FDA approves Herceptin Hylecta for subcutaneous injection in certain HER2-positive breast cancers

Basel, 28 February 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has approved Herceptin Hylecta™ (trastuzumab and hyaluronidase-oysk) for subcutaneous (under the skin) injection for the treatment of certain people with HER2-positive early breast cancer (node-positive, or node-negative and ER/PR-negative or with one high-risk feature) in combination with chemotherapy and HER2-positive metastatic breast cancer in combination with paclitaxel or alone in people who have received one or more chemotherapy regimens for metastatic disease. This new treatment includes the same monoclonal antibody as intravenous Herceptin® (trastuzumab) in combination with recombinant human hyaluronidase PH20, an enzyme that helps to deliver trastuzumab under the skin. Herceptin Hylecta is a ready-to-use formulation that can be administered in two to five minutes, compared to 30 to 90 minutes for intravenous Herceptin.

“Over the past 20 years, Herceptin has significantly advanced treatment of HER2-positive breast cancer,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “The approval of Herceptin Hylecta gives physicians and patients in the United States a new option to select treatment based on individual needs and preferences.”

The FDA approval is based on results from three clinical studies in HER2-positive early breast cancer:

- The phase III HannaH study compared neoadjuvant (before surgery) and adjuvant (after surgery) Herceptin Hylecta to intravenous Herceptin, both in combination with chemotherapy. Subcutaneous administration of Herceptin Hylecta resulted in non-inferior levels of trastuzumab in the blood (pharmacokinetics) and non-inferior clinical efficacy (pathological complete response rate; pCR) compared to intravenous Herceptin.
- The phase III SafeHER study of adjuvant Herceptin Hylecta identified no new safety signals, with safety and tolerability consistent with the known safety profiles of intravenous Herceptin and Herceptin Hylecta.
- The PrefHER patient preference study of adjuvant Herceptin Hylecta followed by intravenous Herceptin, or the reverse sequence, found the majority (86%) of people preferred Herceptin Hylecta over intravenous Herceptin.

The most common side effects in people receiving Herceptin Hylecta for early breast cancer were feeling tired, joint pain, diarrhoea, injection site reaction, upper respiratory tract infection, rash, muscle pain, nausea, headache, swelling, flushing, fever, cough, and pain in extremity.
HannaH, SafeHER and PrefHER study results

<table>
<thead>
<tr>
<th>HannaH</th>
<th>Herceptin Hylecta</th>
<th>Intravenous Herceptin</th>
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<tbody>
<tr>
<td>pCR (absence of invasive cancer cells in the breast)</td>
<td>45.4% (118/260)</td>
<td>40.7% (107/263)</td>
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<td>95% CI 39.2%-51.7%</td>
<td>95% CI 34.7%-46.9%</td>
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<tr>
<td>Mean level of trastuzumab in the blood (C_{trough}) before dosing eighth cycle</td>
<td>78.7 mcg/mL</td>
<td>57.8 mcg/mL</td>
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<td>Geometric mean ratio 1.3 (90% CI 1.2-1.4)</td>
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<td>Most common adverse events (AEs; ≥10%)</td>
<td>Hair loss, nausea, administration-related reactions, feeling tired, decreased neutrophil count, diarrhoea, rash, upper respiratory tract infection, vomiting, mouth blisters or sores, muscle pain, decreased appetite, constipation, radiation skin injury, damage to the nerves (numbness, tingling, pain in the hands/feet), joint pain, headache, flushing, fever, cough, low levels of red blood cells, difficulty breathing, incision site pain, low levels of white blood cells and mucosal inflammation</td>
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SafeHER

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<thead>
<tr>
<th>Herceptin Hylecta</th>
<th>n=1,864</th>
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<tr>
<td>Safety</td>
<td>No new safety signals for Herceptin Hylecta were identified. Safety and tolerability were consistent with the known safety profiles of intravenous Herceptin and Herceptin Hylecta</td>
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<td>Most common AEs (≥10%)</td>
<td>Administration-related reactions, feeling tired, diarrhoea, injection site reaction, weakness, joint pain, rash, muscle pain, nausea, damage to the nerves (numbness, tingling in the hands/feet), headache, swelling, flushing, fever, cough, and pain in extremity</td>
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PrefHER

| Herceptin Hylecta followed by intravenous Herceptin (n=121) or intravenous Herceptin followed by Herceptin Hylecta (n=119) | 86% of people preferred Herceptin Hylecta, 13% preferred intravenous Herceptin, 1% had no preference |
| Patient preference | The most common reason for preferring Herceptin Hylecta was time savings (179/231). The most common reason for preferring intravenous Herceptin was fewer local injection reactions |

About Herceptin Hylecta
Herceptin Hylecta (subcutaneous Herceptin) is a combination of trastuzumab and Halozyme Therapeutics’
Enhanze® drug delivery technology. Trastuzumab is the same monoclonal antibody in intravenous Herceptin 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.\(^3\) Herceptin is designed to block HER2 signalling that is believed to play a role in tumour growth and survival.\(^4\) Binding of Herceptin to HER2 may also signal the body’s immune system to destroy the cancer cells.\(^4\) Halozyme’s Enhanze technology is based on a proprietary recombinant human hyaluronidase PH20 (rHuPH20), an enzyme that temporarily degrades hyaluronan, a glycosaminoglycan or chain of natural sugars in the body, to aid in the dispersion and absorption of other injected therapeutic drugs.

The subcutaneous formulation of Herceptin was first approved in Europe in 2013 and is now approved in 100 countries worldwide.

**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.\(^5\) 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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