

Basel, 8 February 2012

FDA grants Roche's pertuzumab Priority Review for previously untreated HER2-positive metastatic breast cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has accepted the company's Biologics License Application for pertuzumab and granted Priority Review. The proposed indication is pertuzumab in combination with Herceptin (trastuzumab) and docetaxel chemotherapy for people with HER2-positive metastatic or locally recurrent, unresectable breast cancer, who have not received previous treatment or whose disease has relapsed after adjuvant therapy. The FDA confirmed the action date is June 8, 2012.

"We are pleased that the FDA has granted pertuzumab a Priority Review because new medicines are needed for HER2-positive breast cancer," said Hal Barron, M.D., Chief Medical Officer and Head, Global Product Development. "We have been researching HER2-positive breast cancer for more than 30 years, and we hope an expedited review will help us quickly bring another personalized medicine to people battling this aggressive disease."

The pertuzumab application is based on results from the pivotal Phase III CLEOPATRA study. The study demonstrated a 6.1 month improvement in median progression-free survival (PFS) for people who received a pertuzumab-based regimen (pertuzumab combined with Herceptin and docetaxel chemotherapy) compared to those who received Herceptin and chemotherapy alone (median PFS 18.5 vs. 12.4 months). People who received the combination also experienced a 38 percent reduction in the risk of their disease worsening or death (HR=0.62, $p < 0.0001$, according to independent review)¹.

Adverse events (AEs) were consistent with those seen in previous studies of pertuzumab and Herceptin, either in combination or alone.²

About Pertuzumab

Pertuzumab is a humanized monoclonal antibody being studied in early and advanced stages of HER2-positive breast cancer and advanced HER2-positive gastric cancer. Pertuzumab, a HER2 Dimerisation Inhibitor, is unique in that it is designed specifically to prevent the HER2 receptor from pairing (dimerising) with other HER receptors (EGFR/HER1, HER3 and HER4), a process that is believed to play a critical role in the growth and formation of several different cancer types. By preventing receptor pairing, pertuzumab is thought to block cell signalling, which may inhibit cancer cell growth or lead to the death of the cancer cell. Binding of pertuzumab to HER2 may also signal the body's immune system to destroy the cancer cells.

The mechanisms of action of pertuzumab and Herceptin are believed to complement each other, as both bind to the HER2 receptor but on different regions. The goal of combining pertuzumab with Herceptin and chemotherapy is to determine if the combination may provide a more comprehensive blockade of HER signalling pathways.

Roche has also submitted a Marketing Authorization Application to the European Medicines Agency (EMA) for pertuzumab for people with previously untreated HER2-positive mBC.

About the CLEOPATRA Study¹

CLEOPATRA (**C**linical **E**valuation **O**f **P**ertuzumab **A**nd **T**RAstuzumab) is an international, Phase III, randomised, double-blind, placebo-controlled study. The study evaluated the efficacy and safety profile of the pertuzumab-based regimen compared to Herceptin and chemotherapy plus placebo in 808 people with previously untreated HER2-positive mBC. The primary endpoint of the study was PFS as assessed by an independent review committee. Secondary endpoints were overall survival (OS), PFS by investigator assessment, safety profile, overall response rate (ORR), duration of response, time to symptom progression and correlation of biomarkers with clinical outcomes.

Rates of grade ≥ 3 AEs with $>2\%$ difference between arms were observed for neutropenia (low white blood cell count), febrile neutropenia (fever plus low white blood cell count), and diarrhoea with 48.9%, 13.8%, and 7.9% in the pertuzumab, Herceptin and chemotherapy arm compared with 45.8%, 7.6%, and 5.0% in the Herceptin plus chemotherapy arm, respectively. The pertuzumab-based regimen was not associated with a higher incidence of cardiac AEs or left ventricular dysfunction compared with Herceptin and chemotherapy. Left ventricular dysfunction occurred in 8.3% of people in the Herceptin and chemotherapy arm and 4.4% of people in the pertuzumab, Herceptin and chemotherapy arm.

About Breast Cancer

Breast cancer is the most common cancer among women worldwide¹. Each year about 1.4 million new cases of breast cancer are diagnosed worldwide, and over 450,000 women will die of the disease annually². In HER2-positive breast cancer, increased quantities of the human epidermal growth factor receptor 2 (HER2) are present on the surface of the tumour cells. This is known as “HER2 positivity” and affects approximately 15-20 percent of women with breast cancer³. HER2-positive cancer is a particularly aggressive form of breast cancer⁴.

About Herceptin

Herceptin (trastuzumab) is a humanised monoclonal antibody, designed to target and block the function of HER2, a protein produced by a specific gene with cancer-causing potential when it is overexpressed. The mode of action of Herceptin is unique in that it activates the body’s immune system and suppresses HER2 signalling to target and destroy the tumour. Herceptin has demonstrated unprecedented efficacy in treating both early and advanced (metastatic) HER2-positive breast cancer. Given on its own as monotherapy as well as in combination with or following standard chemotherapy, Herceptin has been shown to improve overall survival, response rates and disease-free survival while maintaining quality of life in women with HER2-positive breast cancer. Herceptin is marketed in the United States by Genentech, in Japan by Chugai and internationally by Roche. Since 1998, Herceptin has been used to treat almost 1 million patients with HER2-positive breast cancer worldwide.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world’s largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche’s personalized healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2011, Roche had over 80,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 42.5 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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Additional information

- Roche in Oncology: www.roche.com/de/media/media_backgroundunder/media_oncology.htm

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