Roche's Perjeta significantly extends survival in people with HER2-positive metastatic breast cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced updated survival results from the Phase III CLEOPATRA study, which showed that the combination of Perjeta (pertuzumab), Herceptin (trastuzumab) and docetaxel chemotherapy significantly extended the lives (overall survival) of people with previously untreated HER2-positive metastatic breast cancer (mBC), compared to Herceptin, chemotherapy and placebo. Results showed that the risk of death was reduced by 34 percent for people who received Perjeta, Herceptin and chemotherapy, compared to those who received Herceptin and chemotherapy (HR=0.66; p=0.0008). At the time of the analysis, median overall survival had not yet been reached in people receiving the Perjeta combination, as more than half of these people continued to survive. Median overall survival was more than 3 years (37.6 months) for people who received Herceptin and chemotherapy. Based on these data, people receiving Herceptin and chemotherapy in CLEOPATRA have been offered the option to receive Perjeta. No new safety signals were observed in the study.1

“This treatment combination with Perjeta is the first to have significantly extended survival compared to Herceptin and chemotherapy in people with previously untreated HER2-positive metastatic breast cancer,” said Hal Barron, M.D., Roche’s Chief Medical Officer and Head, Global Product Development. “These data further demonstrate that Perjeta is an important new medicine for people with this aggressive disease.”

Perjeta is a personalised medicine that targets the HER2 receptor, a protein found in high quantities on the outside of cancer cells in HER2-positive cancers. Perjeta is believed to work in a way that is complementary to Herceptin, as the two medicines target different places on the HER2 receptor.

In June 2012, the U.S. Food and Drug Administration (FDA) approved Perjeta in combination with Herceptin and docetaxel chemotherapy for the treatment of people with HER2-positive mBC, who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease, based on the results of the CLEOPATRA study. Perjeta was approved by Swissmedic in August 2012 and in Mexico in September 2012 for the treatment of people with HER2-positive mBC who have not received prior therapy for their metastatic
disease. Roche has submitted a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) for Perjeta for people with previously untreated HER2-positive metastatic breast cancer.

These final, confirmatory survival data from the CLEOPATRA study will be presented at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS; Abstract #P5-18-26, Friday 7th December 2012, 17:00-19:00 CDT Exhibit Hall A-B) by Dr. Sandra Swain, Medstar Washington Hospital Center, USA.

About the CLEOPATRA study

CLEOPATRA (CLinical Evaluation Of Pertuzumab And TRAstuzumab) is an international, Phase III, randomised, double-blind, placebo-controlled study. The study evaluated the efficacy and safety profile of Perjeta combined with Herceptin and docetaxel chemotherapy compared to Herceptin and docetaxel chemotherapy plus placebo in 808 people with previously untreated HER2-positive mBC, or with HER2-positive mBC that had come back after prior therapy in the adjuvant or neo-adjuvant setting.

The primary endpoint of the study was progression-free survival (PFS) as assessed by an independent review committee. Secondary endpoints were overall survival, PFS by investigator assessment, safety profile, overall response rate (ORR), duration of response and time to symptom progression. PFS and safety data from CLEOPATRA were presented at SABCS 2011 and simultaneously published in the *New England Journal of Medicine*.

Progression free survival and safety results

- People who received the combination of Perjeta, Herceptin and chemotherapy had a statistically significant 38 percent reduction in the risk of their disease worsening or death (PFS, HR=0.62, p-value=<0.0001) compared to people who received Herceptin, chemotherapy and placebo.\(^2\)
- The median PFS improved by 6.1 months from 12.4 months for people who received Herceptin and chemotherapy to 18.5 months for those who received Perjeta, Herceptin and chemotherapy.\(^2\)
- The most common adverse events (rate greater than 30 percent) seen with the combination of Perjeta, Herceptin and chemotherapy were diarrhoea, hair loss, low white blood cell count with or without fever, upset stomach, fatigue, rash and peripheral neuropathy (numbness, tingling or damage to the nerves). The most common Grade 3–4 adverse events (rate greater than 2 percent) were low white blood cell count with or without fever, decrease in a certain type of white blood cell, diarrhoea, damage to the nerves, decrease in red blood cell count, weakness and fatigue.\(^2\)
**About Perjeta**

Perjeta is designed specifically to prevent the HER2 receptor from pairing (or ‘dimerising’) with other HER receptors (EGFR/HER1, HER3 and HER4) on the surface of cells, a process that is believed to play a role in tumour growth and survival. Binding of Perjeta to HER2 may also signal the body's immune system to destroy the cancer cells. The mechanisms of action of Perjeta and Herceptin are believed to complement each other, as both bind to the HER2 receptor, but to different places. The combination of Perjeta, Herceptin and docetaxel chemotherapy is thought to provide a more comprehensive blockade of HER signalling pathways.

Roche has spent more than 30 years studying the role of HER2 in cancer, and Perjeta is a result of this research. A companion diagnostic test is used to determine if a person is HER2-positive and whether treatment with Perjeta and Herceptin is appropriate.

**About Herceptin**

Herceptin 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 more than 1.2 million people with HER2-positive breast cancer worldwide.

**About breast cancer**

Breast cancer is the most common cancer among women worldwide. Each year about 1.4 million new cases of breast cancer are diagnosed worldwide, and over 450,000 women will die of the disease annually. 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 cancer. HER2-positive cancer is a particularly aggressive form of breast cancer.
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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