

# Genentech NEWS RELEASE

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## **FOURTH PHASE III STUDY SHOWS HERCEPTIN® PLUS CHEMOTHERAPY IMPROVED DISEASE-FREE SURVIVAL IN EARLY-STAGE HER2-POSITIVE BREAST CANCER**

*-- Interim Analysis of More Than 3,000 Patients in BCIRG Study Showed Reduction in the Risk of Disease Recurrence in Early-Stage HER2-Positive Breast Cancer --*

**SOUTH SAN FRANCISCO, Calif.– September XX, 2005** – Genentech, Inc. (NYSE: DNA) today announced that a planned interim analysis of a Phase III trial of Herceptin® (Trastuzumab) plus chemotherapy in the adjuvant setting showed a significant improvement in the risk of disease recurrence in women with early-stage (or cancer that has not spread beyond the breast and associated lymph nodes) human epidermal growth factor receptor 2 (HER2)- positive breast cancer. The study was supported by Sanofi-Aventis and Genentech, and conducted by the Breast Cancer International Research Group (BCIRG), who will submit the data to the San Antonio Breast Cancer Symposium (SABCS), December 8 to 11, 2005.

The trial evaluated three regimens as adjuvant therapy following initial treatment with surgery: doxorubicin and cyclophosphamide (AC) followed by Herceptin plus Taxotere® (docetaxel) chemotherapy, Taxotere and carboplatin chemotherapies plus Herceptin (TCH) and AC followed by Taxotere alone. This study differs from the two cooperative group trials presented at this year's American Society of Clinical Oncology (ASCO) meeting in that the BCIRG study included a novel regimen of Herceptin plus chemotherapy (TCH), enrolled both node-positive and node-negative patients, included Taxotere, and determined HER2 status by FISH (fluorescent in situ hybridization) testing.

"We are excited that the fourth Phase III trial of Herceptin plus chemotherapy showed an improvement in disease-free survival for women with early-stage HER2-positive breast cancer," said Susan Desmond-Hellmann, M.D., M.P.H., Genentech president, Product Development. "Based on the strength of the data from the two U.S. adjuvant studies presented at this year's ASCO meeting, we continue to anticipate filing a Supplemental

Biologics License Application (sBLA) for Herceptin in the adjuvant setting based on data from the U.S. studies in the first quarter of 2006.”

### **About the BCIRG Study**

This study showed that adding Herceptin to Taxotere following AC chemotherapy or adding Herceptin to Taxotere and carboplatin chemotherapies resulted in improved disease-free survival compared to chemotherapy alone, which is consistent with the results obtained from a joint analysis of the two U.S. cooperative group studies (NSABP and NCCTG).

The reduction in the risk of disease recurrence, the primary endpoint of the study, was 51 percent (95 percent confidence interval of 35 percent to 63 percent) in the arm adding Herceptin to Taxotere following AC and 39 percent (95 percent confidence interval of 21 percent to 53 percent) in the TCH arm. These findings resulted from a planned interim analysis of 3,222 patients after approximately one-third of the required number of relapses had occurred. The comparison of efficacy data from the two Herceptin-containing regimens is not sufficiently mature to reliably determine differences at this time. Insufficient information is available to evaluate the secondary endpoint of overall survival; this data will be available at a later date.

The rate of clinically significant cardiac events, including congestive heart failure (weakening of the heart muscle), in the TCH arm was the same as the control arm AC/Taxotere arm (1.2 percent in each arm). Cardiac events occurred at a rate of 2.3 percent in the AC/Taxotere/Herceptin arm. This study has an independent, external Data Monitoring Committee (IDMC) that reviewed data from the studies, including cardiac safety data. The IDMC monitored safety data on a regular basis and the incidence of cardiac safety in the Herceptin plus chemotherapy arm was deemed acceptable by the IDMC.

"This is the first time in HER2-positive breast cancer research that we have demonstrated that a novel Herceptin-containing regimen without anthracyclines is superior to one of the regimens containing anthracyclines commonly used today in breast cancer," said Dennis Slamon, Ph.D., M.D., Co-Chair of the BCIRG study and Director of Clinical and Translational Research at UCLA's Jonsson Comprehensive Cancer Center. Slamon further noted "In the first interim analysis, this novel regimen appears to avoid the problem of cardiotoxicity that has been reported when Herceptin is used together with anthracyclines."

