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Results From a Randomized Phase II Trial Suggested the Combinations of Avastin(R) Plus Tarceva(R) and Avastin Plus Chemotherapy Improved Progression- Free Survival in Advanced Non-Small Cell Lung Cancer

ATLANTA, June 5 /PRNewswire-FirstCall/ -- Genentech, Inc. (NYSE: DNA) and OSI Pharmaceuticals (Nasdaq: OSIP) today presented results from a Phase II study that compared the combinations of Avastin® (bevacizumab) plus Tarceva® (erlotinib), and Avastin plus chemotherapy, to chemotherapy alone in patients with recurrent or refractory non-small cell lung cancer (NSCLC). The results suggested that the addition of Avastin to either Tarceva or chemotherapy improved progression-free survival (PFS), the primary endpoint, compared to chemotherapy alone. The data were presented by Louis Fehrenbacher, M.D., Vallejo Medical Center, Vallejo, California at the 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO).

This randomized, 120-patient study evaluated three treatment regimens:

- Avastin in combination with Tarceva -- experimental arm, n=39
- Avastin in combination with chemotherapy (either pemetrexed or docetaxel) -- experimental arm, n=40
- Chemotherapy alone (either pemetrexed or docetaxel) -- control arm, n=41

Study Results

The data from this study suggested that the median PFS was 4.8 months in the Avastin plus chemotherapy arm, and 4.4 months in the Avastin plus Tarceva arm, compared to 3.0 months in the chemotherapy-alone arm. The data also suggested that the Avastin plus chemotherapy arm reduced the risk of cancer progression or death by 34 percent compared to chemotherapy alone (based on a hazard ratio of 0.66), and that the Avastin plus Tarceva arm reduced the risk of cancer progression or death by 28 percent compared to chemotherapy alone (based on a hazard ratio of 0.72). Due to the planned exploratory nature and small sample size of the study, these data do not provide definitive conclusions or reach statistical significance with respect to differences among the three treatment arms.

The estimated six-month survival rates -- which represented the percentage of patients alive at six months -- were 78 percent in the Avastin plus Tarceva arm, and 72 percent in the Avastin plus chemotherapy arm, compared to 62 percent in the chemotherapy-alone arm. One-year survival data are not yet mature.

"We are encouraged that these findings support the hypothesis that combining therapies that target different cancer pathways, such as angiogenesis and epidermal growth factor receptor (EGFR) signaling, may improve progression-free survival, possibly without the use of chemotherapy," said Hal Barron, M.D., senior vice president, Development and chief medical officer at Genentech. "Additional research is needed to further explore the safety and efficacy of Avastin in combination with Tarceva in advanced cancers, and we are currently conducting randomized Phase III trials of this combination in relapsed and first-line NSCLC patients."

"We are pleased with the results of this study," stated Gabriel Leung, president, OSI Oncology. "In addition to the encouraging results regarding progression-free survival observed in both experimental arms, the targeted therapy combination of Tarceva and Avastin showed a notable six-month survival rate and fewer reported serious adverse events compared to chemotherapy. As we continue to investigate the combination of Tarceva and Avastin in relapsed and first-line non-small cell lung cancer, we believe this combination may one day provide an important treatment option for patients."

Safety Data

In this study, combination therapy with Avastin plus Tarceva resulted in fewer serious adverse events, compared to either chemotherapy-containing arm. Serious adverse events occurred in 33 percent of patients (n=13) in the Avastin plus Tarceva arm, compared to 40 percent (n=16) in the Avastin plus chemotherapy arm and 53 percent (n=22) in the chemotherapy-alone arm. In addition, there were fewer drug discontinuations due to adverse events in the Avastin plus Tarceva arm (n=4) compared with either the Avastin plus chemotherapy arm (n=10) or the chemotherapy-alone arm (n=10).

No new or unexpected safety signals were observed; the rate of fatal pulmonary hemorrhage was consistent with previous Avastin trials in NSCLC. The most serious adverse events in this study were Grade 5 hemorrhage and venous thromboembolic events. There was one fatal pulmonary hemorrhage in the Avastin plus Tarceva arm; two fatal pulmonary hemorrhages and

one gastrointestinal bleed that led to death in the Avastin plus chemotherapy arm; and one fatal event due to venous thromboembolism and one fatal cardio- pulmonary arrest in the chemotherapy-alone arm.

Other adverse events observed in the Avastin plus Tarceva arm were similar to those observed in previous clinical trials of Avastin in combination with Tarceva. Grade 3/4 diarrhea and Grade 3/4 rash were observed in two patients receiving Avastin plus Tarceva, compared to zero patients treated with chemotherapy alone. In the Avastin plus chemotherapy arm, adverse events observed were similar to those observed in previous clinical trials of Avastin in combination with chemotherapy, and included hypertension and bleeding. Grade 3/4 hypertension was reported in two patients receiving Avastin plus chemotherapy compared to zero patients receiving chemotherapy alone. Adverse events in the chemotherapy alone arm included Grade 3/4 neutropenia in seven patients; arterial thromboembolisms in one patient and venous thromboembolisms in three patients.

