Media Release

Basel, 01 June 2018

European Commission approves Roche’s Perjeta for post-surgery treatment of HER2-positive early breast cancer at high risk of recurrence

- An important new treatment option has been approved for patients in Europe with HER2-positive early breast cancer at high risk of recurrence in a setting where the goal of treatment is cure
- High risk of recurrence is defined as lymph node-positive or hormone receptor-negative disease, based on the large phase III APHINITY study
- One year of treatment with Perjeta, Herceptin and chemotherapy has been shown to reduce the risk of recurrence or death by 23-24% in these high risk subgroups

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission (EC) has approved Perjeta® (pertuzumab) in combination with Herceptin® (trastuzumab) and chemotherapy (the Perjeta®-based regimen) for post-surgery (adjuvant) treatment of adult patients with HER2-positive early breast cancer (eBC) at high risk of recurrence. High risk of recurrence is defined as lymph node-positive or hormone receptor-negative disease. The Perjeta®-based regimen should be administered for a total of one year (up to 18 cycles) as part of a complete regimen for eBC and regardless of the timing of surgery.

HER2-positive breast cancer affects almost 100,000 women in Europe each year.1,2 The majority of these cases are diagnosed at an early stage, when the aim of treatment is cure.3,4 While significant advances have been made in treating HER2-positive eBC, around one in four patients treated with Herceptin and chemotherapy will eventually see their disease return in the long-term.5 It is estimated that two out of three cases of HER2-positive advanced breast cancer (aBC) are a result of recurrence, as opposed to aBC being the initial diagnosis.6 There is no cure for breast cancer that recurs and reaches an advanced stage; in these cases, treatment is aimed at prolonging life for as long as possible.7

“Despite advances in the treatment of HER2-positive early breast cancer, many people still have a recurrence and progress to an incurable stage. In the early breast cancer setting, where the ultimate goal is cure, it is critical that we continue building on existing therapies,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “Today’s approval is great news, as we believe the Perjeta-based regimen has the potential to make a significant impact on the lives of people with HER2-positive early...
breast cancer who are at high risk of recurrence. We are committed to working with EU member states to ensure the Perjeta-based regimen is available to eligible patients as soon as possible.”

“Some patients with early HER2-positive breast cancer are more likely to relapse than others, despite available treatments. Perjeta builds on the efficacy we have already seen with Herceptin and provides a clinically meaningful reduction in the risk of the breast cancer returning or death, for patients at high risk of recurrence,” explained José Baselga, MD, PhD, Physician-in-Chief, Memorial Hospital, Memorial Sloan Kettering Cancer Center. “The only setting where we can potentially cure HER2-positive breast cancer is at the early stage, so the availability of new treatment options is great news for patients.”

The EC approval is based on results from a large phase III study (APHINITY), involving over 4,800 people with HER2-positive eBC, which showed that the Perjeta-based regimen significantly reduced the risk of invasive breast cancer recurrence or death (invasive disease-free survival, iDFS) compared to Herceptin and chemotherapy alone in the overall study population. At the time of primary analysis, the Perjeta-based regimen showed the greatest benefit in certain patients who are at high risk of recurrence:

- For patients with lymph node-positive disease, the risk of recurrence or death was reduced by 23% with the Perjeta-based regimen (HR=0.77; 95% CI 0.62-0.96, p=0.019).
- Among patients with hormone receptor-negative disease, the Perjeta-based regimen reduced the risk of recurrence or death by 24% (HR=0.76; 95% CI 0.56-1.04, p=0.085).

The safety profile of the Perjeta-based regimen was consistent with that seen in previous studies, with a low incidence of cardiac events and no new safety signals.

In the eBC setting, treatment may be given before surgery (neoadjuvant treatment) to shrink tumours and after surgery (adjuvant treatment) to help prevent the cancer from returning. The Perjeta-based regimen is already licensed in the EU, US and many other countries as a neoadjuvant treatment. The adjuvant approval means that eligible patients with HER2-positive eBC in Europe should be treated with the Perjeta-based regimen for a total of one year as part of a complete regimen for eBC, regardless of the timing of surgery. The Perjeta-based regimen is already approved in the US and several other countries for adjuvant treatment of HER2-positive eBC at high risk of recurrence.
The combination has also been previously approved for the treatment of people with advanced HER2-positive breast cancer, where it has been shown to significantly extend survival compared to Herceptin and chemotherapy alone.\textsuperscript{10,11}

