Media Release

CHMP recommends EU approval of Roche's Kadcyla for the adjuvant treatment of people with HER2-positive early breast cancer with residual invasive disease after neoadjuvant treatment

- **Kadcyla cut the risk of disease recurrence or death by half compared to Herceptin in the adjuvant setting for specific patients with HER2-positive early breast cancer**
- **At three years, 88.3% of people treated with Kadcyla did not have their breast cancer return compared to 77.0% treated with Herceptin, an absolute improvement of 11.3%**
- **Kadcyla in early breast cancer represents a new treatment option for this group of patients after neoadjuvant treatment who are known to have a worse prognosis**

Basel, 15 November 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended the approval of Kadcyla® (trastuzumab emtansine) for the adjuvant (after surgery) treatment of adult patients with HER2-positive early breast cancer (eBC) who have residual invasive disease, in the breast and/or lymph nodes, after neoadjuvant (before surgery) taxane-based and HER2-targeted therapy. Based on this recommendation, a final decision regarding approval of Kadcyla in this setting, along with the full details of the approved indication, is expected from the European Commission in the near future.

"In the early breast cancer setting where cure is achievable, it is important to do everything possible to prevent progression to an advanced, incurable stage." said Levi Garraway, MD PhD, Roche's Chief Medical Officer and Head of Global Product Development. "This recommendation therefore marks a significant step forward in bringing a potentially transformative treatment option to patients in Europe with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant therapy."

The recommendation from the CHMP is based on results from the phase III KATHERINE study which showed that Kadcyla 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<0.001) compared to Herceptin as an adjuvant treatment in people with HER2-positive eBC who have residual invasive disease after neoadjuvant taxane and Herceptin-based treatment. At three years, 88.3% of people treated with Kadcyla did not have their breast cancer return compared to 77.0% treated with Herceptin, an absolute improvement of 11.3%. The safety profile of Kadcyla was consistent with that observed in previous studies. [1]

The importance of the KATHERINE data was recognised in May 2019 by the US Food and Drug Administration which accelerated the approval of Kadcyla for the adjuvant treatment of people with HER2-positive eBC with residual invasive disease after neoadjuvant treatment under their Real-Time Oncology Review (RTOR) and Assessment Aid pilot programmes. This led to an approval just over 12 weeks after completing the submission. Kadcyla was the first Roche medicine approved under the RTOR pilot programme, which is exploring a more efficient review process to ensure safe and effective treatments are available to patients as early as possible. [2] This latest milestone is another step towards bringing this new

treatment option to patients in Europe as soon as possible.

About the KATHERINE study[3]

KATHERINE is an international, multi-centre, two-arm, randomised, open-label, phase III study evaluating the efficacy and safety of Kadcyla 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 this study defined as the time from randomisation to the time that the patient is free from invasive breast cancer recurrence or death from any cause. Secondary endpoints include iDFS including second primary non-breast cancer, disease-free survival and overall survival.

KATHERINE study results [1]		
	Kadcyla n=743	**Herceptin n=743**
Median follow-up	~41 months	
Invasive disease-free survival (iDFS)		
Risk reduction	HR=0.50, 95% CI 0.39-0.64, p<0.001	
3-year iDFS	88.3%	77.0%
	11.3% absolute improvement	
Adverse events (AEs)		
Grade ≥3AEs	25.7%%	15.4%
Most common Grade ≥3 AEs (≥1%)		
Thrombocytopenia (decreased platelet count)	5.7%	0.3%
Hypertension (high blood pressure)	2.0%	1.2%

About Kadcyla

Kadcyla is an antibody-drug conjugate (ADC) engineered to deliver potent chemotherapy directly to HER2-positive cancer cells, potentially limiting damage to healthy tissues. [4] 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. [5] Kadcyla is the only ADC approved as a single agent in over 100 countries, including the US and EU, for the treatment of people with HER2-positive metastatic breast cancer who have previously received Herceptin and taxane-based chemotherapy, separately or in combination. Kadcyla is also approved in the US for the adjuvant treatment of people with HER2-positive eBC with residual invasive disease after neoadjuvant treatment that included Herceptin and taxane-based chemotherapy. [6] Roche licenses technology for Kadcyla 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 breast cancer. HER2-positive breast cancer is a particularly aggressive form of the disease that affects approximately 15-20% of patients. [6] Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin® (trastuzumab), Perjeta® (pertuzumab) 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. More than 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 eleventh consecutive year, Roche has been recognised as one of the most sustainable companies 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.

References
[1] Minckwitz G, et al. N Engl J Med. 2018;DOI:10.1056/NEJMoa1814017.
[2] US Food and Drug Administration. Real-Time Oncology Review Pilot Program. [Internet; cited November 2019]. Available from: https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OCE/ucm612927.htm.
[3] ClinicalTrials.gov. A Study of Trastuzumab Emtansine Versus Trastuzumab as Adjuvant Therapy in Patients With HER2-Positive Breast Cancer Who Have Residual Tumor in the Breast or Axillary Lymph Nodes Following Preoperative Therapy (KATHERINE). [Internet; cited November 2019]. Available from: https://clinicaltrials.gov/ct2/show/NCT01772472.
[4] Hurvitz SA, et al. J Clin Oncol. 2013;31(9):1157-63.
[5] Verma S, et al. N Engl J Med. 2012;367(19):1783-91.
[6] Wolff AC, et al. J Clin Oncol. 2013;31(31):3997-4013.

Roche Group Media Relations
Phone: +41 61 688 8888 / e-mail: media.relations@roche.com
- Nicolas Dunant (Head)
- Patrick Barth
- Daniel Grotzky
- Karsten Kleine
- Nathalie Meetz
- Barbara von Schnurbein