About the Patient Population

This randomized, multicenter, Phase II study enrolled 120 patients with recurrent or refractory NSCLC, who had not received previous treatment with Avastin or Tarceva. Patients had an ECOG performance status of 0 - 2, histologically or cytologically confirmed non-squamous NSCLC and had experienced clinical or radiographic disease progression during or following one platinum-based chemotherapy regimen for advanced stage disease (IIIb or IV).

About Avastin

Avastin is a therapeutic antibody designed to inhibit Vascular Endothelial Growth Factor (VEGF), a protein that plays an important role in tumor angiogenesis and maintenance of existing tumor vessels. By inhibiting VEGF, Avastin is designed to interfere with the blood supply to a tumor, a process that is thought to be critical to a tumor's growth and metastasis.

The FDA approved Avastin on February 26, 2004 as a first-line treatment for metastatic colorectal cancer in combination with intravenous 5-FU-based chemotherapy. Based on data showing that VEGF may play a broad role in a range of cancers, Genentech is pursuing a broad development program for Avastin that currently includes 130 clinical trials across 25 different types of cancer. Avastin is being evaluated in Phase III clinical trials for its potential use in adjuvant and metastatic colorectal, renal cell (kidney), breast, pancreatic, non-small cell lung, prostate and ovarian cancers. Avastin is also being evaluated in earlier stage trials as a potential therapy in a variety of solid tumor cancers and hematologic malignancies. For full prescribing information and Boxed Warnings on Avastin and information about angiogenesis, visit http://www.gene.com. For more information on Avastin and clinical trials, please call (888) 662-6728 or visit http://www.avastin.com.

Avastin Safety Profile

Avastin has a well-established safety profile. In Genentech-sponsored studies, the most serious adverse events associated with Avastin were gastrointestinal perforation, wound healing complications, hemorrhage, arterial thromboembolic events, hypertensive crisis, nephrotic syndrome, and congestive heart failure. The most common Grade 3-4 adverse events (occurring in greater than 2 percent of patients in the Avastin arm, compared to the control group) were asthenia, pain, hypertension, diarrhea, and leukopenia. The most common adverse events (occurring in greater than 2 percent of patients in the Avastin arm, compared to the control group) of any severity were asthenia, pain, abdominal pain, headache, hypertension, diarrhea, nausea, vomiting, anorexia, stomatitis, constipation, upper respiratory infection, epistaxis, dyspnea, exfoliative dermatitis, and proteinuria.

About Tarceva

Tarceva is an oral tablet currently approved for use as monotherapy in patients with locally advanced or metastatic non-small cell lung cancer whose disease has progressed after one or more courses of chemotherapy (at a recommended dose of 150 mg/day). 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. Tarceva is also approved in combination with gemcitabine for the treatment of locally advanced or metastatic pancreatic cancer in patients who have not received previous chemotherapy (at a recommended dose of 100 mg/day).

Tarceva is a small molecule designed to target the human epidermal growth factor receptor (EGFR/HER1) pathway, which is one of the factors critical to cell growth in a number of different cancer types. EGFR/HER1 is a component of the HER signaling pathway, which plays a role in the formation and growth of numerous cancers. Tarceva is designed to inhibit the tyrosine kinase activity of the HER1 signaling pathway inside the cell, which may block tumor cell growth. Tarceva is the only EGFR therapy to show, in a Phase III trial, improved survival for advanced NSCLC and advanced pancreatic patients. Additional early-stage trials of Tarceva are being conducted in other solid tumors. For Tarceva full prescribing information, please call (877) TARCEVA or visit http://www.tarceva.com.

Tarceva Safety Profile

In the Phase III NSCLC pivotal trial, the most common adverse reactions in patients receiving Tarceva were rash and diarrhea. Rash and diarrhea each resulted in discontinuation of 1 percent of Tarceva-treated patients. Grade 3-4 rash and diarrhea occurred in 9 and 6 percent of Tarceva-treated patients, respectively. Six and 1 percent of patients needed dose reduction for rash and diarrhea, respectively. In the Phase III trial, severe pulmonary reactions, including potential cases of interstitial lung disease, were infrequent (less than 1 percent) and were equally distributed between treatment arms.

About Non-Small Cell Lung Cancer

According to the World Health Organization, there are more than 1.2 million cases worldwide of lung and bronchial cancer each year, causing approximately 1.1 million deaths annually. It is estimated 162,460 people will die from lung cancer in the United States in 2006, accounting for nearly 29 percent of cancer deaths in this country. According to the National Cancer Institute, lung cancer is the single largest cause of cancer-related deaths of men and women in the United States. NSCLC is the most common form of the disease and accounts for 87 percent of all lung cancers.

