FDA approves Roche’s Kadcyla for adjuvant treatment of people with HER2-positive early breast cancer with residual invasive disease after neoadjuvant treatment

- The approval is based on data showing Kadcyla cut the risk of disease recurring by half compared to Herceptin in the adjuvant setting for specific patients with HER2-positive early breast cancer
- The application was approved in just over 12 weeks under the US FDA’s Real-Time Oncology Review pilot programme

Basel, 6 May 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has approved Kadcyla® (trastuzumab emtansine) for adjuvant (after surgery) treatment of people with HER2-positive early breast cancer (eBC) who have residual invasive disease after neoadjuvant (before surgery) taxane and Herceptin® (trastuzumab)-based treatment.

“This approval is a significant treatment advance for HER2-positive early breast cancer. By working closely with the FDA and participating in the Real-Time Oncology Review pilot programme, we are able to make Kadcyla available for people with residual invasive disease after neoadjuvant therapy much sooner than anticipated,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “With every step forward in reducing the risk of disease recurrence, we come closer to the goal of helping each person with early breast cancer have the greatest opportunity for cure.”

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.[1,2] While we come closer to this goal with each advance, many people still have a disease recurrence in the long-term.[3] Neoadjuvant treatment is given before surgery with the goal of shrinking tumours and helping to improve surgical outcomes.[2] Adjuvant treatment is given after surgery and aims to eliminate any remaining cancer cells in the body to help reduce the risk of the cancer returning.[2]

The FDA rapidly reviewed and approved the application under the FDA’s Real-Time Oncology Review (RTOR) and Assessment Aid pilot programmes, leading to an approval in just over 12 weeks after completing the submission. Kadcyla is 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.[4] For this indication, Kadcyla 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.[5]

This approval is based on results of the phase III KATHERINE study showing 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<0.0001) 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.[6] 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%.[6] People who have residual disease after neoadjuvant treatment have a worse prognosis than those with no detectable disease.[7,8]
The most common Grade 3 or higher side effects (>2%) with Kadcyla in the KATHERINE study were decreased platelet count and high blood pressure. The most common side effects (>25%) with Kadcyla were fatigue; nausea; increased blood levels of liver enzymes; musculoskeletal pain; bleeding; decreased platelet count; headache; numbness, tingling or pain in the hands or feet; and joint pain.\(^6,9\)

**About the KATHERINE study**\(^{10}\)
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 iDFS including second primary non-breast cancer, disease-free survival and overall survival.

### KATHERINE Study Results\(^6\)

<table>
<thead>
<tr>
<th>KATHERINE Study Results(^6)</th>
<th>Kadcyla n=743</th>
<th>Herceptin n=743</th>
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<tbody>
<tr>
<td><strong>Median follow-up</strong></td>
<td>40 months</td>
<td></td>
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<tr>
<td><strong>Invasive disease-free survival (iDFS)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Risk reduction</td>
<td>HR=0.50, 95% CI 0.39-0.64, p&lt;0.0001</td>
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<tr>
<td>3-year iDFS</td>
<td>88.3%</td>
<td>77.0%</td>
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<tr>
<td><strong>Adverse reactions (ARs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade ≥3AR</td>
<td>26%</td>
<td>15%</td>
</tr>
<tr>
<td>Most common Grade ≥3 ARs (&gt;2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia (decreased platelet count)</td>
<td>6%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Hypertension (high blood pressure)</td>
<td>2.0%</td>
<td>1.2%</td>
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</tbody>
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**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.\(^{11,12}\) 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.\(^{13}\) 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. 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 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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