27 May 2026

US FDA decision date extended for SERENA-6 filing of camizestrant to enable review of additional data

The US Food and Drug Administration (FDA) has informed AstraZeneca that it will extend the Prescription Drug User Fee Act (PDUFA) date to review additional data requested to support the New Drug Application (NDA) for camizestrant in combination with a cyclin-dependent kinase (CDK) 4/6 inhibitor (palbociclib, ribociclib or abemaciclib) for the 1st-line treatment of patients with hormone receptor (HR)-positive, HER2-negative advanced breast cancer whose tumours have an emergent *ESR1* mutation.

The NDA is based on positive results from the pivotal SERENA-6 Phase III trial presented at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published in *The New England Journal of Medicine*.[1] The FDA granted Breakthrough Therapy Designation for the camizestrant combination in this setting in May 2025.

In April 2026, the FDA's Oncologic Drugs Advisory Committee did not reach a majority vote in favour of the benefit of switching to camizestrant in combination with a CDK4/6 inhibitor after detection of an *ESR1* mutation in circulating tumour DNA (ctDNA) prior to radiographic progression, based on the SERENA-6 Phase III trial. Subsequently, the Company has provided additional analyses requested by the FDA in support of the application, including ctDNA clearance data linked to longer-term efficacy outcomes that will be presented on 02 June at ASCO 2026.

Susan Galbraith, Executive Vice President, Oncology Haematology R&D, AstraZeneca, said: "We are committed to continuously advancing the clinical landscape in oncology in pursuit of improving outcomes for patients. The SERENA-6 treatment strategy epitomises this approach by monitoring patients for the emergence of *ESR1* mutations in ctDNA and testing if a switch of endocrine backbone therapy at this point improves outcomes. We look forward to continuing the dialogue with the FDA in order to bring the benefits of camizestrant with this innovative treatment strategy to eligible patients in the US as quickly as possible."

On 22 May, the European Medicines Agency's Committee for Medicinal Products for Human Use adopted a positive opinion recommending approval of the camizestrant combination in this setting based on the results of the SERENA-6 Phase III trial.

Camizestrant is approved in the United Arab Emirates and Saudi Arabia in this setting. Regulatory applications are also currently under review in Japan and several other countries based on the SERENA-6 Phase III trial.

Notes

HR-positive breast cancer

Breast cancer is the second most common cancer and one of the leading causes of cancer-related deaths worldwide.[2] More than two million patients were diagnosed with breast cancer in 2022, with more than 665,000 deaths globally.[2] In the US, breast cancer is the most common cancer in women, with more than 300,000 new cases of the disease diagnosed annually, and more than 42,000 deaths.[3] While survival rates are high for those diagnosed with early breast cancer, only about 30% of patients diagnosed with or who progress to metastatic disease are expected to live five years following diagnosis.[4]

HR-positive breast cancer, characterised by the expression of estrogen or progesterone receptors, or both, is the most common subtype of breast cancer with 70% of tumours considered HR-positive and HER2-negative.[4] Estrogen receptor (ERs) often drive the growth of HR-positive breast cancer cells.[5]

Globally, approximately 200,000 patients with HR-positive breast cancer are treated with a medicine in the 1st-line setting; most frequently with endocrine therapies that target ER-driven disease, which are often paired with CDK4/6 inhibitors.[6-8] In the US, approximately 37,000 patients with HR-positive metastatic breast cancer are treated with these therapies in the 1st-line setting.[6-8] However, resistance

to these therapies develops in many patients.[8] Once this occurs, treatment options are limited and survival rates are low with approximately 36% of patients anticipated to live beyond five years after diagnosis.[4,8]

Mutations in the *ESR1* gene are a key driver of endocrine resistance and are associated with poor outcomes, emerging during treatment of the disease and becoming more prevalent as the disease progresses.[9,10] Approximately 30% of patients with endocrine sensitive HR-positive disease develop *ESR1* mutations during 1st-line treatment before disease progression.[6]

The optimisation of endocrine therapy and overcoming resistance to enable patients to continue benefiting from these treatments, as well as identifying new therapies for those who are less likely to benefit, are active areas of focus for breast cancer research.

SERENA-6
SERENA-6 is a Phase III, double-blind, randomised trial evaluating the efficacy and safety of camizestrant in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) versus treatment with an AI (anastrozole or letrozole) in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) in patients with HR-positive, HER2-negative advanced breast cancer (patients with either locally advanced disease, or metastatic disease) whose tumours have an emergent *ESR1* mutation.

The global trial enrolled 315 adult patients with histologically confirmed HR-positive, HER2-negative advanced breast cancer, undergoing treatment with an AI in combination with a CDK4/6 inhibitor as 1st-line treatment. The primary endpoint of the SERENA-6 trial is PFS as assessed by investigator, with secondary endpoints including OS, and PFS2 by investigator assessment.

Camizestrant
Camizestrant is an investigational, potent, next-generation oral selective estrogen receptor degrader (SERD) and complete ER antagonist that is currently in Phase III trials for the treatment of HR-positive breast cancer.