About Genentech BioOncology

Genentech is committed to changing the way cancer is treated by establishing a broad oncology portfolio of innovative, targeted therapies with the goal of improving patients' lives. The company is the leading provider of anti-tumor therapeutics in the United States. Genentech is conducting clinical development programs for Rituxan® (Rituximab), Herceptin® (Trastuzumab), Avastin® (bevacizumab), and Tarceva® (erlotinib), and markets all four products in the United States, either alone (Avastin and Herceptin) or with Biogen Idec Inc. (Rituxan) or OSI Pharmaceuticals, Inc. (Tarceva). Genentech has licensed Rituxan, Herceptin, and Avastin and OSI Pharmaceuticals has licensed Tarceva to Roche for sale by the Roche Group outside of the United States.

The company has a robust pipeline of potential oncology therapies with a focus on four key areas: angiogenesis, apoptosis (i.e., programmed cell death), the HER pathway, and B-cell biology. An investigational antibody directed at the HER pathway is currently in Phase II trials, and in early development, are a small molecule directed at the hedgehog pathway and an investigational agent targeting apoptosis.

Founded 30 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures, and commercializes biotherapeutics for significant unmet medical needs. A considerable number of the currently approved biotechnology products originated from or are based on Genentech science. Genentech manufactures and commercializes multiple biotechnology products and licenses several additional products to other companies. The company has headquarters in South San Francisco, California and is listed on the New York Stock Exchange under the symbol DNA. For additional information about the company, please visit http://www.gene.com.

For the full prescribing information for Tarceva and the full prescribing information and Boxed Warnings for Rituxan, Herceptin, and Avastin please visit http://www.gene.com.

About OSI Pharmaceuticals

OSI Pharmaceuticals is committed to "shaping medicines and changing lives" by discovering, developing, and commercializing high-quality and novel pharmaceutical products that extend life or improve the quality of life for patients with cancer, eye diseases, and diabetes. The Company operates through three business teams, (OSI) Oncology, (OSI) Eyetech, and (OSI) Prosidion. (OSI) Oncology is focused on developing molecular targeted therapies designed to change the paradigm of cancer care. (OSI) Eyetech specializes in the development and commercialization of novel therapeutics to treat diseases of the eye.

(OSI) Prosidion is committed to the generation of novel, targeted therapies for the treatment of type 2 diabetes and obesity. OSI's flagship product, Tarceva® (erlotinib), is the first drug discovered and developed by OSI to obtain FDA approval and the only EGFR inhibitor to have demonstrated the ability to improve survival in both non-small cell lung cancer and pancreatic cancer patients. OSI markets Tarceva through partnerships with Genentech, Inc., in the United States and with Roche throughout the rest of the world. Macugen® (pegaptanib sodium injection) is approved in the United States and Europe for the treatment of neovascular age-related macular degeneration. OSI commercializes Macugen in partnership with Pfizer Inc. For additional information about OSI, please visit http://www.osip.com.

Genentech Safe Harbor Statement

This press release contains a forward-looking statement regarding the potential of combination therapies. Such statement is a prediction and involves risks and uncertainties such that the actual results may differ materially. Among other things, the potential of combination therapies could be affected by unexpected safety, efficacy or manufacturing issues, additional time requirements for data analysis and decision-making, discussions with the FDA, FDA actions, failure to receive FDA approval, competition, reimbursement, pricing, the ability to supply product, or product withdrawal. Please also refer to Genentech's periodic reports filed with the Securities and Exchange Commission. Genentech disclaims and does not undertake any obligation to update or revise this forward-looking statement in this press release.

OSI Safe Harbor Statement

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, the completion of clinical trials, the FDA review process and other governmental regulation, OSI's and its collaborators' abilities to successfully develop and commercialize drug candidates, competition from other pharmaceutical companies, the ability to effectively market products, and other factors described in OSI Pharmaceuticals' filings with the Securities and Exchange Commission.

Genentech Media Contact: Krysta Pellegrino (650) 225-8226

Genentech Investor Contact: Sue Morris (650) 225-6334
OSI Media Contact: Wendy Mensch (631) 962-2000
OSI Investor Contact: Kathy Galante (631) 962-2000

SOURCE Genentech, Inc.

/CONTACT: Media: Krysta Pellegrino, +1-650-225-8226, or Investors: Sue Morris, +1-650-225-6334, both of Genentech; or Media: Wendy Mensch, or Investors: Kathy Galante, both of OSI, +1-631-962-2000/ /Web site: http://www.gene.com/ (DNA OSIP)