The BCIRG study enrolled its first patient in March 2001, and has randomized a total of 3,222 patients.. The study is closed to accrual and the BCIRG cooperative group will continue to monitor patients for longer-term data.

### **About the Herceptin Adjuvant Clinical Trial Program**

In addition to the BCIRG study, interim analyses of three additional adjuvant studies reported earlier this year showed that the addition of Herceptin to a chemotherapy regimen increased disease-free survival for women with early-stage HER2-positive breast cancer.

In April 2005, Genentech announced that a joint interim analysis of two U.S. cooperative group Phase III trials showed an improvement in the primary endpoint of disease-free survival and in the secondary endpoint of overall survival. The trials compared Herceptin plus paclitaxel chemotherapy to paclitaxel chemotherapy alone as adjuvant therapy following initial treatment with surgery for women with early-stage HER2-positive breast cancer.

An interim analysis from a third adjuvant trial called HERA, which was conducted internationally by Roche and Breast International Group (BIG), also showed that treatment with Herceptin plus chemotherapy improved disease-free survival.

### **About Herceptin**

Herceptin is a targeted therapeutic antibody treatment for women with HER2-positive metastatic breast cancer, an especially aggressive form of the disease that affects approximately one-fourth of women with breast cancer. Special testing is required to identify women who are HER2-positive and candidates for treatment with Herceptin.

Herceptin received U.S. Food and Drug Administration (FDA) approval in September 1998 for use in women with metastatic breast cancer who have tumors that overexpress the HER2 protein. It is indicated for weekly treatment of patients both as first-line therapy in combination with paclitaxel and as a single agent in second- and third-line therapy. Herceptin is marketed in the United States by Genentech, in Japan by Chugai, and internationally by Roche.

In clinical trials that resulted in the initial FDA approval of Herceptin, the drug showed a survival benefit when used in combination with chemotherapy. The data showed a 24 percent increase in median overall survival for women with HER2-positive metastatic breast

cancer treated initially with Herceptin and chemotherapy compared to chemotherapy alone (median 25.1 months compared to 20.3 months).

### **Herceptin Safety Profile**

Herceptin therapy does involve risks. Serious side effects have occurred in patients treated with Herceptin in metastatic breast cancer. Herceptin administration can result in the development of ventricular dysfunction and cardiac failure. Severe hypersensitivity reactions (including anaphylaxis), infusion reactions, and pulmonary events have been infrequently reported. Rarely, these were fatal.

Recently, Genentech issued a letter to healthcare providers explaining the cardiac monitoring guidelines under which the two U.S. cooperative group trials of Herceptin in the adjuvant setting were conducted.

Serious reactions were treated by discontinuing Herceptin and administering supportive therapy. In clinical trials, the incidence and severity of cardiac dysfunction was highest in patients receiving Herceptin with anthracycline and cyclophosphamide (AC). Most patients responded to medical therapy, including discontinuation of Herceptin. However, some patients were successfully managed while continuing Herceptin therapy. Patients receiving Herceptin should be monitored for deteriorating cardiac function.

In clinical trials, approximately 40 percent of patients experienced symptoms such as chills and fever during the first infusion. These and other symptoms, including nausea, vomiting, and pain, occurred infrequently with subsequent infusions. In clinical trials, the incidence of moderate to severe neutropenia and of febrile neutropenia were higher in patients receiving Herceptin in combination with myelosuppressive chemotherapy as compared to those receiving chemotherapy alone. There was an increased incidence of anemia leukopenia, diarrhea, and infection when Herceptin was used in combination with chemotherapy.

### **About Breast Cancer**

According to the American Cancer Society, an estimated 211,240 women will be diagnosed with breast cancer and approximately 40,000 women will die of the disease in the United States in 2005. Breast cancer is the most common cause of cancer among women in the

United States and a woman is diagnosed with breast cancer in the United States every three minutes.

### **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 leading 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 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. A therapeutic 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, a therapy targeting apoptosis, and a humanized anti-CD20 antibody for hematology/oncology indications.

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 directly in the United States and licenses several additional products to other companies. 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>.

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*The statements made in this press release relating to the expected timeframe for the sBLA filing for Herceptin is forward looking and the actual result could differ materially. Among*

*other things, the filing timeframe could be delayed by additional time requirements for data analysis or sBLA preparation or FDA actions.*

For full prescribing information, including Boxed Warnings for Avastin, Rituxan and Herceptin, or for Tarceva full prescribing information, please call 800-821-8590 or visit [www.gene.com](http://www.gene.com).