Media & Investor Release

FDA approves Roche's Wilserdly (giredestrant), a next-generation oral SERD, for ER-positive, *ESR1*-mutated advanced breast cancer

- **Wilserdly is the first and only next-generation all-oral SERD combination to significantly outperform standard endocrine combination in a post-CDK4/6 inhibitor setting in a head-to-head phase III trial (evERA)[1]**
- **In *ESR1*-mutated patients Wilserdly plus everolimus significantly delayed disease progression or death by 62% compared to standard endocrine therapy plus everolimus[1]**
- ***ESR1* mutations are considered the primary cause of hormone therapy resistance affecting up to 40% of patients, as detected by an FDA approved test[2,3]**
- **The FDA is also reviewing Wilserdly in the adjuvant setting with a decision expected by 30 November. If approved, Wilserdly will be the first SERD approved for both adjuvant and advanced ER-positive breast cancer**

Basel, 16 November 2026 - Roche (SIX: RO, ROP; OTCQX: RHHBY) announced today that the United States (U.S.) Food and Drug Administration (FDA) has approved Wilserdly™ (giredestrant) in combination with everolimus for the treatment of adults with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, *ESR1*-mutated locally advanced or metastatic breast cancer, as detected by an FDA-authorised test, whose disease has recurred during or after completion of endocrine-based adjuvant therapy, or has progressed on at least one endocrine-based regimen in the metastatic setting.

The approval of Wilserdly addresses an important unmet need for patients developing resistance. Up to 40% of patients with hormone receptor (HR)-positive metastatic breast cancer develop *ESR1* mutations that drive resistance and disease progression.[2,3] Wilserdly plus everolimus addresses this by targeting two different signalling pathways while helping to minimise the impact of treatment on people's lives as an oral regimen without the need for injections.[2,4]

"For patients with *ESR1*-mutated advanced breast cancer, the development of resistance to endocrine therapy remains a substantial challenge - often requiring more intensive treatment," said Levi Garraway, MD, PhD, Roche's Chief Medical Officer and Head of Global Product Development. "By pairing potent oestrogen receptor degradation with everolimus, Wilserdly offers a targeted, all-oral regimen that significantly delays disease progression and allows advanced breast cancer patients to take their treatment from home."

The FDA approval is supported by positive primary endpoint data from the phase III evERA Breast Cancer study published in *The New England Journal of Medicine*. In adult patients with *ESR1*-mutated, ER-positive, HER2-negative locally advanced or metastatic breast cancer

progressing after prior cyclin-dependent kinase (CDK)4/6 inhibitor therapy, the all-oral combination of Wilserdly plus everolimus significantly prolonged progression-free survival, achieving a 62% reduction in the risk of disease progression or death compared to standard endocrine therapy plus everolimus (stratified hazard ratio=0.38; 95% confidence interval: 0.27–0.54; p<0.0001).[1,5]

“Patients with advanced breast cancer progressing on endocrine therapies often face difficult choices and deteriorating quality of life as options narrow,” said Dr Erica L. Mayer, Director of Breast Cancer Clinical Research at the Dana-Farber Cancer Institute. “The evERA trial demonstrates that the oral giredestrant combination regimen directly targets the primary genomic drivers of resistance, offering patients prolonged disease control through a fully oral therapeutic option.”

“For more than three decades, Roche has transformed care across oncology, and this first approval for Wilserdly marks a pivotal leap forward in addressing aggressive, treatment-resistant breast cancer,” said Teresa Graham, Chief Executive Officer, Roche Pharmaceuticals. “We remain focused on maximising the clinical impact of Wilserdly across the continuum of care, including early-stage disease.”

Roche has also submitted a New Drug Application for Wilserdly as an adjuvant treatment for adults with ER-positive, HER2-negative, stage I, II, and III breast cancer at intermediate to high risk of recurrence based on the phase III lidERA Breast Cancer study, which was accepted under Priority Review.[6] The FDA has set a Prescription Drug User Fee Act date of 30 November 2026. If approved, this would represent the first new adjuvant endocrine therapy in over 20 years, with potential to establish a new standard of care in this setting.[6-8]

Roche’s broad and robust Wilserdly clinical development programme spans distinct treatment settings and lines of therapy, reflecting our commitment to deliver innovative medicines to as many people with HR-positive breast cancer as possible. Additional regulatory filings and development activities are underway in markets outside the US.

