

Roche's fixed-dose subcutaneous combination of Perjeta and Herceptin comparable to intravenous formulations in people with HER2-positive breast cancer

- **Fixed-dose combination administered under the skin in just minutes, compared to hours with intravenous administration, significantly reducing time spent receiving treatment**
- **Phase III FeDeriCa study showed non-inferior pharmacokinetics and comparable efficacy and safety with the fixed-dose combination when compared to intravenous formulations**
- **Data will be submitted to health authorities globally, including the US Food and Drug Administration and European Medicines Agency**

Basel, 12 December 2019 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new data from the phase III FeDeriCa study which showed the investigational fixed-dose combination (FDC) of Perjeta® (pertuzumab) and Herceptin® (trastuzumab), administered by subcutaneous (SC) injection in combination with intravenous (IV) chemotherapy, demonstrated non-inferior levels of Perjeta in the blood (pharmacokinetics) and comparable efficacy and safety to standard IV infusions of Perjeta plus Herceptin and chemotherapy in eligible people with HER2-positive early breast cancer (eBC).¹

These new data, from a primary analysis of the FeDeriCa study, will be presented in a spotlight session at 07.00 CST today at the 2019 San Antonio Breast Cancer Symposium (SABCS) in Texas, US (Abstract #PD4-07).

SC administration of the FDC takes approximately eight minutes for the initial loading dose and approximately five minutes for each subsequent maintenance dose. This is compared to approximately 150 minutes for infusion of a loading dose of Perjeta and Herceptin using the standard IV formulations, and between 60 to 150 minutes for subsequent maintenance infusions of the two medicines.^{2,3,4}

“This fixed-dose subcutaneous combination has the potential to provide a quicker and less invasive method of administration for people with HER2-positive breast cancer being treated with Perjeta and Herceptin,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “This is the first time that we have brought together two of our targeted antibodies as a single subcutaneous injection that can be administered in just minutes.”

The FeDeriCa study met its primary endpoint, with SC administration of the FDC showing non-inferior levels of Perjeta in the blood during a given dosing interval (C_{trough}) when compared to IV administration of Perjeta. The geometric mean ratio (GMR; a type of average used when assessing pharmacokinetics) for the primary endpoint was 1.22 (90% CI: 1.14 to 1.31), with the lower limit of the 90% CI of the GMR=1.14 \geq 0.80 (the pre-specified non-inferiority margin). A secondary endpoint of non-inferior C_{trough} of Herceptin was also met, with blood concentrations for people receiving the FDC non-inferior to those receiving IV Herceptin (GMR=1.33 [90% CI: 1.24 to 1.43]; lower limit of 90% CI of GMR=1.24 \geq 0.80). A non-inferiority endpoint

was chosen for the study to ensure that people were receiving sufficient dosing with Perjeta and Herceptin as compared to the established IV doses at the same treatment intervals. In addition, rates of total pathological complete response (pCR), a secondary endpoint, were comparable between the treatment arms, with 59.7% of patients receiving the FDC and 59.5% of patients treated with IV Perjeta and Herceptin achieving a total pCR – a difference of 0.15% (95% CI: -8.67 to 8.97).¹

The safety profile of the FDC in combination with chemotherapy was comparable to that of IV administration of Perjeta plus Herceptin and chemotherapy and no new safety signals were identified, including no meaningful difference in cardiac toxicity. The most common adverse events in both arms were alopecia, nausea, diarrhoea and anaemia.¹

In previous studies, SC administration has been shown to be strongly preferred by the majority of patients compared to IV administration of the same medicine, with the most common reason being that administration required less time in the clinic.⁵ Roche is currently investigating patient preference for SC administration of the FDC compared to standard IV administration of Perjeta and Herceptin in people with HER2-positive eBC in the PHranceSCa study. Interim results of this phase II study will be presented at a future medical meeting.

About the FeDeriCa study⁶

FeDeriCa is an international, multi-centre, two-arm, randomised, open-label, phase III study evaluating the pharmacokinetics, efficacy and safety of SC injection of the FDC of Perjeta and Herceptin in combination with chemotherapy, compared with standard IV infusions of Perjeta and Herceptin in combination with chemotherapy in 500 people with HER2-positive eBC who are being treated in the neoadjuvant (before surgery) and adjuvant (after surgery) settings. The primary endpoint of the study is minimum levels of Perjeta in the blood during a given dosing interval (C_{trough}). Secondary endpoints include safety; minimum levels of Herceptin in the blood during a given dosing interval (C_{trough}); and total pCR, meaning there is no tumour tissue detectable in the tissue removed at the time of surgery.

About the FDC of Perjeta and Herceptin

The FDC of Perjeta and Herceptin is a new SC formulation that combines Perjeta and Herceptin with Halozyme Therapeutics' Enhance[®] drug delivery technology.

Trastuzumab in the FDC is the same monoclonal antibody as in IV Herceptin and pertuzumab in the FDC is the same monoclonal antibody as in IV Perjeta. The mechanisms of action of Perjeta and Herceptin are believed to complement each other as both bind to the HER2 receptor, but in different locations. The combination of Perjeta and Herceptin is thought to provide a more comprehensive, dual blockade of the HER signaling pathways.^{7,8}

The standard IV formulation of Perjeta in combination with IV Herceptin and chemotherapy (the Perjeta-based regimen) is approved in over 100 countries for the treatment of both early and metastatic HER2-positive breast cancer. In the neoadjuvant eBC setting, the Perjeta-based regimen has been shown to almost double the rate of pCR compared to Herceptin and chemotherapy.⁹ Additionally, the combination has been shown to significantly reduce the risk of recurrence of invasive disease or death in the adjuvant eBC setting.¹⁰

In the metastatic setting, the combination has shown an unprecedented survival benefit in previously untreated (first-line) patients with HER2-positive metastatic breast cancer.¹¹

Halozyme's Enhance drug delivery technology may enable and optimise SC drug delivery for appropriate co-administered therapeutics. The 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.¹²

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 metastatic HER2-positive disease. HER2-positive breast cancer is a particularly aggressive form of the disease that affects approximately 15-20% of patients.¹³ 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.

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