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Phase III Trials of Tarceva Plus Chemotherapy in First-Line Non-Small Cell Lung Cancer Do Not Meet Primary Efficacy Endpoint

Ongoing Program Continues to Study Tarceva in a Variety of Solid Tumor Types

SOUTH SAN FRANCISCO, Calif.; MELVILLE, N.Y. & BASEL, Switzerland, Oct 1, 2003 (BUSINESS WIRE) -- Genentech, Inc. (NYSE:DNA), OSI Pharmaceuticals, Inc. (Nasdaq:OSIP), and Roche (SWX Zurich) today announced that two first-line Phase III studies (called TRIBUTE in the U.S. and TALENT outside of the U.S.) of Tarceva™ (erlotinib HCl) plus standard chemotherapy in metastatic non-small cell lung cancer (NSCLC) did not meet their primary endpoints of improving overall survival. In the TRIBUTE study, one of the secondary endpoints, time to symptomatic progression, did achieve statistical significance, but this did not translate into improvements in overall survival or time to disease progression. These results do not affect Genentech's previous earnings per share growth projections for the current or future years.

The studies, conducted by Genentech in the United States and Roche in countries outside of the United States, evaluated Tarceva at 150 mg/day in combination with standard chemotherapy. Tarceva is a small molecule oral therapy designed to inhibit the tyrosine kinase activity of the HER1/EGFR signaling pathway inside the cell, which may block tumor growth.

"We are disappointed, but not completely surprised based on previously announced failures of EGFR inhibitors in this setting, that Tarceva in combination with chemotherapy did not improve overall survival as a first-line therapy in these studies. We believe that further work is needed to provide more insight into the role of EGFR inhibitors in this setting, either as a single agent or in combination with other targeted agents or chemotherapy," said Susan D. Hellmann, M.D., M.P.H., Genentech's executive vice president, Development and Product Operations, and chief medical officer. "In order to optimize the therapeutic potential of EGFR inhibition in NSCLC, we will use clinical data and conduct pre-specified analyses of tumor biopsy material to identify potential subsets of patients who may be more likely to benefit from treatment with Tarceva in combination with chemotherapy. The alliance of Genentech, OSI and Roche remains on track with our clinical development program and believes Tarceva may have utility in treating a variety of cancers."

The addition of Tarceva to chemotherapy was generally well tolerated and adverse events were similar to those previously reported with chemotherapy treatment and with Tarceva. Adverse events that occurred more often with Tarceva included diarrhea and rash.

About the Phase III Studies

The multi-center, randomized, controlled Phase III studies evaluated Tarceva at 150 mg/day in combination with standard chemotherapy in patients with stage IIIB/IV metastatic non-small cell lung cancer. The 1,050 patients enrolled in the TRIBUTE study were randomized to receive Tarceva plus standard chemotherapy (carboplatin and paclitaxel) or standard chemotherapy plus a Tarceva placebo. The TALENT study randomized 1,200 patients to receive either Tarceva in combination with standard chemotherapy (gemcitabine and cisplatin) or standard chemotherapy plus a Tarceva placebo.

Comprehensive Clinical Trial Program

These two Phase III studies are part of a comprehensive clinical development program in lung cancer, which includes a Phase III study of Tarceva as a single agent in a second-/third-line setting, a Phase II study of Tarceva as a single agent in bronchioloalveolar cell carcinoma (BAC) and a Phase I/II trial of Tarceva in combination with Avastin™ (bevacizumab).

"It is important to note that Tarceva has shown activity in a number of solid tumor types, including relapsed NSCLC, BAC and glioblastoma (brain cancer). Consequently, we remain optimistic about the alliance's prospects for success in the Phase III second-/third-line monotherapy trial in NSCLC and are encouraged by the response rates observed in the Phase I glioblastoma study, Phase II BAC study and in the combination trial with Genentech's Avastin," said Colin Goddard, Ph.D., chief executive officer of OSI.

