26 May 2026

Datroway approved in the US as first TROP2-directed antibody drug conjugate for 1st-line treatment of patients with metastatic triple-negative breast cancer who are not PD-1/PD-L1 inhibitor candidates

AstraZeneca and Daiichi Sankyo's Datroway is the only TROP2-directed antibody drug conjugate to prolong overall survival in this setting vs. chemotherapy, with an unprecedented median overall survival of approximately two years based on the TROPION-Breast02 Phase III trial

Datroway has the potential to become the new standard of care in this setting

AstraZeneca and Daiichi Sankyo's *Datroway* (datopotamab deruxtecan) has been approved in the US for the treatment of adult patients with unresectable or metastatic triple-negative breast cancer (TNBC) who are not candidates for PD-1/PD-L1 inhibitor therapy.

The approval follows Priority Review by the Food and Drug Administration (FDA) based on results from the TROPION-Breast02 Phase III trial which were presented at the 2025 European Society for Medical Oncology Congress and published in *Annals of Oncology*.

Tiffany A. Traina, MD, FASCO, Section Head, Triple-Negative Breast Cancer Clinical Research Programme, Memorial Sloan Kettering Cancer Centre and investigator for TROPION-Breast02, said: "Datopotamab deruxtecan is the first and only medicine to significantly prolong overall survival in the 1st-line setting compared to chemotherapy in patients with metastatic triple-negative breast cancer who are not candidates for immunotherapy. This approval will bring a much-needed treatment option for these patients."

Arlene Brothers, Executive Director, Triple Negative Breast Cancer Foundation, said: "For seven out of 10 patients with metastatic triple-negative breast cancer who are not candidates for immunotherapy, chemotherapy has remained the only treatment option. Today's approval of *Datroway* means that for the first time, these patients will have a new standard of care beyond traditional chemotherapy at the outset of their treatment."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "Triple-negative breast cancer is notoriously difficult to treat. Patients with metastatic disease, especially those who are unable to receive immunotherapy, urgently need more effective, durable and tolerable treatment options, which extend survival. With today's approval, we are proud to bring *Datroway* to a broad population of advanced triple-negative breast cancer patients and we continue to study its promise as a mainstay treatment across tumours, stages and settings."

Ken Keller, Global Head of Oncology Business, and President and CEO, Daiichi Sankyo, Inc., said: "As the first antibody drug conjugate to demonstrate a median overall survival of two years in the 1st-line metastatic setting of triple-negative breast cancer, *Datroway* has the potential to redefine the treatment landscape for these patients. With this approval, *Datroway* is now approved for three indications in the US, including two for breast cancer, underscoring its potential to play an important role across tumour types."

In the trial, *Datroway* demonstrated a statistically significant and clinically meaningful 5.0-month improvement in median overall survival (OS) (hazard ratio [HR] 0.79; 95% confidence interval [CI] 0.64-0.98; p=0.0290) and a 43% reduction in patients' risk of disease progression or death (HR 0.57; 95% CI 0.47-0.69; p<0.0001) compared to chemotherapy as 1st-line treatment in this patient population. *Datroway* was also associated with more robust treatment responses, including an objective response rate (ORR) of 64% compared to an ORR of 30% with chemotherapy.[1]

The safety profile of *Datroway* in TROPION-Breast02 was consistent with previous clinical trials of *Datroway* in breast cancer.

This application was reviewed under Project Orbis, which provides a framework for concurrent submission and review of oncology medicines among participating international partners. As part of Project Orbis, reviews are ongoing in Australia, Canada, Singapore and Switzerland. This initiative is designed to bring effective cancer treatments to patients as early as possible. Additional reviews are underway in the EU, China and Japan.

Based on the results of TROPION-Breast02, datopotamab deruxtecan (*Datroway*) has been included in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a Category 1 Preferred 1st-line treatment option for patients with metastatic TNBC who are not candidates for immunotherapy. See NCCN Guidelines® for detailed recommendations.[2]

Datroway is a specifically engineered TROP2-directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo and being jointly developed and commercialised by AstraZeneca and Daiichi Sankyo.

