

## **FDA accepts Roche's Biologics License Application for fixed-dose subcutaneous combination of Perjeta and Herceptin for 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**
- **US Food Drug and Administration is expected to decide on approval by 18 October 2020**

Basel, 25 February 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has accepted the company's Biologics License Application (BLA) for the fixed-dose combination (FDC) of Perjeta® (pertuzumab) and Herceptin® (trastuzumab) with hyaluronidase, administered by subcutaneous (SC) injection in combination with intravenous (IV) chemotherapy, for the treatment of eligible patients with HER2-positive breast cancer. The BLA for the FDC is based on results from the phase III FeDeriCa study, which 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.<sup>1</sup>

“For more than two decades, our medicines have redefined the standard of care for people with HER2-positive breast cancer,” said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. “Today's acceptance builds upon our commitment by potentially offering patients a faster way to administer Perjeta and Herceptin. We're working with the FDA to bring this treatment option to patients as quickly as possible.”

SC administration of the FDC takes approximately eight minutes for the initial loading dose and approximately five minutes for each subsequent maintenance dose.<sup>1</sup> This is compared to approximately 150 minutes for infusion of a loading dose of Perjeta and Herceptin using the standard IV formulations, and between 60-150 minutes for subsequent maintenance infusions of the two medicines.<sup>2,3,4</sup>

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<sub>trough</sub>) when compared to IV administration of Perjeta. A secondary endpoint of non-inferior C<sub>trough</sub> of Herceptin was also met. 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), another secondary endpoint, were comparable between the treatment arms. 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.<sup>1</sup>

In previous studies of other SC formulations, 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.<sup>5,6</sup> In the PHranceSCa study, 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 early breast cancer (eBC).<sup>7</sup> Interim results of this phase II study will be presented at a future medical meeting.

#### **About the FeDeriCa study<sup>8</sup>**

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<sub>trough</sub>). Secondary endpoints include safety; minimum levels of Herceptin in the blood during a given dosing interval (C<sub>trough</sub>); 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<sup>®</sup> drug delivery technology.

Pertuzumab in the FDC is the same monoclonal antibody as in IV Perjeta, and trastuzumab in the FDC is the same monoclonal antibody as in IV Herceptin. 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.<sup>9,10</sup>

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.<sup>11</sup> Additionally, the combination has been shown to significantly reduce the risk of recurrence of invasive disease or death in the adjuvant eBC setting.<sup>12</sup> In the metastatic setting, the combination has shown an unprecedented survival benefit in previously untreated (first-line) patients with HER2-positive metastatic breast cancer.<sup>13</sup>

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.<sup>14</sup>

### **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.<sup>15</sup> Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin® (trastuzumab), Perjeta® (pertuzumab) and Kadcyła® (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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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](http://www.roche.com).

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## **Roche Group Media Relations**

Phone: +41 61 688 8888 / e-mail: [media.relations@roche.com](mailto:media.relations@roche.com)

- Nicolas Dunant (Head)
- Patrick Barth
- Daniel Grotzky
- Karsten Kleine
- Nathalie Meetz
- Barbara von Schnurbein