Media Release

Roche's fixed-dose subcutaneous combination of Perjeta and Herceptin showed non-inferiority when compared to intravenous formulations for people with HER2-positive breast cancer

- **New fixed-dose combination is administered under the skin in just minutes, significantly reducing the time spent receiving treatment**
- **Data will be submitted to health authorities around the world, including the US Food and Drug Administration and European Medicines Agency**
- **Results will be presented at an upcoming medical meeting**

Basel, 13 September 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced the phase III FeDeriCa study met its primary endpoint. The study showed a new 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) compared to standard IV infusion of Perjeta plus Herceptin and chemotherapy in people with HER2-positive early breast cancer (eBC). The safety profile of the FDC of Perjeta and Herceptin was consistent with that of Perjeta and Herceptin administered intravenously.[1, 2]

"With this single injection under the skin, people with HER2-positive breast cancer receiving Perjeta and Herceptin can have a faster treatment option," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "Our medicines have helped millions of people living with HER2-positive breast cancer and this latest development is particularly exciting as, for the first time, we have combined two therapeutic antibodies as a single subcutaneous formulation."

SC administration of the FDC takes approximately 8 minutes for the initial loading dose, and approximately 5 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 for the combination.[1, 2, 3]

Full data from the FeDeriCa study will be submitted for presentation at an upcoming medical meeting and to health authorities around the world.

About the FeDeriCa study
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 people with HER2-positive eBC who are being treated in the neoadjuvant (before surgery) and adjuvant (after surgery) settings.[4] The primary endpoint of the study is minimum levels of Perjeta in the

blood during a given dosing interval (Ctrough). Secondary endpoints include safety; minimum levels of Herceptin in the blood during a given dosing interval (Ctrough); and total pCR, meaning there is no tumour tissue detectable at the time of surgery.[4]

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' Enhanze® drug delivery technology.

Trastuzumab in the FDC is the same monoclonal antibody as in IV Herceptin and pertuzumab 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 to different places.[5] The combination of Perjeta and Herceptin is thought to provide a more comprehensive, dual blockade of the HER signaling pathways.[5]

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.[6] Additionally, the combination has been shown to significantly reduce the risk of recurrence of invasive disease or death in the adjuvant eBC setting.[7] In the metastatic setting, the combination has shown an unprecedented survival benefit in previously untreated (first-line) patients with HER2-positive metastatic breast cancer.[8]

Halozyme's Enhanze 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.[9]

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.[10] 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 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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