

## **European Commission approves Roche's Phesgo (fixed-dose combination of Perjeta and Herceptin for subcutaneous injection) for people with HER2-positive breast cancer**

- **Subcutaneous administration is preferred by patients, physicians and healthcare providers, and is associated with a reduction in healthcare costs<sup>1,2,3</sup>**
- **Treatment with Phesgo is over 90% faster, administered under the skin in just minutes compared to hours with intravenous (IV) infusion of Perjeta plus Herceptin<sup>4,5,6</sup>**
- **Approval is based on results from the pivotal phase III FeDeriCa trial, which showed that Phesgo delivered non-inferior levels of Perjeta and Herceptin in the blood and comparable efficacy and safety versus IV formulations<sup>7</sup>**

Basel, 23 December 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission has approved Phesgo<sup>®</sup>, a fixed-dose combination of Perjeta<sup>®</sup> (pertuzumab) and Herceptin<sup>®</sup> (trastuzumab) with hyaluronidase, administered by subcutaneous (SC; under the skin) injection for the treatment of early and metastatic HER2-positive breast cancer.

“This approval represents a significant step forward in the treatment of HER2-positive breast cancer,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “The innovation of Phesgo significantly reduces the time people spend receiving standard of care therapy with Perjeta and Herceptin, helping to minimise the impact of treatment on their everyday lives. It also addresses the increasing demand across healthcare systems for faster and more flexible treatment solutions.”

Phesgo is available as a single-dose vial for SC injection and enables over 90% faster treatment than IV administration of standard of care therapy with Perjeta and Herceptin. SC administration of Phesgo 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 60-150 minutes for subsequent maintenance infusions of the two medicines.<sup>4,5,6</sup>

The approval of Phesgo in Europe is based on results from the pivotal phase III FeDeriCa study, which showed that treatment with Phesgo produced non-inferior levels of Perjeta and Herceptin in the blood and demonstrated comparable efficacy versus IV administration of the two medicines. The safety profile of Phesgo with chemotherapy was comparable to IV administration of Perjeta plus Herceptin and chemotherapy. No new safety signals were identified, including no meaningful difference in cardiac toxicity.<sup>7</sup>

The development of Phesgo highlights Roche's commitment to improving patients' experience of cancer treatment, looking beyond efficacy outcomes and focusing on more flexible treatment solutions. Phesgo has the potential to help minimise pressure on healthcare systems by reducing administration time, as well as other costs associated with treatment, such as time spent in the infusion chair and drug preparation.<sup>8,9</sup> The

COVID-19 pandemic has further highlighted the need to utilise novel approaches that help to manage healthcare capacity to free-up time and resources.

### **About the FeDeriCa study<sup>7,10</sup>**

FeDeriCa is an international, multi-centre, two-arm, randomised, open-label, pivotal phase III study evaluating the pharmacokinetics, efficacy and safety of subcutaneous injection of Phesgo in combination with chemotherapy, compared with standard intravenous (IV) infusions of Perjeta and Herceptin in combination with chemotherapy, in 500 people with HER2-positive early breast cancer 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 ( $C_{\text{trough}}$ ), when compared to IV administration of Perjeta. Secondary endpoints include safety; minimum levels of Herceptin in the blood during a given dosing interval ( $C_{\text{trough}}$ ); and total pathological complete response, meaning there is no tumour tissue detectable in the tissue removed at the time of surgery.

Data from the FeDeriCa study were presented at the San Antonio Breast Cancer Symposium in December 2019. The FeDeriCa study met its primary endpoint of non-inferior levels of Perjeta in the blood. 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 levels of Herceptin was also met, with blood concentrations for people receiving Phesgo 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.

### **About Phesgo**

Phesgo combines the same monoclonal antibodies as Perjeta and Herceptin with Halozyme Therapeutics' Enhance<sup>®</sup> drug delivery technology in a novel formulation for subcutaneous (SC) use.<sup>4,11</sup> This is the first time that Roche has combined two monoclonal antibodies that can be administered by a single SC injection.

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>11</sup>

Pertuzumab in Phesgo is the same monoclonal antibody as in intravenous (IV) Perjeta, and trastuzumab in Phesgo 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 signalling pathways.<sup>12,13</sup>

Phesgo is approved in the US for the treatment of early and metastatic HER2-positive breast cancer. The approved indications for Phesgo mirror those of Perjeta.

The standard IV formulation of Perjeta in combination with IV Herceptin and chemotherapy (the Perjeta-based regimen) is approved in more than 100 countries for the treatment of both early and metastatic HER2-positive breast cancer. In the neoadjuvant (before surgery) early breast cancer (eBC) setting, the Perjeta-based regimen has been shown to almost double the rate of pathological complete response compared to Herceptin and chemotherapy.<sup>14</sup> Additionally, the combination has been shown to significantly reduce the risk of recurrence of invasive disease or death in the adjuvant (after surgery) eBC setting.<sup>15</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>16</sup>

#### **About Roche's medicines for HER2-positive breast cancer**

Roche has been leading research into the HER2 pathway for more than 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 25-30% of patients.<sup>17</sup> Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin, Perjeta 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 twelfth 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).

All trademarks used or mentioned in this release are protected by law.

