This announcement contains inside information

14 September 2026

Update on SERENA-4 Phase III trial of *Etcamah* in combination with palbociclib in upfront 1st-line advanced ER-positive breast cancer

SERENA-4 trial did not meet primary objective of statistically significant improvement in progression-free survival, however a numerical improvement was observed

Etcamah is the only oral SERD to demonstrate benefit in 1st-line setting and is approved for patients with an emergent ESR1 tumour mutation based on SERENA-6

The SERENA-4 Phase III trial of AstraZeneca's *Etcamah* (camizestrant) in combination with palbociclib, a cyclin-dependent kinase (CDK) 4/6 inhibitor, did not meet the primary endpoint of progression-free survival (PFS), however a numerical improvement was observed in the upfront 1st-line treatment of patients with estrogen receptor (ER)-positive, HER2-negative advanced breast cancer who have not received any systemic treatment for advanced disease. The trial evaluated the *Etcamah* combination versus treatment with an aromatase inhibitor (anastrozole) in combination with palbociclib.

Susan Galbraith, Executive Vice President, Oncology Haematology R&D, AstraZeneca, said: "Whilst we are disappointed by the SERENA-4 outcome, it sharpens our focus on maximising the number of patients who can benefit from *Etcamah* today based on SERENA-6 and reinforces the importance of *ESR1* testing for patients on first-line therapy. Early breast cancer represents an important opportunity, and we remain confident in the long-term potential of *Etcamah* in the early setting as we advance our broader programme."

The safety profile of *Etcamah* in combination with palbociclib in SERENA-4 was consistent with the known safety profile of each medicine, with no new safety concerns identified. Data will be shared in due course.

Etcamah in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) is approved in the US, EU, Japan and several other countries for the treatment of adult patients with hormone receptor (HR)-positive (or ER-positive), HER2-negative locally advanced or metastatic breast cancer upon detection or emergence of *ESR1* mutation during 1st-line endocrine-based therapy, based on the results from the SERENA-6 Phase III trial.

Etcamah is currently being evaluated in the most comprehensive oral SERD development programme in early breast cancer. Encompassing approximately 10,000 patients, the CAMBRIA-1 and CAMBRIA-2 Phase III trials are designed for patients at both intermediate and high risk of recurrence in the adjuvant setting, evaluating *Etcamah* as a monotherapy, in combination with CDK4/6 inhibitors and following CDK4/6 inhibitor treatment to address areas of unmet need in HR-positive, HER2-negative breast cancer.

Notes

ER-positive breast cancer

Breast cancer is the second most common cancer and one of the leading causes of cancer-related deaths worldwide.[1] More than two million patients were diagnosed with breast cancer in 2024, with more than 690,000 deaths globally.[1] 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.[2]

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.[2] ERs often drive the growth of HR-positive breast cancer cells.[3] More than 97% of HR-positive breast cancer tumours are ER-positive.[4,5]

SERENA-4
SERENA-4 is a Phase III, double-blind, randomised trial evaluating the efficacy and safety of camizestrant in combination with palbociclib, a CDK4/6 inhibitor, versus treatment with an aromatase inhibitor (AI) (anastrozole) in combination with palbociclib in patients with ER-positive, HER2-negative advanced breast cancer (patients with either locally advanced disease, or metastatic disease).

The global trial enrolled 1,371 adult patients, newly diagnosed with Stage IV *de novo* or recurrent disease who had not received any systemic treatment for metastatic disease. Patients with recurrence from early-stage disease had received at least 24 months of standard adjuvant endocrine therapy (AI or tamoxifen), and at least 12 months had elapsed since the last dose of adjuvant AI therapy without disease progression on treatment.

The primary endpoint of the SERENA-4 trial is PFS as assessed by investigator, with secondary endpoints including OS, PFS2, and health-related quality of life (HRQOL).

Etcamah
Etcamah is a potent, next-generation oral selective estrogen receptor degrader (SERD) and complete ER antagonist, administered orally, once daily. The recommended dose of *Etcamah* in combination with a CDK4/6 inhibitor is 75mg.

Etcamah in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) is approved in the US, EU, Japan and several other countries for the treatment of adult patients with HR-positive (or ER-positive), HER2-negative locally advanced or metastatic breast cancer upon detection or emergence of *ESR1* mutation during 1st-line endocrine-based therapy, based on the results from the SERENA-6 Phase III trial.

The broad, robust and innovative *Etcamah* clinical development programme, including the CAMBRIA-1 and CAMBRIA-2 Phase III trials, is evaluating the safety and efficacy of *Etcamah* 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.

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 are exploring 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* (fulvestrant) 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, *Etcamah*.

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 *Etcamah* or endocrine therapy 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
For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

References

1. Sung H, et al. Global cancer statistics 2024: GLOBOCAN estimates of incidence and mortality worldwide for 34 cancers in 186 countries. *CA Cancer J Clin*. 2026; DOI: 10.3322/caac.70090.
2. National Cancer Institute. Cancer Stat facts: Female breast cancer subtypes. Available at: https://seer.cancer.gov/statfacts/html/breast-subtypes.html. Accessed September 2026.
3. 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.
4. Bae S, et al. Poor prognosis of single hormone receptor positive breast cancer: similar outcome as triple-negative breast cancer. *BMC Cancer*. 2015; 15:138.
5. Cserni G, et al. Estrogen Receptor Negative and Progesterone Receptor Positive Breast Carcinomas-How Frequent are they? *Pathol. Oncol. Res*. 2011; 17:663-668.

Matthew Bowden
Company Secretary
AstraZeneca PLC

This announcement contains information that AstraZeneca PLC is obliged to make public pursuant to the EU Market Abuse Regulation (596/2014) and the assimilated EU Market Abuse Regulation (596/2014) as it forms part of the law of the United Kingdom by operation of the European Union (Withdrawal) Act 2018. This announcement was submitted for publication, through the agency of the contact person(s) set out above, at 21:15 BST 11 September 2026.