Media & Investor Release

Ten-year APHINITY data show Roche's Perjeta-based regimen reduced the risk of death by 17% in people with HER2-positive early-stage breast cancer

- **Long term follow-up in this curative setting demonstrated clinically meaningful survival benefit when adding adjuvant Perjeta® (pertuzumab) to Herceptin® (trastuzumab) and chemotherapy[1]**
- **21% reduction in the risk of death was seen in the pre-specified subgroup of people with lymph node-positive disease[1]**
- **Data to be presented as a late-breaking abstract at the 2025 European Society for Medical Oncology (ESMO) Breast Cancer Congress**

Basel, 13 May 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY), the Breast International Group (BIG), Institut Jules Bordet Clinical Trials Support Unit and Frontier Science Foundation, announced today statistically significant final overall survival (OS) results from the phase III APHINITY study in people with human epidermal growth factor receptor 2 (HER2)-positive early-stage breast cancer.[1] After ten years, the risk of death was reduced by 17% for people treated with Perjeta® (pertuzumab), Herceptin® (trastuzumab) and chemotherapy (the Perjeta-based regimen) for a year as post-surgery (adjuvant) treatment, compared with individuals who received Herceptin, chemotherapy, and placebo.[1]

"Early treatment of breast cancer can provide substantial patient benefit and also increases the chance for cure. For people with early-stage HER2-positive disease, the APHINITY results validate the sustained benefits of the Perjeta-based regimen," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "These long-term data reinforce the regimen's value as a well-established standard-of-care treatment in the curative setting."

"After 10 years, the APHINITY trial clearly shows a statistically significant and clinically meaningful improvement of the overall survival," said Prof. Sibylle Loibl, APHINITY Study Chair, Chair of the German Breast Group (GBG) and the Chief Executive Officer of the GBG Forschungs GmbH. "Adding Perjeta to a standard adjuvant treatment is most beneficial for people with HER2-positive breast cancer with lymph-node positive disease who are at high risk of recurrence."

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After ten years, results show:

- 91.6% of people treated with the Perjeta-based regimen were alive at ten years versus 89.8% of those treated with Herceptin, chemotherapy, and placebo (hazard ratio [HR]=0.83, 95% CI: 0.69-1.00, p-value=0.044).[1]
- A 21% reduction in the risk of death was seen in the prespecified subgroup of people with lymph node-positive disease (HR=0.79, 95% CI: 0.64-0.97).[1]
- The previously reported invasive disease-free survival (primary endpoint) benefit was maintained (HR=0.79, 95% CI: 0.68-0.92), strengthening results from earlier APHINITY analyses.[1,2] No benefit was seen in the node negative subgroup.[1]
- The safety profile, including cardiac safety, was consistent with previous studies and no new or unexpected safety signals were identified.[1,2]

Full results will be presented as a late-breaking abstract on Thursday, 15 May at the 2025 European Society for Medical Oncology Breast Cancer Congress.

“The international collaborations in APHINITY have facilitated important insights about HER2-positive breast cancer and are continuing to yield promising findings,” said Liz Frank, Independent Research Advocate. “Scientists and clinicians are working together with the broader goal of improving our understanding of HER2-positive breast cancer, improving the quality of life for people living with the disease and ultimately, helping them to live longer with no disease occurring.”

The collaborative efforts of Roche, BIG, and study partners enabled the initiation of pivotal trials such as APHINITY and HERA. These studies led to Herceptin and Perjeta becoming standards of care and helped improve outcomes for people with early-stage HER2-positive breast cancer.[3]

About the APHINITY study

APHINITY (Adjuvant Pertuzumab and Herceptin IN Initial TherapY in Breast Cancer, NCT01358877/ BO25126/ BIG 4-11) is a global, phase III, randomised, double-blind, placebo-controlled, two-arm study evaluating the efficacy and safety of Perjeta® (pertuzumab) plus Herceptin® (trastuzumab) and chemotherapy, compared with Herceptin and chemotherapy, as post-surgery (adjuvant) treatment in 4,804 people with operable human epidermal growth factor receptor 2-positive early-stage breast cancer.[4]

The primary endpoint is invasive disease-free survival, which in this study is defined as the time a patient lives without recurrence of invasive breast cancer (when the cancer returns

locally or spreads into the surrounding breast tissue and/or beyond) or death from any cause after post-surgery treatment.[4] Secondary endpoints include cardiac and overall safety, overall survival and health-related quality of life.[4]

About the Perjeta-based regimen (intravenous (IV) Perjeta® (pertuzumab), Herceptin® (trastuzumab) and chemotherapy)