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 Wilserdly™ (giredestrant) in combination with everolimus versus standard 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.[9]

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.[9] Approximately 40% of people with HR-positive metastatic breast cancer who received first-line endocrine therapy have *ESR1* mutations.[3] Key secondary endpoints include overall survival, objective response rate, duration of response, clinical benefit rate and safety.[9]

About Wilserdly™ (giredestrant)

Wilserdly is a next-generation, potent, oral selective oestrogen receptor degrader (SERD) and full antagonist designed to achieve deep and sustained inhibition of oestrogen receptor (ER) signalling.[10] Wilserdly is designed to block oestrogen from binding to the ER, triggering the breakdown of the ER protein (known as degradation) and stopping or slowing down the growth of cancer cells.[11]

Key mechanisms of resistance to a cyclin-dependent kinase (CDK)4/6 inhibitor and endocrine therapy include activation of the PAM (PI3K/AKT/mTOR) signalling pathway while maintaining dependency on ER.[2] Wilserdly's antiproliferative activity is synergistically enhanced when combined with an mTOR inhibitor, addressing a key resistance mechanism.[1,12]

Pre-clinical data have demonstrated improved clinical potency versus other oral SERDs potentially enabling treatment at one of the lowest doses among oral SERDs.[12,13]

Wilserdly has an extensive clinical development programme including six company-sponsored phase III clinical trials across multiple treatment settings and lines of therapy:

Study	Intervention	Patient population
Positive primary study readouts completed		
lidERA Breast Cancer; NCT04961996	Wilserdly versus standard endocrine therapy as adjuvant treatment[14]	ER-positive, human epidermal growth factor receptor 2 (HER2)-negative early-stage breast cancer[14]
evERA Breast Cancer; NCT05306340	Wilserdly plus everolimus versus standard endocrine therapy plus everolimus[9]	ER-positive, HER2-negative, locally advanced or metastatic breast cancer[9]
Primary study readouts pending		
pionERA Breast Cancer; NCT06065748	Wilserdly plus investigator's choice of a cyclin-dependent kinase (CDK)4/6 inhibitor versus fulvestrant plus an investigator's choice CDK4/6 inhibitor[15]	ER-positive, HER2-negative advanced breast cancer resistant to adjuvant endocrine therapy[15]

Study	Intervention	Patient population
heredERA Breast Cancer; NCT05296798	Wilserdly plus Phesgo® (pertuzumab, trastuzumab, and hyaluronidase subcutaneous) versus Phesgo plus optional standard endocrine therapy at investigator's discretion[16]	ER-positive, HER2-positive locally advanced or metastatic breast cancer[16]
novERA Breast Cancer; NCT07541079	Wilserdly, evaluating adherence, tolerability, and patient-reported outcomes [17]	Patients with ER-positive, HER2-negative early-stage breast cancer who are intolerant to adjuvant aromatase inhibitor treatment[17]
kalitERA; NCT07827573	Wilserdly, evaluating treatment adherence, tolerability, and patient-reported outcomes[18]	ER-positive, HER2-negative early-stage breast cancer[18]

About hormone receptor (HR)-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.[19] Breast cancer remains the number one cause of cancer-related deaths amongst women, and the second most common cancer type.[20]

HR-positive, human epidermal growth factor receptor 2-negative breast cancer accounts for approximately 70% of breast cancer cases and more than 90% are diagnosed in the early-stage.[21-25] A defining feature of HR-positive breast cancer is that its tumour cells have receptors that attach to hormones like oestrogen, which can contribute to tumour growth.[26]

Despite treatment advances, HR-positive breast cancer remains particularly challenging to treat due to its biological complexity.[2] Patients often face the risk of disease progression, treatment side effects and resistance to endocrine therapy.[2,27] There is an urgent need for more effective treatments that can delay clinical progression and reduce the burden of treatment on people's lives.[2,27]

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 includes setting and redefining standards of care with pioneering treatments such as Herceptin® (trastuzumab) and Kadcyla® (trastuzumab emtansine), and we continue to build on this with next-generation innovations such as Wilserdly™ (giredestrant), pushing 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

Roche (SIX: RO, ROP; OTCQX: RHHBY) is a healthcare company uniquely placed to prevent, stop and cure diseases by uniting leading science and technology across diagnostics, medicines and digital solutions.

Roche was founded in Basel, Switzerland in 1896 and today is a leading provider of transformative medicines and diagnostics for millions of people in over 150 countries around the world. It is dedicated to tackling healthcare challenges that place the greatest strain on patients, families, communities and healthcare systems. Across its Diagnostics and Pharmaceutical divisions, Roche focuses on areas including oncology, neurology, cardiovascular and metabolic diseases, ophthalmology, infectious diseases and immunology with the aim of providing real and positive change for patients, the people they love and the professionals who care for them.

Genentech in the United States is a fully owned subsidiary in the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, a major innovator in the Japanese therapeutic antibody market.

For more information, please visit www.roche.com.

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