Media & Investor Release

FDA accepts New Drug Application for Roche's giredestrant in *ESR1*-mutated, ER-positive advanced breast cancer

- **Filing acceptance based on phase III data showing giredestrant plus everolimus reduced the risk of disease progression or death by 44% and 62% in ITT and *ESR1*-mutated populations, respectively, versus standard-of-care endocrine therapy plus everolimus[1]**
- **Strength of evERA data demonstrate potential for giredestrant combination to help address resistance to standard-of-care therapies, and could be the first and only oral SERD combination approved in the post-CDK4/6 inhibitor setting[1]**
- **The FDA has set a Prescription Drug User Fee Act date of 18 December**

Basel, 20 February 2026 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the United States (U.S.) Food and Drug Administration (FDA) has accepted the company's New Drug Application for giredestrant, an investigational oral therapy, in combination with everolimus for the treatment of adult patients with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2-negative, *ESR1*-mutated locally advanced or metastatic breast cancer following recurrence or progression on a prior endocrine-based regimen. The FDA is expected to make a decision on the approval by 18 December 2026. Giredestrant plus everolimus could be the first and only oral selective oestrogen receptor degrader (SERD) combination approved in the post-cyclin-dependent kinase (CDK)4/6 inhibitor setting.

"The clinically meaningful benefit seen with giredestrant could enable an important new treatment option to help delay disease progression or death in people with advanced, ER-positive breast cancer," said Levi Garraway, MD, PhD, Roche's Chief Medical Officer and Head of Global Product Development. "This acceptance marks a first step towards establishing the giredestrant combination as a new standard of care in this population."

The filing acceptance is based on the phase III evERA Breast Cancer study results, which showed that giredestrant plus everolimus reduced the risk of disease progression or death by 44% and 62% in the intention-to-treat (ITT) and *ESR1*-mutated populations, respectively, compared with standard-of-care endocrine therapy plus everolimus.[1] In the *ESR1*-mutated population, the median progression-free survival (PFS) was 9.99 months compared with 5.45 months in the giredestrant and comparator arm, respectively (stratified hazard ratio [HR]=0.38, 95% CI: 0.27-0.54, p-value=<0.0001).[1] In the ITT population, the median PFS was 8.77 months compared with 5.49 months in the giredestrant and comparator arms, respectively (HR=0.56, 95% CI: 0.44-0.71, p-value=<0.0001).[1]

Overall survival (OS) data were immature at the time of analysis, but a clear positive trend has been observed in the ITT (HR=0.69, 95% CI: 0.47-1.00, p-value=0.0473) and *ESR1*-mutated

populations (HR=0.62, 95% CI: 0.38-1.02, p-value=0.0566).[1] Follow-up for OS will continue to the next analysis. Adverse events for the giredestrant combination were manageable and consistent with the known safety profiles of the individual medicines.[1] No unexpected safety findings were observed, including no photopsia.[1]

Data from evERA are being used to support filing submissions to other global health authorities.

ER-positive breast cancer accounts for approximately 70% of breast cancer cases.[2] Resistance to endocrine therapies, particularly in the post-CDK inhibitor setting, increases the risk of disease progression and is associated with poor outcomes.[2,3] Oral combination therapies, such as giredestrant plus everolimus, could address this by targeting two different signalling pathways while helping to minimise the impact of treatment on people's lives without the need for injections.[4,5]

evERA was the first positive phase III readout for giredestrant, followed by lidERA Breast Cancer in the early-stage setting.[1,6] The scientific rationale for lidERA was supported by prior results in the neoadjuvant setting, including the coopERA trial showing that giredestrant was superior to an aromatase inhibitor in reducing malignant cell division (Ki67 levels).[7] 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.[1,6,7] In the coming weeks, Roche will submit the giredestrant phase III lidERA data in early-stage breast cancer to health authorities worldwide, including the FDA. The persevERA readout in first-line ER-positive breast cancer is expected in the first half of this year, which will provide further evidence for giredestrant in the ER-positive breast cancer treatment paradigm.

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.

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 (ER)-positive, human epidermal growth factor receptor 2-negative locally advanced or metastatic breast cancer who have had previous treatment with cyclin-dependent kinase (CDK)4/6 inhibitor and endocrine therapy, either in the adjuvant or locally advanced/metastatic setting.[8]

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.[8] 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.[9,10] Key secondary endpoints include overall survival, objective response rate, duration of response, clinical benefit rate and safety.[8]

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 (ER), 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 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)[7]
- 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 (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)[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.[4] Patients often face the risk of disease progression, treatment side effects and resistance to endocrine therapy.[4,20] There is an urgent need for more effective treatments that can delay clinical progression and reduce the burden of treatment on people's lives.[4,20]

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.

All trademarks used or mentioned in this release are protected by law.

