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FDA grants Priority Review for Roche's Perjeta (pertuzumab) for adjuvant treatment of HER2-positive early breast cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced the US Food and Drug Administration (FDA) has accepted the company's supplemental Biologics License Application (sBLA) and granted Priority Review for Perjeta® (pertuzumab), in combination with Herceptin® (trastuzumab) and chemotherapy (the Perjeta-based regimen), for adjuvant (after surgery) treatment of HER2-positive early breast cancer (eBC). The FDA is expected to make a decision on approval by 28 January 2018. The sBLA is based on results of the phase III APHINITY study. A Priority Review designation is granted to medicines that the FDA has determined to have the potential to provide significant improvements in the treatment, prevention or diagnosis of a disease.

"We are pleased to receive Priority Review for the Perjeta-based regimen for the adjuvant treatment of HER2-positive early breast cancer," said Sandra Horning, M.D., Roche's Chief Medical Officer and Head of Global Product Development. "The goal of treating breast cancer early is to provide people with the best chance for a cure. Despite advances in the treatment of this disease, many people treated with the current standard of care still see their cancer return."

The combination of Perjeta, Herceptin and chemotherapy is licensed as a neoadjuvant (before surgery) treatment for people with HER2-positive eBC in more than 85 countries worldwide following approvals by the European Medicines Agency (EMA) and the US FDA. In the US, the regimen is currently available under the FDA Accelerated Approval Program. This sBLA seeks to convert the current accelerated approval to full approval in the US. Additionally, the APHINITY trial reflects the commitment to evaluate the Perjeta-based regimen as part of a complete treatment approach for eBC. Perjeta in combination with Herceptin and docetaxel chemotherapy is also approved in the US and the European Union for people with previously untreated HER2-positive metastatic breast cancer.

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About APHINITY[1]

APHINITY (**A**djuvant **P**ertuzumab and **H**erceptin **IN** **I**nitial **T**herap**Y** 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.

APHINITY Study Results[1] Median follow-up for intent-to-treat (ITT) population 45.4 months (381 events)		
Primary endpoint: invasive disease-free survival (iDFS), HR=0.81; 95% CI 0.66-1.00, p=0.045		
	Perjeta + Herceptin + chemotherapy n=2,400	**Placebo + Herceptin + chemotherapy** n=2,404
iDFS at 3 years		
ITT population n=4,804	94.1% 171 events	93.2% 210 events
	HR=0.81; 95% CI 0.66-1.00, p=0.045	
Node-positive subgroup n=3,005	92.0% 139 events	90.2% 181 events
	HR=0.77; 95% CI 0.62-0.96, p=0.019	
Node-negative subgroup n=1,799	97.5% 32 events	98.4% 29 events
	HR=1.13; 95% CI 0.68-1.86, p=0.644	
Hormone receptor-positive subgroup n=3,082	94.8% 100 events	94.4% 119 events
	HR=0.86; 95% CI 0.66-1.13, p=0.277	
Hormone receptor-negative subgroup n=1,722	92.8% 71 events	91.2% 91 events
	HR=0.76; 95% CI 0.56-1.04, p=0.085	

Estimate of iDFS at 4 years*		
ITT population n=4,804	92.3%	90.6%
Node-positive subgroup n=3,005	89.9%	86.7%
Node-negative subgroup n=1,799	96.2%	96.7%
Hormone receptor-positive subgroup n=3,082	93.0%	91.6%
Hormone receptor-negative subgroup n=1,722	91.0%	88.7%
Safety		
Grade 3 or higher adverse event (AE)	64.2%	57.3%
Fatal AE	0.8%	0.8%
Primary cardiac event**	0.7%	0.3%
	Difference 0.4%; 95% CI 0.0-0.8%	
Most common (≥5%) severe (Grade 3 or higher) AEs		
Neutropenia *Decrease in a certain type of white blood cell*	16.3%	15.7%
Febrile neutropenia *Fever associated with decrease in a certain type of white blood cell*	12.1%	11.1%
Diarrhoea	9.8%	3.7%
Diarrhoea *Onset after chemotherapy, during targeted therapy*	0.5%	0.2%
Neutrophil count decreased *Decrease in a certain type of white blood cell*	9.6%	9.6%
Anaemia *Decrease in red blood cells or haemoglobin*	6.9%	4.7%

** iDFS at four years was calculated based on data available at the time of primary analysis with median follow-up of 45.4 months*
*** Primary cardiac events included heart failure New York Heart Association (NYHA) class III or IV with left ventricular ejection fraction (LVEF) drop ≥10 points from baseline and to below 50%; and cardiac death*

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.[2,3] 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.[4,5]

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 20% of patients.[6] 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 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 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.

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