breastfeeding while taking Tarceva. Patients should call their doctor right away if they have these signs or symptoms: new or worsening skin rash; serious or ongoing diarrhea, nausea, loss of appetite, vomiting, or stomach pain; new or worsening shortness of breath or cough; fever; eye irritation. Rash and diarrhea were the most common side effects associated with Tarceva in the non-small cell lung cancer clinical study. Fatigue, rash, nausea, loss of appetite, and diarrhea were the most common side effects associated with Tarceva plus gemcitabine therapy in the pancreatic cancer clinical study.

For full prescribing information, please call 1-877-TARCEVA or visit <http://www.tarceva.com>.

### **About OSI Pharmaceuticals**

OSI Pharmaceuticals is committed to "shaping medicine and changing lives" by discovering, developing and commercializing high-quality, novel and differentiated targeted medicines designed to extend life and improve the quality of life for patients with cancer and diabetes/obesity. For additional information about OSI, please visit <http://www.osip.com>.

*This news release contains forward-looking statements. These statements are subject to known and unknown risks and uncertainties that may cause actual future experience and results to differ materially from the statements made. Factors that might cause such a difference include, among others, OSI's and its collaborators' abilities to effectively market and sell Tarceva and to expand the approved indications for Tarceva, OSI's ability to protect its intellectual property rights, safety concerns regarding Tarceva, competition to Tarceva and OSI's drug candidates from other biotechnology and pharmaceutical companies, the completion of clinical trials, the effects of FDA and other governmental regulation, including pricing controls, OSI's ability to successfully develop and commercialize drug candidates, and other factors described in OSI Pharmaceuticals' filings with the Securities and Exchange Commission.*

SOURCE: OSI Pharmaceuticals, Inc.

#### **OSI Pharmaceuticals, Inc.**

Investors/Media:

Kathy Galante, 631-962-2043

Senior Director

or

Media:

Kim Wittig, 631-962-2135

Director

or

**Burns McClellan, Inc. (representing OSI)**

Media:

Justin Jackson/Kathy Nugent, 212-213-0006

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