

Roche presents first phase II data on giredestrant, a next generation selective oestrogen receptor degrader, in untreated oestrogen receptor (ER)-positive, early breast cancer

- New interim data for giredestrant showed superior anti-proliferative activity compared to anastrozole and a tolerable safety profile in neoadjuvant ER-positive breast cancer¹
- Recently published data in the *Journal of Medicinal Chemistry* demonstrates giredestrant's exceptional preclinical profile in the treatment of hormone receptor-positive breast cancer²
- Giredestrant has a comprehensive development programme across a broad range of settings and treatment combinations

Basel, 17 September 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced interim data from the randomised phase II coopERA Breast Cancer trial evaluating neoadjuvant treatment with giredestrant (formerly known as GDC-9545), an investigational next generation oral selective oestrogen receptor degrader (SERD), in post-menopausal women with ER-positive, HER2-negative early breast cancer. In the window of opportunity phase, after 14 days of treatment, giredestrant showed a reduction in Ki67, a prognostic marker that measures tumour proliferation, compared to anastrozole (80% versus 67% respectively, $p=0.0222$). The safety profile of giredestrant remained consistent with previous trials and fewer patients experienced side effects assessed as related to giredestrant versus anastrozole.¹ Interim analysis results from the coopERA Breast Cancer study will be presented at the European Society for Medical Oncology (ESMO) Congress 2021 and the primary analysis data will be presented at an upcoming medical meeting.

“We are pleased to share the first randomised phase II data for giredestrant, which shows encouraging activity and safety in early HR-positive, HER2-negative breast cancer,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “Our ongoing comprehensive programme in HR-positive breast cancer aims to address significant unmet needs for people who still experience a profound impact on their quality of life, including the risk of treatment resistance and disease recurrence.”

The interim analysis data from 83/202 patients enrolled in the coopERA Breast Cancer study demonstrated superior anti-proliferative activity of giredestrant compared with anastrozole and a favourable safety profile in HR-positive, HER2-negative breast cancer¹:

- During the window of opportunity phase (1-14 days) in this neoadjuvant (pre-operative) study, the pharmacodynamic effect of giredestrant was assessed using the relative Ki67 reduction as proliferation biomarker, which indicates the ability of a therapy to suppress tumour growth:
 - Giredestrant showed a mean Ki67 reduction of 80% (95% CI: -85%, -72%) versus 67% for anastrozole (95% CI; 95% CI: -75%, -56%) $p=0.0222$.

- Consistent Ki67 suppression was observed in patients with baseline Ki67 $\geq 20\%$ (83% reduction for giredestrant versus 71% for anastrozole) or baseline Ki67 $< 20\%$ (65% vs 24% respectively).
- After 14 days of treatment, 25% of tumours exhibited Complete Cell Cycle Arrest Rate (CCCA) with giredestrant versus 5% with anastrozole ($\Delta 20\%$; 95% CI: -37%, -3%).
- The safety profile of giredestrant was consistent with its mechanism of action, with fewer patients experiencing side effects assessed as related to giredestrant (28%) versus anastrozole (38%) by the reporting investigators. No Grade ≥ 3 adverse events (AEs) or serious AEs were giredestrant-related.

Further data from the primary analysis of this study are expected to be presented at an upcoming medical meeting and will include results from the full population of the window of opportunity phase and early results from the neoadjuvant phase of the study, which evaluates giredestrant plus palbociclib versus anastrozole plus palbociclib.

Roche is currently enrolling patients into a second phase II study (acelERA Breast Cancer) evaluating giredestrant in second/third-line oestrogen receptor (ER)-positive early breast cancer, as well as two phase III studies: persevERA Breast Cancer, evaluating giredestrant plus palbociclib against letrozole plus palbociclib in patients with ER-positive, HER2-negative locally advanced or metastatic breast cancer and lidERA Breast Cancer, evaluating adjuvant giredestrant versus endocrine therapy of physician's choice in patients with medium- and high-risk ER-positive and HER2-negative early breast cancer.^{3,4,5} In August 2021, the first patient was enrolled in the lidERA study, the first study to evaluate an oral SERD in the adjuvant setting.⁶ Data was also recently published in the *Journal of Medicinal Chemistry*; with giredestrant shown to be a potent SERD and a full antagonist, with best in class potential due to its better anti-proliferative activity than other known SERDs. Among the various SERDs reported so far, giredestrant 'stands out in its overall preclinical package'.^{2,7}

Giredestrant received U.S. Food and Drug Administration (FDA) Fast Track Designation (FTD) for ER-positive, HER2-negative, second and third-line metastatic breast cancer on 15 December 2020. FTD is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need.⁸

About giredestrant

Giredestrant is a next generation investigational SERD, designed to fully block ER signalling with robust receptor occupancy and demonstrates an exceptional preclinical profile. Oestrogen encourages ER-positive breast cancer cells to grow by attaching to the ER. Giredestrant works by blocking this receptor to prevent the action of oestrogen, and in the process causes the receptor to be degraded. This investigational medicine has also shown efficacy regardless of ESR1 mutation status (mutations in the ESR1 gene are important mechanisms of resistance to hormone therapy).^{9,10,11,12}

Orally given, giredestrant delivers an encouraging clinical efficacy and safety profile and has shown superior pre-clinical potency over other SERDs in development.^{2,11,13} The oral administration of giredestrant has the potential to transform the treatment experience for patients, offering greater convenience and a less painful option compared to therapies administered via intramuscular injection.

Giredestrant has a comprehensive development programme across a broad range of settings and treatment combinations for patients with HR-positive, HER2-negative breast cancer. A standardised once-daily 30 mg dose has been selected for the giredestrant development programme, both as a monotherapy and in combination studies.

About coopERA (NCT04436744)¹⁴

An open-label, two-arm, phase II study to evaluate the efficacy, safety, and pharmacokinetics of giredestrant versus anastrozole (in the window of opportunity phase) and giredestrant plus palbociclib compared with anastrozole plus palbociclib (in the neoadjuvant phase) in postmenopausal women with untreated, ER-positive, HER2-negative early breast cancer. The primary endpoint of the study is the geometric change in Ki67 scores (a measure of how quickly cancer cells are proliferating) from baseline to week 2 during the window of opportunity phase. Secondary endpoints include overall response rate, CCCA, safety outcomes and plasma concentration of giredestrant.

About Roche in breast cancer

Roche has been advancing breast cancer research for more than 30 years with the goal of helping as many people with the disease as possible. Our medicines, along with companion diagnostic tests, have contributed to bringing breakthrough innovations in HER2-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 all forms of early and advanced breast cancer, including triple-negative and hormone receptor-positive.

Our targeted medicines Herceptin® (trastuzumab), Perjeta® (pertuzumab), Phesgo®, Kadcyła® (trastuzumab emtansine) and Tecentriq® (atezolizumab) are continuing to transform the treatment of early and advanced HER2-positive and triple-negative breast cancers and, through our clinical programmes, we hope to bring new treatment combinations to people with breast cancer, ultimately improving outcomes.

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, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

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. In recent years, Roche has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

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 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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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