

Brussels, 02 March 2017

Phase III APHINITY study shows Roche's Perjeta® regimen helped people with an aggressive type of early breast cancer live longer without their disease returning compared to Herceptin® and chemotherapy

- **Perjeta plus Herceptin and chemotherapy showed a statistically significant improvement in invasive disease-free survival (iDFS) for people with HER2-positive early breast cancer (eBC) compared to Herceptin and chemotherapy alone**
- **Data will be discussed with health authorities, including the US Food and Drug Administration (FDA) and European Medicines Agency (EMA)**

Roche (SIX: RO, ROG; OTCQX: RHHBY), the Breast International Group (BIG), Breast European Adjuvant Study Team (BrEAST) and Frontier Science Foundation (FS) today announced positive results from the phase III APHINITY study. The study met its primary endpoint and showed that adjuvant (after surgery) treatment with the combination of Perjeta® (pertuzumab), Herceptin® (trastuzumab) and chemotherapy (the Perjeta-based regimen) achieved a statistically significant reduction in the risk of recurrence of invasive disease or death (invasive disease-free survival; iDFS) in people with HER2-positive early breast cancer (eBC) compared to Herceptin and chemotherapy alone. The safety profile of the Perjeta-based regimen was consistent with that seen in previous studies¹, and no new safety signals were identified. Full results from the APHINITY trial will be presented at an upcoming medical meeting in 2017.

“These results from the positive APHINITY study represent an important addition to the body of data for Perjeta in the treatment of people with HER2-positive early breast cancer,” said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development at Roche. “We look forward to discussing these adjuvant results with global regulatory authorities.”

Gunter von Minckwitz, MD, study coordinator from the Breast International Group and academic study partners, added, “APHINITY provides yet another example of the importance of industry-academic collaborations and their value in advancing cancer care for people affected by this challenging disease.”

HER2-positive breast cancer is an aggressive form of the disease, which affects approximately one in five people with breast cancer² and is associated with a poor prognosis if left untreated.³ Despite advancements in the treatment of HER2-positive eBC, up to one in three people treated with Herceptin and chemotherapy may eventually see their cancer return.^{4,5} Treatment options are needed to improve the outcomes of people with this aggressive disease. Treating breast cancer early, before it has spread, may improve the chance of preventing the disease from returning and potentially reaching an incurable stage.⁶ Adjuvant therapy is given after surgery and is aimed at killing any remaining cancer cells to reduce the risk of the cancer returning.⁶

The combination of Perjeta, Herceptin and chemotherapy is licenced as a neoadjuvant (before surgery) treatment for people with HER2-positive eBC in more than 75 countries worldwide following approvals by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA).^{1,7} In the US, the regimen is currently available under the FDA accelerated approval programme. The APHINITY trial reflects the commitment to evaluate the Perjeta-based regimen as part of a complete treatment approach for eBC. These data will be discussed with health authorities across the world, including the US FDA with the hope to convert the current US accelerated approval to a full approval.

About APHINITY[®]

APHINITY (**A**djuvant **P**ertuzumab and **H**erceptin **I**N **I**nitial **T**herap**Y** in Breast Cancer, NCT01358877/BO25126/ BIG 4-11) is an international, phase III, randomised, double-blind, placebo-controlled, two-arm study evaluating the efficacy and safety of Perjeta plus Herceptin and chemotherapy compared to Herceptin and chemotherapy as an adjuvant therapy in 4,805 people with operable HER2-positive eBC.

People enrolled in the study underwent surgery and were randomised to one of two arms (1:1) to receive either:

- Six to eight cycles of chemotherapy (anthracycline or non-anthracycline-containing regimen) with Perjeta and Herceptin, followed by Perjeta and Herceptin every three weeks for a total of one year (52 weeks) of treatment.
- Six to eight cycles of chemotherapy (anthracycline or non-anthracycline-containing regimen) with placebo and Herceptin, followed by placebo and Herceptin every three weeks for a total of one year (52 weeks) of treatment.

Radiotherapy and/or endocrine therapy could be initiated at the end of adjuvant chemotherapy. The APHINITY study allowed for a range of standard chemotherapy regimens to be used and both lymph node-positive and lymph node-negative participants were eligible for enrolment. The primary efficacy endpoint of the APHINITY study is iDFS, which is the time a patient lives without return of invasive breast cancer at any site or death from any cause after adjuvant treatment. Secondary endpoints include cardiac and overall safety, overall survival, disease-free survival and health-related quality of life.

About Perjeta

Perjeta is a medicine 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.^{9,10} Perjeta is designed specifically to prevent the HER2 receptor from pairing (or 'dimerising') with other HER receptors (EGFR/HER1, HER3 and HER4) on the surface of cells, a process that is believed to play a role in tumour growth and survival. Binding of Perjeta to HER2 may also signal the body's immune system to destroy the cancer cells. 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. The combination of Perjeta and Herceptin is thought to provide a more comprehensive, dual blockade of HER signalling pathways, thus preventing tumour cell growth and survival.^{11,12}

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 advanced HER2-positive disease. HER2-positive breast cancer is a particularly aggressive form of the disease that affects approximately 20% of patients.² Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin, Perjeta 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.¹

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. Twenty-nine 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry eight years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 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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About the Breast International Group (BIG)

The Breast International Group (BIG) is a not-for-profit organisation for academic breast cancer research groups from around the world, based in Brussels, Belgium.

Global collaboration is crucial to make significant advances in breast cancer research, reduce unnecessary duplication of effort, share data, contribute to the faster development of better treatments, and increase the likelihood of cures for patients. Therefore BIG facilitates breast cancer research at an international level, by stimulating cooperation between its members and other academic networks, and collaborating with, but working independently from, the pharmaceutical industry.

Founded by leading European opinion leaders in 1999, BIG now constitutes a network of 56 collaborative groups from Europe, Canada, Latin America, Asia and Australasia. These entities are tied to several thousand specialised hospitals and research centres worldwide. More than 30 clinical trials are run or are under development under the BIG umbrella at any one time. BIG also works closely with the US National Cancer Institute (NCI) and the North American Breast Cancer Groups (NABCG), so that together they act as a strong integrating force in the breast cancer research arena.

www.BIGagainstbreastcancer.org

About the Breast European Adjuvant Studies Team (BrEAST)

The Breast European Adjuvant Studies Team (BrEAST) is a specialised clinical trials unit (data centre) located at the Institut Jules Bordet, Brussels, Belgium. It was created in 1997 in order to conduct large, international phase III studies in breast cancer aiming to register new drugs. The unit is responsible for setting up, coordinating and managing the data collected in these trials, which are run in collaboration with pharmaceutical companies and the Breast International Group (BIG). BrEAST manages complex trials involving more than 20,000 patients in over 40 countries.

About Frontier Science Foundation (FS)

Frontier Science Foundation (FS) is a not-for-profit corporation that has gained an international reputation as a highly capable data management and statistical organisation, collaborating with research networks, pharmaceutical companies and others in the design, conduct and execution of clinical trials and long-term observation studies.

Founded in 1975, Frontier Science provides innovative data management and analysis for clinical trials in a variety of disease settings throughout the world. Some of the significant advancements in the treatment of AIDS and cancer have resulted from studies in which Frontier Science played a major role.

Frontier Science has biostatistics, IT, data management and support staff in five locations in the United States, Greece and Scotland.

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