

Roche submits supplemental biologics license application to the US FDA for Kadcyła for adjuvant treatment of people with HER2-positive early breast cancer with residual disease after neoadjuvant treatment

- **Roche's application is being reviewed under the US FDA's Real-Time Oncology Review and Assessment Aid pilot programmes**
- **Kadcyła was granted Breakthrough Therapy Designation for this application**

Basel, 05 February 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced completing the submission of a supplemental Biologics License Application to the US Food and Drug Administration (FDA) for Kadcyła^{*} (trastuzumab emtansine) for adjuvant (after surgery) treatment of people with HER2-positive early breast cancer (eBC) with residual disease after neoadjuvant (before surgery) treatment. The FDA is reviewing the application under the Real-Time Oncology Review and Assessment Aid pilot programmes, which aim to explore a more efficient review process to ensure safe and effective treatments are available to patients as early as possible.^{1,2} For this indication, Kadcyła was also granted Breakthrough Therapy Designation, which is designed to expedite the development and review of medicines intended to treat serious or life-threatening diseases.³

“Kadcyła was granted Breakthrough Therapy Designation and is also the first Roche medicine to be reviewed under the FDA's Real-Time Oncology Review pilot programme; both FDA initiatives aim to expedite reviews and bring medicines to patients sooner” said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. “We are working closely with the FDA to bring Kadcyła to people with HER2-positive early breast cancer who have residual disease after neoadjuvant therapy as early as possible.”

This application is based on results of the phase III KATHERINE study showing Kadcyła significantly reduced the risk of invasive breast cancer recurrence or death from any cause (invasive disease-free survival; iDFS) by 50% (HR=0.50, 95% CI 0.39-0.64, p<0.0001) compared to Herceptin^{*} (trastuzumab) as an adjuvant treatment in people with HER2-positive eBC who have residual disease present following neoadjuvant treatment.⁴ People who have residual disease after neoadjuvant treatment have a worse prognosis than those with no detectable disease. At three years, 88.3% of people treated with Kadcyła did not have their breast cancer return compared to 77.0% treated with Herceptin, an absolute improvement of 11.3%.⁴

The most common Grade 3-4 side effects ($\geq 1\%$) with Kadcyła in the KATHERINE study were decreased platelet count; high blood pressure; radiation-induced skin injury; numbness, tingling or pain in the hands or feet; decreased neutrophil count; low blood potassium level; fatigue and decrease in red blood cells.⁴

About the KATHERINE study⁵

KATHERINE is an international, multi-centre, two-arm, randomised, open-label, phase III study evaluating the efficacy and safety of Kadcyła versus Herceptin as an adjuvant therapy in people with HER2-positive eBC who have pathological invasive residual disease in the breast and/or axillary lymph nodes following neoadjuvant therapy that included Herceptin and taxane-based chemotherapy. The primary endpoint of the study is iDFS, which in this study is defined as the time from randomisation free from invasive breast cancer recurrence or death from any cause. Secondary endpoints include disease-free survival and overall survival.

About Kadcyła

Kadcyła is an antibody-drug conjugate (ADC) engineered to deliver potent chemotherapy directly to HER2-positive cancer cells, potentially limiting damage to healthy tissues.^{6,7} It combines two anti-cancer properties joined together by a stable linker: the HER2-targeting properties of trastuzumab (the active ingredient in Herceptin) and the chemotherapy agent DM1.⁸ Kadcyła is the only ADC approved as a single agent in 104 countries including the US and EU for the treatment of people with HER2-positive metastatic breast cancer who have previously received Herceptin and taxane chemotherapy, separately or in combination. Roche licenses technology for Kadcyła under an agreement with ImmunoGen, Inc.

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.⁹ Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin (trastuzumab), Perjeta® (pertuzumab) and Kadcyła (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. Moreover, for the tenth consecutive year, Roche has been recognised as the most sustainable company in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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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Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Simone Oeschger
- Anja von Treskow