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Datroway (datopotamab deruxtecan) approved in the US for patients with previously treated metastatic HR-positive, HER2-negative breast cancer

First approval in the US for AstraZeneca and Daiichi Sankyo's Datroway based on TROPION-Breast01 results showing 37% reduction in the risk of disease progression or death vs. chemotherapy

Datroway is the eighth new medicine of the 20 AstraZeneca has set out to deliver by 2030

Datroway (datopotamab deruxtecan or Dato-DXd) has been approved in the US for the treatment of adult patients with unresectable or metastatic hormone receptor (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. The approval by the US Food and Drug Administration (FDA) was based on results from the TROPION-Breast01 Phase III trial.

Aditya Bardia, MD, MPH, Program Director of Breast Oncology and Director of Translational Research Integration at the UCLA Health Jonsson Comprehensive Cancer Center and Global Principal Investigator for TROPION-Breast01, said: "Despite considerable progress in the HR-positive, HER2-negative metastatic breast cancer treatment landscape, new therapies are still needed to tackle the frequent and complex challenge of disease progression after endocrine and initial chemotherapy. The approval of datopotamab deruxtecan, a novel TROP2-directed antibody drug conjugate, marks a major therapeutic milestone and provides patients with metastatic breast cancer a new treatment alternative to conventional chemotherapy."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "With this first approval of *Datroway* in the US, we continue to deliver on our ambition for antibody drug conjugates to improve upon and replace conventional chemotherapy for the treatment of multiple cancers. We are proud to bring *Datroway* to people living with metastatic HR-positive, HER2-negative breast cancer, and this approval marks the eighth new medicine of the 20 we have set out to deliver across AstraZeneca by 2030."

Ken Keller, Global Head of Oncology Business, and President and CEO, Daiichi Sankyo, Inc., said: "The approval of *Datroway* provides patients with HR-positive, HER2-negative breast cancer previously treated with endocrine-based therapy and traditional chemotherapy with the opportunity to be treated with a new TROP2-directed antibody drug conjugate earlier in the metastatic setting. *Datroway* is the latest addition to our portfolio of innovative cancer treatments and marks the fourth medicine from our oncology pipeline to receive approval in the US."

Caitlin Lewis, Senior Vice President of Strategy & Mission, Living Beyond Breast Cancer, said: "Only one in three patients with metastatic HR-positive, HER2-negative breast cancer live more than five years following diagnosis, highlighting the urgent need for additional effective therapies. The approval of *Datroway* is a significant advance, offering patients with metastatic HR-positive breast cancer a new and much-needed treatment option."

In TROPION-Breast01, *Datroway* significantly reduced the risk of disease progression or death by 37% compared to investigator's choice of chemotherapy (hazard ratio [HR] 0.63; 95% confidence interval [CI] 0.52-0.76; p<0.0001) in patients with HR-positive, HER2-negative metastatic breast cancer as assessed by blinded independent central review (BICR). Median progression-free survival (PFS) was 6.9 months in patients treated with *Datroway* versus 4.9 months with chemotherapy.

The safety profile of *Datroway* was consistent with the known profile of this medicine with no new safety concerns identified. In the *Datroway* arm, the interstitial lung disease (ILD) rate was 4.2% and the majority of events were low grade.

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

Additional regulatory submissions for *Datroway* in breast cancer are under review in the EU, China and other regions.

Notes

HR-positive breast cancer

In the US, more than 300,000 cases of breast cancer are diagnosed annually.[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]

Approximately 70% of diagnosed cases are considered what has been historically called HR-positive, HER2-negative breast cancer (measured as HER2 score of IHC 0, IHC 1+ or IHC 2+/ISH-).[2] Endocrine therapies are widely given consecutively in the early lines of treatment for HR-positive metastatic breast cancer.[3] However, after initial treatment, further efficacy from endocrine therapy is often limited.[3] The current standard of care following endocrine therapy is chemotherapy, which is associated with poor response rates and outcomes.[3-6]

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TROPION-Breast01

TROPION-Breast01 is a global, randomised, multicentre, open-label Phase III trial evaluating the efficacy and safety of intravenous *Datroway* (6 mg/kg) once per 21-day cycle versus investigator's choice of single-agent chemotherapy (eribulin, capecitabine, vinorelbine or gemcitabine) in adult patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have progressed on and are not suitable for endocrine therapy per investigator assessment and have received at least one prior line of chemotherapy for unresectable or metastatic disease.

Following disease progression or discontinuation of *Datroway* or chemotherapy, patients had the option to receive a subsequent treatment at the discretion of their physician. Crossover between trial arms was not permitted.

The dual primary endpoints of TROPION-Breast01 are PFS as assessed by BICR and OS. Key secondary endpoints include ORR, duration of response, investigator-assessed PFS, disease control rate, time to first subsequent therapy and safety. The PFS data and additional results for key secondary endpoints of TROPION-Breast01 were published in the *Journal of Clinical Oncology*.

TROPION-Breast01 enrolled 732 patients in Africa, Asia, Europe, North America and South America. For more information visit ClinicalTrials.gov.

Datroway

Datroway (datopotamab deruxtecan-dlnk in the US; datopotamab deruxtecan in rest of world) is a TROP2-directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, *Datroway* is one of six 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 (6mg/kg) is approved in the US and Japan 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 the results from the TROPION-Breast01 Phase III 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 non-small cell lung cancer, triple-negative breast cancer (TNBC) and HR-positive, HER2-negative breast cancer. The programme includes seven Phase III trials in lung cancer and five Phase III trials in breast cancer evaluating *Datroway* as a monotherapy and in combination with other anticancer 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 starting to challenge, and redefine, 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*, a HER2-directed ADC, AstraZeneca and Daiichi Sankyo are aiming to improve outcomes in previously treated HER2-positive and HER2-low 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* and *Zoladex* (goserelin) and aims to reshape the HR-positive space with first-in-class AKT inhibitor, *Truqap* (capivasertib), and next-generation SERD and potential new medicine camizestrant. AstraZeneca is also collaborating with Daiichi Sankyo to explore the potential of TROP2-directed ADC, *Datroway*, in this setting.

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 and to explore its potential in earlier disease.

To bring much-needed treatment options to patients with TNBC, an aggressive form of breast cancer, AstraZeneca is evaluating the potential of *Datroway* alone and in combination with immunotherapy *Imfinzi* (durvalumab), *Truqap* in combination with chemotherapy, and *Imfinzi* in combination with other oncology medicines, including *Lynparza* and *Enhertu*.

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/Nasdaq: 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

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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