

Basel, June 26, 2015

## **Roche's Perjeta recommended for approval in EU for use before surgery in HER2-positive early breast cancer**

- The Perjeta regimen is the first neoadjuvant (pre-surgery) breast cancer treatment recommended for approval in the EU based on the benefit in achieving pathological complete response (pCR)

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the EU Committee for Medicinal Products for Human Use (CHMP) has recommended that the European Commission approves the use of Perjeta® (pertuzumab) in combination with Herceptin® (trastuzumab) and chemotherapy for the neoadjuvant treatment (use before surgery) of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence. The EU filing was based primarily on data from the Phase II NeoSphere study, which showed that nearly 40% of people receiving the Perjeta regimen had no evidence of tumour tissue detectable at the time of surgery in the affected breast and local lymph nodes (known as a pathological complete response, or pCR) compared to 21.5% of people who received Herceptin and taxane chemotherapy alone.<sup>1</sup> This is the first CHMP recommendation in the neoadjuvant setting based on pCR.

Every year, approximately 100,000 people in Europe are diagnosed with HER2-positive breast cancer, an aggressive type of the disease that is likely to progress more quickly than cancer that is HER2-negative.<sup>2,3</sup> The majority of breast cancer cases are diagnosed at an early stage of the disease, before the cancer has spread to other parts of the body.<sup>4,5</sup>

“Breast cancer treatment has the greatest impact in the early stage, where it can potentially prevent the disease from returning and spreading. Consequently, there is a need to bring promising treatments to patients with early breast cancer,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We are very pleased that the use of pCR as a novel clinical trial endpoint may hopefully soon allow us to make the Perjeta regimen available to patients with early breast cancer in Europe.”

The CHMP opinion was provided in the context of the totality of Perjeta data available to date, including the biological rationale for the combination of Perjeta, Herceptin and taxane chemotherapy, its established safety profile and the efficacy results in the advanced breast cancer (aBC) setting. The submission was supported by efficacy and safety data from two neoadjuvant studies, NeoSphere and TRYPHAENA, as well as long-term safety results from the CLEOPATRA trial in people with previously untreated HER2-positive aBC. Data from the ongoing Phase III

APHINITY study in the adjuvant (post-surgery) setting will provide additional insights into the broader role of Perjeta in the treatment of HER2-positive early breast cancer (eBC).

Perjeta is already approved as a neoadjuvant treatment for people with HER2-positive eBC in the U.S. and 20 other countries.

Follow-up data from the NeoSphere study were presented at the American Society of Clinical Oncology (ASCO) 2015 Annual Meeting.<sup>6</sup> These data suggest that, at three years, people who received the Perjeta regimen prior to surgery were 31% less likely to experience disease worsening, recurrence or death (progression-free survival, PFS HR=0.69; 95% CI, 0.34–1.40) compared to those who received Herceptin and chemotherapy.<sup>6</sup> People treated with the Perjeta regimen were also 40% less likely to experience disease recurrence or death (disease-free survival, DFS HR=0.60; 95% CI, 0.28–1.27).<sup>6</sup>

### **About Perjeta**

Perjeta is a medicine that targets the HER2 receptor, a protein found on the outside of many normal cells and in high quantities on the outside of cancer cells in HER2-positive cancers. 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 and Herceptin is thought to provide a more comprehensive blockade of HER signalling pathways, thus preventing tumour cell growth and survival.

### **About the NeoSphere trial**

The NeoSphere trial<sup>1</sup> (**Neoadjuvant Study of Pertuzumab and Herceptin in an Early Regimen Evaluation**) is a randomised, multicentre, international Phase II study in 417 people with newly diagnosed HER2-positive, operable, locally advanced or inflammatory eBC. Participants were randomised to one of four study arms and received four cycles (12 weeks) of neoadjuvant treatment followed by surgery and a year of adjuvant treatment with Herceptin plus chemotherapy. The primary endpoint was pCR. Secondary endpoints included clinical response, time to clinical response, safety profile, DFS, PFS, breast-conserving surgery rate and biomarker assessment. Study data showed the following:

- Treatment with Perjeta, Herceptin and docetaxel chemotherapy significantly improved the rate of pCR in the breast and local lymph nodes by 17.8% compared to Herceptin and chemotherapy alone (39.3% vs. 21.5%, p=0.0063).
  - pCR of 21.5% for Herceptin and chemotherapy
  - pCR of 39.3% for Perjeta, Herceptin and chemotherapy
  - pCR of 11.2% for Perjeta and Herceptin
  - pCR of 17.7% for Perjeta and chemotherapy
- The Perjeta regimen was not associated with a significant increase in adverse events (AEs), compared to Herceptin and chemotherapy alone.