## References

- [1] O'Shaughnessy J, et al. Patient (pt) preference for the pertuzumab-trastuzumab fixed-dose combination for subcutaneous use (PH FDC SC) in HER2-positive early breast cancer (EBC): Primary analysis of the open-label, randomised crossover PHranceSCa study. Presented at ESMO, 2020 Sept 19-21. Abstract #165MO.
- [2] Xavier P, et al. Preference for subcutaneous or intravenous administration of trastuzumab in patients with HER2-positive early breast cancer (PrefHer): an open-label randomised study. *Lancet Oncol.* 2013;14(10):962-70.
- [3] Tjalma, et al. Trastuzumab IV versus SC: A time, motion and cost assessment in a lean operating day care oncology unit. Presented at: SABCS; 2016 Dec 6-10; San Antonio, TX, USA. Abstract #P4-21-15.
- [4] US Food and Drug Administration. Prescribing information for Phesgo. [Internet; cited December 2020]. Available from: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2020/761170s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761170s000lbl.pdf).
- [5] US Food and Drug Administration. Prescribing Information for Herceptin. [Internet; cited December 2020]. Available from: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/](https://www.accessdata.fda.gov/drugsatfda_docs/label/).
- [6] US Food and Drug Administration. Prescribing information for Perjeta. [Internet; cited December 2020]. Available from: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/125409lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/125409lbl.pdf).
- [7] Tan A. et al. Subcutaneous administration of the fixed-dose combination of trastuzumab and pertuzumab in combination with chemotherapy in HER2-positive early breast cancer: Primary analysis of the phase III, multicenter, randomized, open-label, two-arm FeDeriCa study. Presented at SABCS; 2019 Dec 10-14; San Antonio, Texas. Abstract #PD4-07.
- [8] Sripada et al. Subcutaneous fixed-dose combination of pertuzumab and trastuzumab for the treatment of metastatic breast cancer in Canada - a budget impact analysis. Presented at SABCS; 2020 Dec 08-11; San Antonio Texas: PS9-55.
- [9] Roche data on file.
- [10] Clinical trials.gov. A Study to Evaluate the Pharmacokinetics, Efficacy, and Safety of Subcutaneous Administration of the Fixed-Dose Combination of Pertuzumab and Trastuzumab in Combination With Chemotherapy in Participants With HER2-Positive Early Breast Cancer (FeDeriCa). [Internet: December 2020]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03493854>.
- [11] Halozyme. Enhance<sup>®</sup> Drug Delivery Technology. [Internet; cited December 2020]. Available from: <https://www.halozyme.com/enhance/overview/default.aspx>.
- [12] Iqbal N, Iqbal N. Human Epidermal Growth Factor Receptor 2 (HER2) in Cancers: Overexpression and Therapeutic Implications. *Mol Biol Int.* 2014;2014:852748.
- [13] Baselga J, Swain SM. Novel anticancer targets: revisiting ERBB2 and discovering ERBB3. *Nat Rev Cancer* 2009;9:463-75.
- [14] Gianni L, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. *Lancet Oncol.* 2012;13(1):25-32.
- [15] Minckwitz G, et al. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. *N Engl J Med.* 2017;13;377(2):122-31.
- [16] Swain SM, et al. Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. *N Engl J Med.* 2015;19;372(8):724-34.
- [17] Jarrett A, et al. Experimentally-driven mathematical modelling to improve combination targeted and cytotoxic therapy for HER2+ breast cancer. *Sci Rep.* 2019;9:12830.

## Roche Group Media Relations

**F. Hoffmann-La Roche Ltd**

4070 Basel  
Switzerland

Group Communications  
Roche Group Media Relations

Tel. +41 61 688 88 88  
[www.roche.com](http://www.roche.com)

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

Dr. Nicolas Dunant  
Phone: +41 61 687 05 17

Patrick Barth  
Phone: +41 61 688 44 86

Dr. Daniel Grotzky  
Phone: +41 61 688 31 10

Karsten Kleine  
Phone: +41 61 682 28 31

Nina Mähltitz  
Phone: +41 79 327 54 74

Nathalie Meetz  
Phone: +41 61 687 43 05

Dr. Barbara von Schnurbein  
Phone: +41 61 687 89 67

#### **Roche Investor Relations**

Dr. Karl Mahler  
Phone: +41 61 68-78503  
e-mail: [karl.mahler@roche.com](mailto:karl.mahler@roche.com)

Jon Kaspar Bayard  
Phone: +41 61 68-83894  
e-mail: [jon\\_kaspar.bayard@roche.com](mailto:jon_kaspar.bayard@roche.com)

Dr. Sabine Borngräber  
Phone: +41 61 68-88027  
e-mail: [sabine.borngraeber@roche.com](mailto:sabine.borngraeber@roche.com)

Dr. Bruno Eschli  
Phone: +41 61 68-75284  
e-mail: [bruno.eschli@roche.com](mailto:bruno.eschli@roche.com)

Dr. Birgit Masjost  
Phone: +41 61 68-84814  
e-mail: [birgit.masjost@roche.com](mailto:birgit.masjost@roche.com)

Dr. Gerard Tobin  
Phone: +41 61 68-72942  
e-mail: [gerard.tobin@roche.com](mailto:gerard.tobin@roche.com)

#### **Investor Relations North America**

Loren Kalm  
Phone: +1 650 225 3217  
e-mail: [kalm.loren@gene.com](mailto:kalm.loren@gene.com)

Dr. Lisa Tuomi  
Phone: +1 650 467 8737  
e-mail: [tuomi.lisa@gene.com](mailto:tuomi.lisa@gene.com)