On 30 April, the EC also approved the use of Perjeta with a subcutaneous (SC) formulation of Herceptin as an alternative to the previously approved co-administration of Perjeta with Herceptin intravenous (IV) formulation.\textsuperscript{11} The Herceptin SC formulation allows Herceptin to be delivered to patients in two to five minutes via an injection under the skin, compared to 30 to 90 minutes required for the original IV formulation.\textsuperscript{12}

Perjeta works in combination with Herceptin to provide a more comprehensive, dual blockade of the HER2 receptor, thus preventing tumour cell growth and survival.\textsuperscript{13}

For more information about HER2-positive breast cancer and the goals of treatment, visit our Breast Cancer Hub on roche.com.

\* Prespecified subgroup analyses without adjusting for multiple comparisons. Results are considered descriptive.

**About APHINITY**

APHINITY (Adjuvant Pertuzumab and Herceptin IN Initial TherapY in Breast Cancer, NCT01358877/BO25126/ BIG 4-11) is an international, phase III, randomised, double-blind, placebo-controlled, two-arm study evaluating the efficacy and safety of Perjeta plus Herceptin and chemotherapy, compared to Herceptin and chemotherapy, as adjuvant therapy in 4,805 people with operable HER2-positive eBC. The primary efficacy endpoint of the APHINITY study is invasive disease-free survival (iDFS), which in this study is defined as the time a patient lives without return of invasive breast cancer at any site or death from any cause after adjuvant treatment. Secondary endpoints include cardiac and overall safety, overall survival, disease-free survival and health-related quality of life. The study will continue to follow participants for ten years.

At the time of the primary analysis, with a median follow-up of 45.4 months, the Perjeta-based regimen significantly reduced the risk of invasive breast cancer recurrence or death by 19% compared to Herceptin and chemotherapy alone in the overall study population (HR=0.81, 95% CI 0.66-1.00, p=0.045). Estimates of iDFS rates were 94.1% vs. 93.2% at three years and 92.3% vs. 90.6% at four years\textsuperscript{1} in Perjeta-treated patients vs. placebo-treated patients, respectively.
The subgroup results were as follows:

- **Lymph node-positive subgroup (HR=0.77, 95% CI 0.62-0.96)**
  - Estimate of iDFS at three years 92.0% vs. 90.2%
  - Estimate of iDFS at four years 89.9% vs. 86.7%

- **Lymph node-negative subgroup (HR=1.13, 95% CI 0.68-1.86)**
  - Estimate of iDFS at three years 97.5% vs. 98.4%
  - Estimate of iDFS at four years 96.2% vs. 96.7%

- **Hormone receptor-negative subgroup (HR=0.76, 95% CI 0.56-1.04)**
  - Estimate of iDFS at three years 92.8% vs. 91.2%
  - Estimate of iDFS at four years 91.0% vs. 88.7%

- **Hormone receptor-positive subgroup (HR=0.86, 95% CI 0.66-1.13)**
  - Estimate of iDFS at three years 94.8% vs. 94.4%
  - Estimate of iDFS at four years 93.0% vs. 91.6%

The most common severe (Grade 3-4) side effects with the Perjeta-based regimen are low levels of white blood cells with or without a fever, diarrhoea, decrease in certain types of white blood cells, decrease in red blood cells, fatigue, nausea and mouth blisters or sores. The most common side effects are diarrhoea, nausea, hair loss, fatigue, nerve damage and vomiting.

* Prespecified subgroup analyses without adjusting for multiple comparisons. Results are considered descriptive.

† iDFS at four years was calculated based on data available at the time of primary analysis with median follow-up of 45.4 months.

**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.\(^{14,15}\) 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, dual blockade of HER signalling pathways, thus preventing tumour cell growth and survival.\(^{13,16}\)
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 of people with both early and advanced HER2-positive disease. HER2-positive breast cancer is a particularly aggressive form of the disease that affects approximately 15-20% of patients.\(^1\) Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin, Perjeta and Kadcyla* (trastuzumab emtansine).

Eligibility for treatment with Roche’s HER2-targeted medicines is determined via a diagnostic test, which identifies people who will likely benefit from these medicines at the onset of their disease.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people’s lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare - a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world’s largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. Thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 billion. 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). All trademarks used or mentioned in this release are protected by law.
Roche Group Media Relations
Phone: +41 61 688 8888 / e-mail: media.relations@roche-global.com
- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Simone Oeschger
- Anja von Treskow

References