AstraZeneca's broad, robust and innovative clinical development programme, including the SERENA-6, SERENA-4, CAMBRIA-1 and CAMBRIA-2 trials, is evaluating the safety and efficacy of camizestrant when used as a monotherapy or in combination with CDK4/6 inhibitors to address a number of areas of unmet need in HR-positive, HER2-negative breast cancer.

Camizestrant has demonstrated anti-cancer activity across a range of preclinical models, including those with ER-activating mutations. In the SERENA-2 Phase II trial, camizestrant demonstrated a statistically significant and clinically meaningful improvement in PFS versus *Faslodex* (fulvestrant) in the overall trial population, including in patients with *ESR1* tumour mutations irrespective of prior treatment with CDK4/6 inhibitors in patients with ER-positive locally advanced or metastatic breast cancer, previously treated with endocrine therapy. The SERENA-1 Phase I trial demonstrated that camizestrant is well tolerated and has a promising anti-tumour profile when administered alone or in combination with palbociclib, ribociclib and abemaciclib; three widely used CDK4/6 inhibitors.

AstraZeneca in breast cancer
Driven by a growing understanding of breast cancer biology, AstraZeneca is challenging, and redefining, the current clinical paradigm for how breast cancer is classified and treated to deliver even more effective treatments to patients in need - with the bold ambition to one day eliminate breast cancer as a cause of death.

AstraZeneca has a comprehensive portfolio of approved and promising compounds in development that leverage different mechanisms of action to address the biologically diverse breast cancer tumour environment.

With *Enhertu* (trastuzumab deruxtecan), a HER2-directed antibody drug conjugate (ADC), AstraZeneca and Daiichi Sankyo are aiming to improve outcomes in previously treated HER2-positive, HER2-low and HER2-ultralow metastatic breast cancer, and expanding its potential in earlier lines of treatment and in new breast cancer settings.

In HR-positive breast cancer, AstraZeneca continues to improve outcomes with foundational medicines *Faslodex* and *Zoladex* (goserelin) and aims to reshape the HR-positive space with first-in-class AKT inhibitor, *Truqap* (capivasertib), the TROP-2-directed ADC, *Datroway* (datopotamab deruxtecan), and next-generation oral SERD and potential new medicine camizestrant.

PARP inhibitor *Lynparza* (olaparib) is a targeted treatment option that has been studied in early and metastatic breast cancer patients with an inherited *BRCA* mutation. AstraZeneca with MSD (Merck & Co., Inc. in the US and Canada) continue to research *Lynparza* in these settings. AstraZeneca is also exploring the potential of saruparib, a potent and selective inhibitor of PARP1, in combination with camizestrant in *BRCA*-mutated, HR-positive, HER2-negative advanced breast cancer.

To bring much-needed treatment options to patients with triple-negative breast cancer, an aggressive form of breast cancer, AstraZeneca is collaborating with Daiichi Sankyo to evaluate the potential of *Datroway* alone and in combination with immunotherapy *Imfinzi* (durvalumab).

AstraZeneca in oncology
AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

AstraZeneca
AstraZeneca (LSE/STO/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Disease, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Social Media @AstraZeneca.

Contacts
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References

1. Bidard FC, et al. First-Line Camizestrant for Emerging ESR1-Mutated Advanced Breast Cancer. *N Engl J Med* 2025; DOI: 10.1056/NEJMoa2502929.
2. Bray F, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024; 1- 35. DOI:10.3322/caac.21834.
3. American Cancer Society. Key Statistics for Breast Cancer. Available at: https://www.cancer.org/cancer/types/breast-cancer/about/how-common-is-breast-cancer.html. Accessed May 2026.
4. National Cancer Institute. Cancer Stat facts: Female breast cancer subtypes. Available at: https://seer.cancer.gov/statfacts/html/breast-subtypes.html. Accessed May 2026.
5. Scabia V, et al. Estrogen receptor positive breast cancers have patient specific hormone sensitivities and rely on progesterone receptor. *Nat Commun*. 2022; 10.1038/s41467-022-30898-0.
6. Cerner CancerMPact database. Accessed May 2026.
7. Lin M, et al. Comparative Overall Survival of CDK4/6 Inhibitors Plus Endocrine Therapy vs. Endocrine Therapy Alone for Hormone receptor-positive, HER2-negative metastatic breast cancer. *J Cancer*. 2020; 10.7150/jca.48944.
8. Lloyd M R, et al. Mechanisms of Resistance to CDK4/6 Blockade in Advanced Hormone Receptor-positive, HER2-negative Breast Cancer and Emerging Therapeutic Opportunities. *Clin Cancer Res*. 2022; 28(5):821-30.

9. Brett O, et al. ESR1 mutation as an emerging clinical biomarker in metastatic hormone receptor-positive breast cancer. *Breast Cancer Res*. 2021; 23:85.
10. Zundelevich A, et al. ESR1 mutations are frequent in newly diagnosed metastatic and loco-regional recurrence of endocrine-treated breast cancer and carry worse prognosis. *Breast Cancer Res*. 2020; 22:16.

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