

Ad hoc announcement pursuant to Art. 53 LR

Roche provides update on phase III persevERA study in ER-positive advanced breast cancer

- **persevERA Breast Cancer study did not meet the primary objective of a statistically significant improvement in progression-free survival, but a numerical improvement was observed**
- **Giredestrant plus palbociclib was well tolerated and adverse events were consistent with the known safety profiles of each individual treatment**
- **Roche is committed to transforming ER-positive breast cancer care, anchored by the landmark success of lidERA in early-stage disease and evERA in the advanced setting^{1,2}**
- **The FDA recently accepted the New Drug Application based on evERA data; phase III lidERA data will be submitted to the FDA in the coming weeks**
- **persevERA is the first of two distinct phase III studies in the first-line setting; pionERA study of giredestrant in combination with physician's choice of CDK4/6 inhibitor in endocrine-resistant ER-positive breast cancer is expected to readout in 2027^{3,4}**

Basel, 9 March 2026 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today results from the phase III persevERA Breast Cancer study evaluating investigational giredestrant in combination with palbociclib for people with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer. The study did not meet its primary objective of a statistically significant improvement in progression-free survival in the intent-to-treat population versus letrozole plus palbociclib, but a numerical improvement was observed. The adverse events for the giredestrant combination were manageable and consistent with the known safety profiles of each individual treatment.

“While persevERA didn’t meet its primary objective, we are confident in the potential of giredestrant to become a new standard-of-care endocrine therapy in early and advanced ER-positive breast cancer,” said Levi Garraway, MD, PhD, Roche’s Chief Medical Officer and Head of Global Product Development. “We believe there is a path forward for combining giredestrant with a CDK4/6 inhibitor in the adjuvant setting and we are conducting further studies. The efficacy demonstrated in evERA and lidERA provides clear validation of the clinical activity of giredestrant and reinforces the strength of our expanding clinical development programme.”

The giredestrant clinical development programme is made up of distinct studies designed to reflect the specific disease biology of each stage of breast cancer.³⁻⁷ Roche will continue to advance the clinical development programme to identify the people with ER-positive breast cancer who can derive the greatest benefit from giredestrant.

Giredestrant phase III clinical development programme

Trial	Indication	Regimen
lidERA Breast Cancer ⁵	Adjuvant ER+/HER2- breast cancer	Giredestrant vs. standard-of-care endocrine therapy (SoC ET)
persevERA Breast Cancer ³	1L ER+/HER2- metastatic breast cancer (endocrine-sensitive)	Giredestrant + palbociclib vs. letrozole plus palbociclib
pionERA Breast Cancer ⁴	1L ER+/HER2- metastatic breast cancer (endocrine-resistant)	Giredestrant + physician's choice of CDK4/6 inhibitor vs. fulvestrant + physician's choice of CDK4/6 inhibitor
evERA Breast Cancer ⁶	2L+ ER+/HER2- metastatic breast cancer	Giredestrant + everolimus vs. SoC ET + everolimus
heredERA Breast Cancer ⁷	1L maintenance ER+/HER2+ metastatic breast cancer	Giredestrant + Phesgo [®] (pertuzumab, trastuzumab, and hyaluronidase subcutaneous) vs. Phesgo

evERA was the first positive phase III readout for giredestrant, followed by lidERA in the early-stage setting.^{8,9} The scientific rationale for lidERA was supported by prior results in the neoadjuvant setting, including the phase II coopERA trial showing that giredestrant was superior to an aromatase inhibitor in reducing malignant cell division (Ki67 levels).¹⁰ This growing body of evidence underscores the potential of giredestrant to become a new standard-of-care endocrine therapy across ER-positive early-stage and advanced breast cancer.

persevERA is the first of two distinct phase III studies in the first-line setting; the pionERA study of giredestrant in combination with physician's choice of cyclin-dependent kinase (CDK)4/6 inhibitor in endocrine-resistant ER-positive, HER2-negative breast cancer is expected to readout in 2027.^{3,4}

The United States Food and Drug Administration (FDA) recently accepted the New Drug Application based on the evERA data. In the coming weeks, Roche will submit the giredestrant phase III lidERA data in early-stage breast cancer to the FDA.

The full results from persevERA will be presented at an upcoming medical meeting.

About the persevERA Breast Cancer study

persevERA Breast Cancer [[NCT04546009](#)] is a phase III, randomised, double-blind, placebo-controlled, multicentre study evaluating the efficacy and safety of giredestrant plus palbociclib versus letrozole plus palbociclib as first-line treatment for people with oestrogen receptor-positive, human epidermal growth factor receptor 2-negative, locally advanced or metastatic breast cancer.³ The study enrolled 992 patients globally.³

The primary endpoint is investigator-assessed progression-free survival.³ Key secondary endpoints include overall survival, objective response rate, duration of response and safety.³

About giredestrant

Giredestrant is an investigational, oral, potent next-generation selective oestrogen receptor degrader and full antagonist.¹¹

Giredestrant is designed to block oestrogen from binding to the oestrogen receptor, triggering its breakdown (known as degradation) and stopping or slowing down the growth of cancer cells.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 oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative early-stage breast cancer (lidERA Breast Cancer; [NCT04961996](#))⁵
- Giredestrant plus everolimus versus SoC ET plus everolimus in ER-positive, HER2-negative, locally advanced or metastatic breast cancer (evERA Breast Cancer; [NCT05306340](#))⁶
- 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](#))³
- Giredestrant plus investigator's choice of a cyclin-dependent kinase (CDK)4/6 inhibitor versus fulvestrant plus a CDK4/6 inhibitor in ER-positive, HER2-negative advanced breast cancer resistant to adjuvant endocrine therapy (pionERA Breast Cancer; [NCT06065748](#))⁴
- 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](#))⁷

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.¹³ Breast cancer remains the number one cause of cancer-related deaths amongst women, and the second most common cancer type.¹⁴

ER-positive breast cancer accounts for approximately 70% of breast cancer cases.¹⁵ In the US and EU5, an estimated 273,000 people are diagnosed in the early-stage setting, 88,000 people are diagnosed in first-line and 106,000 in the second and third-line setting combined.¹⁶

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.¹⁷

Despite treatment advances, ER-positive breast cancer remains particularly challenging to treat due to its biological complexity.¹⁸ In the early-stage setting, up to a third of people eventually experience disease recurrence on or after adjuvant endocrine therapy treatment.¹⁹⁻²¹ Additionally, many have to interrupt or stop treatment early due to safety or tolerability issues, thereby increasing the risk of death.²² In advanced settings, resistance to endocrine therapy – particularly following treatment with cyclin-dependent kinase inhibitors – increases the risk of disease progression and is associated with poor outcomes.^{15,23}

There is an urgent need for more effective treatments that can delay clinical progression and reduce the burden of treatment on people's lives.^{18,20,22-24}

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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