The Phase III randomized study in second-/third-line metastatic NSCLC is assessing Tarceva as a single agent (150 mg/day) with survival as the primary endpoint. This 700-patient study is being conducted by OSI in collaboration with the National Cancer Institute Canada Clinical Trials Group (NCIC CTG), and completed enrollment in January 2003. This is the first single-agent controlled Phase III study of an EGFR-targeted agent designed to detect a survival advantage in second-/third-line NSCLC, and data are expected in early 2004.

The alliance, through OSI, is also conducting a Phase III trial evaluating Tarceva in 450 patients with previously-untreated

metastatic pancreatic cancer. The Phase III study also is being conducted in collaboration with the NCIC CTG, and is a randomized, placebo-controlled study assessing the use of Tarceva in combination with gemcitabine, the only approved first-line chemotherapy treatment for pancreatic cancer. Improvement in patient survival is the primary endpoint in this study and data are expected in mid-2004.

Based on activity seen to date in a Phase I study of Tarceva in glioblastoma, Genentech initiated a Phase II study in glioblastoma earlier this year. The companies also announced that the U.S. Food and Drug Administration (FDA) has granted orphan drug status for Tarceva in patients with glioblastoma. This is the first HER1/EGFR-inhibitor to receive such classification.

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. According to the National Cancer Institute, lung cancer is the single largest cause of cancer deaths in the United States and is responsible for nearly 30 percent of cancer deaths in the country. Non-small cell lung cancer is the most common form of the disease and accounts for almost 80 percent of all lung cancer.

About Tarceva

Tarceva is a small molecule designed to target the human epidermal growth factor receptor 1 (HER1) pathway, which is critical to cell growth in many cancers. HER1, also known as EGFR, is a key component of the HER signaling pathway, which often is involved 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 blocks tumor cell growth. Tarceva currently is being studied as an oral dosage tablet.

About the Alliance

Genentech is a leading biotechnology company that discovers, develops, manufactures, and commercializes biotherapeutics for significant unmet medical needs. Sixteen of the currently approved biotechnology products originated from, or are based on Genentech science. Genentech manufactures and commercializes 11 biotechnology products in the United States. The company has headquarters in South San Francisco, Calif., and is traded on the New York Stock Exchange under the symbol DNA. For additional information about the company, please visit http://www.gene.com.

OSI Pharmaceuticals is a leading biotechnology company focused on the discovery, development, and commercialization of high-quality, next-generation oncology products that both extend and improve the quality-of-life for cancer patients worldwide. OSI has a balanced pipeline of oncology drug candidates that includes both next-generation cytotoxic agents and novel mechanism-based, gene-targeted therapeutics focused in the areas of signal transduction and apoptosis. OSI has a commercial presence in the U.S. oncology market where it exclusively markets Novantrone® (mitoxantrone concentrate for injection) for approved oncology indications, and Gelclair™ for the relief of pain associated with oral mucositis.

Headquartered in Basel, Switzerland, Roche is one of the world's leading innovation-driven healthcare groups. Its core businesses are pharmaceuticals and diagnostics. Roche is number one in the global diagnostics market and is the leading supplier of pharmaceuticals for cancer and a leader in virology and transplantation. As a supplier of products and services for the prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche employs roughly 65,000 people in 150 countries. The Group has alliances and research and development agreements with numerous partners, including majority ownership interests in Genentech and Chugai.

The statements made in this press release relating to the expected time frames for data availability from the Phase III studies in second-/third line metastatic NSCLC and metastatic pancreatic cancer and Tarceva's potential utility in treating a variety of cancers, including second-/third-line NSCLC and glioblastoma, are forward-looking and actual results could differ materially. Among other things, the timing of data availability could be affected by the length of time to achieve study endpoints, additional time requirements for data analysis or discussions with the FDA and Tarceva's potential utility in treating variety of cancers could be affected by insufficient efficacy or safety results.

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