- The most common severe (Grade 3 or higher) AEs for the Perjeta regimen were neutropenia (decrease in a certain type of white blood cell, 44.9%), febrile neutropenia (fever associated with decrease in a certain type of white blood cell, 8.4%), leukopenia (decrease in overall white blood cells, 4.7%) and diarrhoea (5.6%).

pCR means that there is no tumour tissue detectable at the time of surgery either in the affected breast or in the affected breast and local lymph nodes following completion of neoadjuvant treatment.

### **About the TRYPHAENA trial**

The TRYPHAENA trial<sup>7</sup> (ToleRabilitY of Pertuzumab, Herceptin and AnthracyclinEs in NeoAdjuvant breast cancer) is a randomised, multicentre Phase II study that was conducted in 225 people with HER2-positive, operable, locally advanced or inflammatory eBC with tumours greater than two centimetres. Participants were randomised to one of three neoadjuvant Perjeta regimens. The primary endpoint was cardiac safety. Secondary endpoints included pCR, clinical response, breast-conserving surgery rate, DFS, PFS, overall survival (OS) and biomarker assessment. Study data showed the following:

- The study was not powered to compare the three study arms. The rates of total pCR in the breast and local lymph nodes in the three arms were as follows:
  - pCR of 56.2% for Perjeta, Herceptin and anthracycline-based chemotherapy, followed by Perjeta, Herceptin and chemotherapy
  - pCR of 54.7% for anthracycline-based chemotherapy, followed by Perjeta, Herceptin and chemotherapy
  - pCR of 63.6% for the anthracycline-free arm (Perjeta, Herceptin, chemotherapy and carboplatin chemotherapy)
- No new or unexpected cardiac AEs, or other AEs, were observed in any of the study arms. AEs observed were consistent with those seen in previous studies of Perjeta, Herceptin and chemotherapy, either in combination or alone.
- The most common severe (Grade 3 or higher) AEs in any of the three study arms were:
  - In the concurrent arm: neutropenia (47.2%), leukopenia (19.4%) and febrile neutropenia (18.1%)
  - In the sequential arm: neutropenia (42.7%), leukopenia (12.0%), febrile neutropenia (9.3%), diarrhoea (5.3%) and left ventricular dysfunction (4.0%)
  - In the anthracycline-free arm: neutropenia (46.1%), febrile neutropenia (17.1%), anaemia (decrease in red blood cells, 17.1%); the AEs of diarrhoea, leukopenia, anaemia and thrombocytopenia (decrease in platelets) all had an incidence of 11.8%

### **About Roche's medicines for HER2-positive breast cancer**

Roche has been leading research into the HER2 pathway for over 30 years and is committed to improving the health, quality of life and survival for people with both early and advanced HER2-positive disease.

Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin, Perjeta and Kadcyła. HER2-positive breast cancer is a

particularly aggressive form of the disease that affects approximately 20% of patients.<sup>3</sup> Over the past 15 years, the outlook for people with HER2-positive disease has improved to the extent that those with this form of the disease treated with these innovative medicines now typically experience better outcomes than people with less aggressive HER2-negative disease.<sup>8</sup>

Eligibility for treatment with Roche's HER2-targeted medicines is determined via a diagnostic test, saving time from the outset by identifying patients who will likely benefit from these medicines at the onset of their disease.

### **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, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-nine medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy.

In 2014, the Roche Group employed 88,500 people worldwide, invested 8.9 billion Swiss francs in R&D and posted sales of 47.5 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit [www.roche.com](http://www.roche.com).

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### **Additional information**

- Roche in Oncology: [www.roche.com/media/media\\_backgrounder/media\\_oncology.htm](http://www.roche.com/media/media_backgrounder/media_oncology.htm).
- Follow us via @roche on Twitter and on LinkedIn at <https://www.linkedin.com/company/1602>.

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- <sup>7</sup> Schneeweiss A, et al. *Cancer Res* 2011; 71(suppl 24):S5-6.
- <sup>8</sup> Dawood S, et al. *J Clin Oncol* 2010; 28:92.