The Perjeta-based regimen is approved in more than 120 countries/regions for the treatment of both early-stage and metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer. In the neoadjuvant (before surgery) early-stage breast cancer setting, the Perjeta-based regimen has been shown to almost double the rate of pathological complete response compared to Herceptin and chemotherapy.[5] Additionally, the combination has been shown to significantly reduce the risk of recurrence of invasive disease or death in the adjuvant (after surgery) early-stage breast cancer setting.[6] In the metastatic setting, the combination has shown an unprecedented survival benefit in previously untreated (first-line) patients with HER2-positive metastatic breast cancer.[7] Phesgo® – a subcutaneous fixed-dose combination of Perjeta and Herceptin – is also approved in more than 120 countries/regions and provides faster and more flexible administration of Perjeta and Herceptin under the skin in approximately eight minutes, compared to hours with standard IV administration.[8,9] The European Medicines Agency's Committee for Medicinal Products for Human Use recently recommended updating Phesgo's label in the European Union to allow administration outside of a clinical setting (such as in a person's home) by a healthcare professional, which can help to alleviate treatment burden and free up cancer care capacity in clinics.[10]

About Roche's medicines for human epidermal growth factor receptor 2 (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-stage and advanced HER2-positive disease. HER2-positive breast cancer affects approximately 15-20% of people with breast cancer.[11]

Survival outcomes for people with HER2-positive breast cancer, once seen as an aggressive type of the disease, have been transformed through the development of targeted therapies, including Roche molecules Herceptin® (trastuzumab), Perjeta® (pertuzumab), Kadcyla® (trastuzumab emtansine) and Phesgo® (pertuzumab, trastuzumab, and hyaluronidase subcutaneous).[12,13] Long-term survival is now a possibility for many people, which also contributes to societal and economic benefits.[14]

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 in breast cancer

Our medicines, along with companion diagnostic tests, have contributed to bringing breakthrough outcomes in human epidermal growth factor 2-positive and triple-negative breast cancers. As our understanding of breast cancer biology rapidly improves, we are working to identify new biomarkers and approaches to treatment for other subtypes of the disease, including oestrogen receptor-positive breast cancer, which is a form of hormone receptor-positive breast cancer, the most prevalent type of all breast cancers.

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

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.

About Breast International Group

The Breast International Group (BIG) is an international 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 international level, by stimulating cooperation between its

members and other academic networks, and collaborating with, but working independently from, the pharmaceutical industry.

In 1999, BIG was founded by Dr Martine Piccart and the late Dr Aron Goldhirsch with the aim to address fragmentation in European breast cancer research. Research groups from other parts of the world rapidly expressed interest in joining BIG and, more than 25 years later, BIG represents a network of over 55 like-minded research groups from around the world. These entities are tied to several thousand specialised hospitals, research centres and world-class breast cancer experts across approximately 70 countries on 6 continents. 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 National Clinical Trials Network (NCTN), so that together they act as a strong integrating force in the breast cancer research arena.

BIG's research is supported in part by its philanthropy unit, known as ***BIG against breast cancer***. This denomination is used to interact with the general public and donors, and to raise funds for BIG's purely academic breast cancer trials and research programmes.
For more information, visit www.BIGagainstbreastcancer.org

Frontier Science & Technology Research Foundation (FSTRF)
FSTRF is a non-profit, research organisation which supports research networks, pharmaceutical companies and investigators to conduct scientifically meaningful high-quality clinical trials. The APHINITY trial involved research staff in the US and in the Affiliate office in Scotland.

FSTRF works with scientists and technicians in more than 800 laboratories, universities and medical centres around the world to provide a comprehensive range of research services throughout the clinical trial process including design, analysis and reporting.

Through its work, FSTRF aims to advance the application of statistical science and practice and data management techniques in science, healthcare and education.

About Institut Jules Bordet Clinical Trials Support Unit
As an academic non-profit organisation, the Clinical Trials Support Unit (CTSU) of the comprehensive cancer centre Institut Jules Bordet (IJB) is fighting cancer through the design, set-up and conduct of innovative clinical trials that matter to patients. IJB-CTSU's multidisciplinary team strongly believes that its work contributes to improve the understanding of the disease and to optimise diagnosis, care and cancer treatments.

The IJB-CTSU manages the operational activities both for investigator-initiated trials and for clinical trials sponsored by pharmaceutical companies, biotech companies or other academic institutions.

The IJB-CTSU expertise covers project management, regulatory affairs, contract management, pharmacovigilance, data management, sites monitoring, central imaging review and biosamples management. Moreover, the IJB-CTSU benefits from a close collaboration with the IJB medical team and IJB statistical team.

In 2013, the BrEAST (Breast Adjuvant Study Team) joined the IJB-CTSU as its data management unit. This unit is responsible for the data management activities implemented for all clinical studies managed by the IJB-CTSU.

For more information, please visit https://ctsu.bordet.be

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