Media Release

Roche's Kadcyla cut the risk of disease recurring by half compared to Herceptin in people with HER2-positive early breast cancer with residual disease after neoadjuvant treatment

- **At three years, 88.3% of people treated with Kadcyla in the adjuvant HER2-positive early breast cancer setting did not have their breast cancer return compared to 77.0% treated with Herceptin, an 11.3% improvement**
- **People who have residual disease after neoadjuvant treatment have a worse prognosis than those with no detectable disease**
- **Data from the phase III KATHERINE study will be submitted to health authorities globally, including the US Food and Drug Administration and European Medicines Agency**
- **Results are being presented at the 2018 San Antonio Breast Cancer Symposium, featured in the press programme and simultaneously published in the *New England Journal of Medicine* on Wednesday, 5 December 2018**

Basel, 5 December 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the phase III KATHERINE study met its primary endpoint, showing Kadcyla® (trastuzumab emtansine) as a single agent significantly reduced the risk of disease recurrence or death (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 (after surgery) treatment in people with HER2-positive early breast cancer (eBC) who have residual disease (pathological invasive residual disease in the breast and/or axillary nodes) present following neoadjuvant (before surgery) treatment. [1] 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 11.3% improvement. [1] Kadcyla improved iDFS irrespective of hormone receptor status, lymph node status and prior HER2-targeted treatment regimen received in the neoadjuvant setting.[1] The safety profile of Kadcyla was consistent with that seen in previous studies, and no unexpected or new safety signals were identified.[1,2,3]

"The KATHERINE results demonstrate a significant reduction in the risk of recurrence of HER2-positive early breast cancer in people with residual disease after neoadjuvant therapy, and we look forward to submitting these data to health authorities as soon as possible," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "We come closer to the goal of helping each person with early breast cancer have the greatest opportunity for cure with every advance in reducing disease recurrence."

The goal in treating eBC is to provide people with the best chance for a cure, which may involve treatment before and after surgery as part of a comprehensive treatment approach. [4;5] While we come closer to this goal with each advance, many people still have a disease recurrence in the long-term. [6] Neoadjuvant treatment is given before surgery with the goal of shrinking tumours and helping to improve surgical outcomes. [5;7;8] Adjuvant treatment is given after surgery and is aimed at eliminating any remaining cancer cells in the body to help reduce the risk of the cancer returning. [5]

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These results are being presented in an oral session today at the 2018 San Antonio Breast Cancer Symposium (SABCS) at 11.00 am CST (abstract GS1-10) and featured in the official SABCS press programme at 07.15 am CST. These results will simultaneously be published in the *New England Journal of Medicine*.

About the KATHERINE study [9]

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, 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.

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<0.0001	
3-year iDFS	88.3%	77.0%
	11.3% improvement	
Overall survival (OS)		
Risk reduction	HR=0.70, 95% CI 0.47-1.05, p=0.0848 *Data immature at this interim analysis*	
Adverse events (AEs)		
Grade ≥3 AE	25.7%	15.4%
Serious AE	12.7%	8.1%
Most common Grade ≥3 AEs		
Thrombocytopenia *(decreased platelet count)*	5.7%	0.3%
Hypertension *(high blood pressure)*	2.0%	1.2%
Radiation-induced skin injury	1.4%	1.0%
Peripheral neuropathy *(numbness, tingling or pain in the hands or feet)*	1.4%	0.0%
Neutropenia *(decreased neutrophil count)*	1.2%	0.7%
Hypokalaemia *(low blood potassium level)*	1.2%	0.1%
Fatigue	1.1%	0.1%
Anaemia *(decrease in red blood cells)*	1.1%	0.1%

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. [2;3] 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.[10] Kadcyla 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 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 disease. HER2-positive breast cancer is a particularly aggressive form of the disease that affects approximately 15-20% of patients. [11] 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. 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 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.

References

[1] Geyer, et al. KATHERINE trial. Presented at SABCS; 2018 Dec 4-8; San Antonio, TX, USA. Abstract #GS1-10.
[2] Hurvitz SA, et al. J Clin Oncol. 2013;31(9):1157-63.
[3] Verma S, et al. N Engl J Med. 2012;367(19):1783-91.
[4] Scharl A, et al. Geburtshilfe Frauenheilkd. 2015;75(7):683-91.
[5] Johns Hopkins. Neoadjuvant and Adjuvant Chemotherapy. [Internet; cited 2018 November 29]. Available from: http://www.hopkinsmedicine.org/breast_center/treatments_services/medical_oncology/neoadjuvant_adjuvant_chemotherapy.html.
[6] Slamon D, et al. BCIRG 006 trial. Presented at: SABCS; 2015 Dec 6-10; San Antonio, TX, USA. Abstract #S5-04.
[7] Abt NB, et al. JAMA Surg. 2014;149(10):1068-76.
[8] Kaufmann M, et al. Ann Surg Oncol. 2012;19(5):1508-16.
[9] 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 2018 November 29]. Available from: https://clinicaltrials.gov/ct2/show/NCT01772472.
[10] Junttila TT, et al. Breast Cancer Res Treat. 2011;128:347–56.
[11] Wolff AC, et al. J Clin Oncol. 2013;31(31):3997-4013.

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