References

[1] Mayer E, et al. Giredestrant (GIRE), an oral selective oestrogen receptor (ER) antagonist and degrader, + everolimus (E) in patients (pts) with ER-positive, HER2-negative advanced breast cancer (ER+, HER2– aBC) previously treated with a CDK4/6 inhibitor (i): Primary results of the Phase III evERA BC trial. Presented at: European Society for Medical Oncology (ESMO) Annual Meeting; 2025 October 17-21; Berlin, Germany. LBA #16.
[2] Kinslow C, et al. Prevalence of Estrogen Receptor Alpha (ESR1) Somatic Mutations in Breast Cancer. JNCI Cancer Spectrum; 2022 Oct;6(5):pkac060.
[3] Sahin T, et al. Post-progression treatment options after CDK4/6 inhibitors in hormone receptor-positive, HER2-negative metastatic breast cancer. Cancer Treatment Reviews. 2025 April;135:102924.
[4] Hanker A, et al. Overcoming Endocrine Resistance in Breast Cancer. Canc Cell. 2020 Apr 13;37(4):496–513.
[5] Wood L. A review on adherence management in patients on oral cancer therapies. Eur J Oncol Nurs. 2012 Sept; 16(4):432-38.
[6] Bardia A, et al. Giredestrant vs standard-of-care endocrine therapy as adjuvant treatment for patients with estrogen receptor-positive, HER2-negative early breast cancer: Results from the global Phase III lidERA Breast Cancer trial. Presented at: San Antonio Breast Cancer Symposium (SABCS); 2025 December 9-12; San Antonio, Texas, United States. #GS1-10.
[7] Hurvitz SA, et al. Neoadjuvant palbociclib plus either giredestrant or anastrozole in oestrogen receptor-positive, HER2-negative, early breast cancer (coopERA Breast Cancer): an open-label, randomised, controlled, phase 2 study. Lancet Oncol. 2023;24:1029–1041.
[8] ClinicalTrials.gov. A Study Evaluating the Efficacy and Safety of Giredestrant Plus Everolimus Compared With the Physician's Choice of Endocrine Therapy Plus Everolimus in Participants With Estrogen Receptor-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer (evERA Breast Cancer) [Internet; cited 2026 February]. Available from: https://clinicaltrials.gov/study/NCT05306340.
[9] Meisel J L, et al. Real-world estrogen receptor 1 (ESR1) testing patterns and results in U.S. patients with metastatic breast cancer, 2018-2024. JCO Oncol Pract. 2025;21:579.
[10] Chaudhary N, et al. CDK4/6i-treated HR+/HER2- breast cancer tumors show higher ESR1 mutation prevalence and more altered genomic landscape. npj Breast Cancer. 2024;10,15.
[11] Martin M, et al. Giredestrant (GDC-9545) vs physician choice of endocrine monotherapy (PCET) in patients (pts) with ER+, HER2– locally advanced/metastatic breast cancer (LA/mBC): Primary analysis of the phase 2, randomised, open-label acelERA BC study. Presented at: The ESMO Annual Meeting; 2022 September 9-13; Paris, France. Abstract #211MO.
[12] Metcalfe C, et al. GDC-9545: A novel ER antagonist and clinical candidate that combines desirable mechanistic and pre-clinical DMPK attributes. Presented at: SABCS; 2018 December 4-8; San Antonio, Texas, USA. Abstract #P5-04-07.
[13] ClinicalTrials.gov. A Study Evaluating the Efficacy and Safety of Adjuvant Giredestrant Compared With Physician's Choice of Adjuvant Endocrine Monotherapy in Participants With Estrogen Receptor-Positive, HER2-Negative Early Breast Cancer (lidERA Breast Cancer) [Internet; cited 2026 February]. Available from: https://clinicaltrials.gov/study/NCT04961996.
[14] ClinicalTrials.gov. A Study Evaluating the Efficacy and Safety of Giredestrant Combined With Palbociclib Compared With Letrozole Combined With Palbociclib in Participants With Estrogen Receptor-Positive, HER2-Negative Locally Advanced or Metastatic Breast Cancer (persevERA Breast Cancer) [Internet; cited 2026 February]. Available from: https://clinicaltrials.gov/study/NCT04546009.

[15] ClinicalTrials.gov. A Study to Evaluate Efficacy and Safety of Giredestrant Compared With Fulvestrant (Plus a CDK4/6 Inhibitor), in Participants With ER-Positive, HER2-Negative Advanced Breast Cancer Resistant to Adjuvant Endocrine Therapy (pionERA Breast Cancer) [Internet; cited 2026 February]. Available from: https://clinicaltrials.gov/study/NCT06065748.
[16] ClinicalTrials.gov. A Study to Evaluate the Efficacy and Safety of Giredestrant in Combination With Phesgo (Pertuzumab, Trastuzumab, and Hyaluronidase-zzxf) Versus Phesgo in Participants With Locally Advanced or Metastatic Breast Cancer (heredERA Breast Cancer) [Internet; cited 2026 February]. Available from: https://clinicaltrials.gov/study/NCT05296798.
[17] World Health Organization. Breast Cancer [Internet; cited 2026 February]. Available from: https://www.who.int/news-room/fact-sheets/detail/breast-cancer.
[18] World Health Organization. Cancer Today [Internet; cited 2026 February]. Available from: https://gco.iarc.fr/today/en/dataviz/bars?mode=cancer&types=1&group_populations=1&sexes=2&key=asr&age_end=14.
[19] National Cancer Institute. Hormone Therapy for Breast Cancer [Internet; cited 2026 February]. Available from: https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet.
[20] Başaran G, et al. Ongoing unmet needs in treating estrogen receptor-positive/HER2-negative metastatic breast cancer. Cancer Treat Rev. 2018 Feb;63:144-55.

Roche Global Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

Hans Trees, PhD
Phone: +41 79 407 72 58

Lorena Corfas
Phone: +41 79 568 24 95

Karsten Kleine
Phone: +41 79 461 86 83

Yvette Petillon
Phone: +41 79 961 92 50

Nathalie Altermatt
Phone: +41 79 771 05 25

Simon Goldsborough
Phone: +44 797 32 72 915

Kirti Pandey
Phone: +49 172 6367262

Dr Rebekka Schnell
Phone: +41 79 205 27 03

Roche Investor Relations

Dr Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com