Notes

Triple-negative breast cancer
TNBC accounts for approximately 15% of all breast cancer cases, with an estimated 345,000 diagnoses globally each year.[3,4] In the US, an estimated 32,000 to 48,000 cases of TNBC were diagnosed in 2025, and approximately 11,000 patients with TNBC receive treatment in the 1st-line setting each year.[5-7] TNBC is diagnosed more frequently in younger and premenopausal women, and is more prevalent in Black and Hispanic women.[8-10] Metastatic TNBC is the most aggressive type of breast cancer and has one of the worst prognoses, with median OS of just 12 to 18 months and only about 15% of patients living five years following diagnosis.[8,11,12]

While some breast cancers may test positive for oestrogen receptors, progesterone receptors or overexpression of HER2, TNBC tests negative for all three.[8] Due to its aggressive nature and absence of common breast cancer receptors, TNBC is characteristically difficult to treat.[8] For patients with metastatic disease with PD-L1 expressing tumours, the addition of immunotherapy to chemotherapy has improved outcomes in the 1st-line setting.[13,14] However, for approximately 70% of patients with metastatic TNBC who are not candidates for immunotherapy, prior to the approval of *Datroway*, chemotherapy was the only approved 1st-line treatment.[15]

TROP2 is a protein broadly expressed in several solid tumours, including TNBC.[16] TROP2 is associated with increased tumour progression and poor survival in patients with breast cancer.[17,18]

TROPION-Breast02

TROPION-Breast02 is a global, multicentre, randomised, open-label Phase III trial evaluating the efficacy and safety of *Datroway* versus investigator's choice of chemotherapy (paclitaxel, nab-paclitaxel, capecitabine, carboplatin or eribulin) in patients with previously untreated locally recurrent inoperable or metastatic TNBC for whom immunotherapy was not an option. This included patients whose tumours did not express PD-L1 as well as patients with PD-L1 expressing tumours who could not receive immunotherapy due to prior exposure in early-stage disease, comorbidities or immunotherapy not being accessible in their geography. Enrolment included patients with de novo or recurrent disease, regardless of disease-free interval, and those with poor prognostic factors such as stable brain metastases.

The dual primary endpoints of TROPION-Breast02 are progression-free survival (PFS) as assessed by blinded independent central review and OS. Secondary endpoints include PFS as assessed by investigator, ORR, duration of response, disease control rate, pharmacokinetics and safety.

TROPION-Breast02 enrolled 644 patients at sites in Africa, Asia, Europe, North America and South America. For more information, visit ClinicalTrials.gov.

Datroway
Datroway (datopotamab deruxtecan; datopotamab deruxtecan-dlnk in the US only) is a TROP2-directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, *Datroway* is one of seven DXd ADCs in the oncology pipeline of Daiichi Sankyo, and one of the most advanced programmes in AstraZeneca's ADC scientific platform. *Datroway* is comprised of a humanised anti-TROP2 IgG1 monoclonal antibody, developed in collaboration with Sapporo Medical University,

attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

Datroway is also approved in more than 40 countries/regions worldwide for the treatment of adult patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease based on results from the TROPION-Breast01 trial.

Datroway is available in the US under accelerated approval for the treatment of adult patients with locally advanced or metastatic *EGFR*-mutated non-small cell lung cancer (NSCLC) who have received prior *EGFR*-directed therapy and platinum-based chemotherapy based on results from the TROPION-Lung05 and TROPION-Lung01 trials. Continued approval for this indication in the US may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Datroway clinical development programme
A comprehensive global clinical development programme is underway with more than 20 trials evaluating the efficacy and safety of *Datroway* across multiple cancers, including NSCLC, TNBC and urothelial cancer. The programme includes eight Phase III trials in lung cancer, five Phase III trials in breast cancer, and one Phase III trial and one Phase II/III trial in urothelial cancer evaluating *Datroway* as a monotherapy and in combination with other cancer treatments in various settings.

Daiichi Sankyo collaboration
AstraZeneca and Daiichi Sankyo entered into a global collaboration to jointly develop and commercialise *Enhertu* (trastuzumab deruxtecan) in March 2019 and *Datroway* in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights for each ADC. Daiichi Sankyo is responsible for the manufacturing and supply of *Enhertu* and *Datroway*.

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*, 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* (fulvestrant) and *Zoladex* (goserelin) and aims to reshape the HR-positive space with first-in-class AKT inhibitor, *Truqap* (capivasertib), the TROP2-directed ADC, *Datroway*, 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 Diseases, 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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2. Referenced with permission from the NCCN Guidelines. © National Comprehensive Cancer Network® 2026. All rights reserved. Accessed May 2026. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
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Disclosure: Dr. Traina provides consulting and advisory services to AstraZeneca (and Daiichi Sankyo).

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