Media & Investor Release

Positive phase III results show Roche's giredestrant significantly improved progression-free survival in ER-positive advanced breast cancer

- **evERA met its co-primary endpoints; giredestrant plus everolimus demonstrated significant benefit in ITT and *ESR1*-mutated populations in post-CDK inhibitor setting, compared with standard of care plus everolimus**
- **The all-oral combination was well tolerated and adverse events were consistent with the known safety profiles of the individual study treatments; no new safety signals were observed**
- **evERA is the first positive head-to-head phase III trial investigating an all-oral selective oestrogen receptor degrader-containing regimen versus a standard of care combination[1]**
- **Data will be presented at an upcoming medical meeting and shared with health authorities**

Basel, 22 September 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive results from the phase III evERA study evaluating investigational giredestrant in combination with everolimus in people with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer previously treated with cyclin-dependent kinase (CDK) 4/6 inhibitor and endocrine therapy. The study met both co-primary endpoints, demonstrating a statistically significant and clinically meaningful improvement in progression-free survival (PFS) in both the intention-to-treat and *ESR1*-mutated populations, compared with standard-of-care endocrine therapy plus everolimus. Overall survival (OS) data were immature, but a clear positive trend was observed. Follow-up continues to the next OS analysis. The giredestrant combination was well tolerated and adverse events were consistent with the known safety profiles of the individual study treatments, and no new safety signals were observed. This is the first positive head-to-head phase III trial investigating an all-oral selective oestrogen receptor degrader-containing regimen versus a standard of care combination.[1]

"These results show that the giredestrant combination provided a meaningful benefit for ER-positive breast cancer patients whose disease has progressed following treatment with a CDK inhibitor," said Levi Garraway, Roche's Chief Medical Officer and Head of Global Product Development. "We look forward to discussing these results with regulatory authorities with the goal of making this giredestrant-based regimen available to many people with advanced ER-positive breast cancer."

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ER-positive breast cancer accounts for approximately 70% of breast cancer cases.[2] Despite treatment advances, ER-positive breast cancer remains particularly challenging to treat due to its biological complexity.[3] Resistance to endocrine therapies, particularly in the post-CDK inhibitor setting, increases the risk of disease progression and is associated with poor outcomes.[2,4] Combination therapies, such as giredestrant plus everolimus, could address this by targeting two different signalling pathways, with the potential for improved patient outcomes.[3] Additionally, as an all-oral combination, this regimen could help minimise the impact of treatment on people's lives without the need for injections.[5]

Our extensive giredestrant clinical development programme spans multiple treatment settings and lines of therapy, reflecting our commitment to deliver innovative medicines to as many people with ER-positive breast cancer as possible.

Data from the evERA study will be submitted to health authorities with the view of bringing this potential treatment option to patients as soon as possible.

About the evERA Breast Cancer study

evERA Breast Cancer [NCT05306340] is a phase III, randomised, open-label, multicentre study evaluating the efficacy and safety of giredestrant in combination with everolimus versus standard-of-care endocrine therapy in combination with everolimus in people with oestrogen receptor-positive, human epidermal growth factor receptor 2-negative locally advanced or metastatic breast cancer who have had previous treatment with cyclin-dependent kinase 4/6 inhibitor and endocrine therapy, either in the adjuvant or locally advanced/metastatic setting.[1]

The co-primary endpoints are investigator-assessed progression-free survival in the intention-to-treat and *ESR1*-mutated populations, defined as the time from randomisation to the time when the disease progresses or a patient dies from any cause. The trial has been enriched for *ESR1*-mutated patients above the natural prevalence to assess the efficacy in this population. In the post-CDK inhibitor setting, up to 40% of people with ER-positive disease have *ESR1* mutations[4]. Key secondary endpoints include overall survival, objective response rate, duration of response, clinical benefit rate and safety.[1]

About giredestrant

Giredestrant is an investigational, oral, next-generation selective oestrogen receptor degrader (SERD) and full antagonist.[6]

Giredestrant is designed to block oestrogen from binding to the oestrogen receptor (ER), triggering its breakdown (known as degradation) and stopping or slowing down the growth of cancer cells.[7,10-12]

Giredestrant has an extensive clinical development programme and is being investigated in

five company-sponsored phase III clinical trials that span multiple treatment settings and lines of therapy to benefit as many people as possible:

- Giredestrant versus standard-of-care endocrine therapy (SoC ET) as adjuvant treatment in ER-positive, human epidermal growth factor receptor 2 (HER2)-negative early-stage breast cancer (lidERA Breast Cancer; NCT04961996)[13]
- Giredestrant plus everolimus versus SoC ET plus everolimus in ER-positive, HER2-negative, locally advanced or metastatic breast cancer (evERA Breast Cancer; NCT05306340)[1]
- Giredestrant plus palbociclib versus letrozole plus palbociclib in ER-positive, HER2-negative, endocrine-sensitive, recurrent locally advanced or metastatic breast cancer (persevERA Breast Cancer; NCT04546009)[14]
- Giredestrant plus investigator's choice of a cyclin-dependent kinase 4/6 (CDK 4/6) inhibitor versus fulvestrant plus a CDK 4/6 inhibitor in ER-positive, HER2-negative advanced breast cancer resistant to adjuvant endocrine therapy (pionERA Breast Cancer; NCT06065748)[15]
- Giredestrant plus Phesgo® (pertuzumab, trastuzumab, and hyaluronidase subcutaneous) versus Phesgo in ER-positive, HER2-positive locally advanced or metastatic breast cancer (heredERA Breast Cancer; NCT05296798)[16]

About oestrogen receptor (ER)-positive breast cancer

Globally, the burden of breast cancer continues to grow, with 2.3 million women diagnosed and 670,000 dying from the disease every year.[17] Breast cancer remains the number one cause of cancer-related deaths amongst women, and the second most common cancer type.[18]

ER-positive breast cancer accounts for approximately 70% of breast cancer cases.[2] A defining feature of ER-positive breast cancer is that its tumour cells have receptors that attach to oestrogen, which can contribute to tumour growth.[19]

Despite treatment advances, ER-positive breast cancer remains particularly challenging to treat due to its biological complexity.[3] Patients often face the risk of disease progression, treatment side effects and resistance to endocrine therapy.[3,20] There is an urgent need for more effective treatments that can delay clinical progression and reduce the burden of treatment on people's lives.[3,20]

About Roche in breast cancer

Roche has been advancing breast cancer research for more than 30 years, and it continues to be a major focus of research and development. Our legacy began with the development of the first targeted therapy for human epidermal growth factor receptor 2-positive breast cancer,

and we continue to push the boundaries of science to address the complexities of all breast cancer subtypes.

By leveraging our dual expertise in pharmaceuticals and diagnostics, we are dedicated to providing tailored treatment approaches and improving outcomes for every patient, from early to advanced stages of the disease. Together with our partners, we are relentlessly pursuing a cure, as we strive for a future where no one dies from breast cancer.

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.

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