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AstraZeneca PLC
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Datroway approved in the US for patients with previously treated advanced _EGFR_-mutated non-small cell lung cancer

Based on TROPION-Lung05 results and supported by data from TROPION-Lung01

First and only TROP2-directed therapy approved in the US for the treatment of lung cancer

Datroway (datopotamab deruxtecan or Dato-DXd) has been approved in the US 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.

This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DoR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

The approval follows Priority Review and Breakthrough Therapy Designation by the Food and Drug Administration (FDA) based on results from a subgroup analysis of the TROPION-Lung05 Phase II trial and supported by data from the TROPION-Lung01 Phase III trial.

Jacob Sands, MD, Medical Oncology, Dana-Farber Cancer Institute and investigator in both trials, said: "Addressing disease progression in patients with advanced *EGFR*-mutated lung cancer after prior targeted therapy and chemotherapy is very challenging with limited later-line treatment options available. The US approval of datopotamab deruxtecan introduces a novel and needed treatment option to patients with advanced disease."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "This first approval of *Datroway* in lung cancer provides a much-needed option to patients with advanced *EGFR*-mutated lung cancer whose disease has become resistant to past treatments, regardless of the driving mutation. We have long supported patients with *EGFR*-mutated lung cancer and are proud to bring another innovative treatment option to this community."

Ken Keller, Global Head of Oncology Business, and President and CEO, Daiichi Sankyo, Inc, said: "With today's accelerated approval, *Datroway* is now the first TROP2-directed medicine available for certain patients in the US living with lung cancer. We remain committed to our extensive clinical development programme to further identify where *Datroway* may be used in other types of lung and breast cancer."

Andrea E. Ferris, President and CEO, LUNGevity, said: "For people with advanced *EGFR*-mutated non-small cell lung cancer whose disease progresses on initial treatments, additional options are limited. Today's approval of *Datroway* offers a new treatment option for patients whose disease has progressed following treatment with an *EGFR*-directed therapy and chemotherapy."

In TROPION-Lung05 and TROPION-Lung01, *Datroway* demonstrated a confirmed ORR of 45% (95% confidence interval [CI]: 35-54) in patients with previously treated locally advanced or metastatic *EGFR*-mutated NSCLC (n=114) as assessed by blinded independent central review (BICR). Complete responses were seen in 4.4% of patients and partial responses were seen in 40% of patients. The median DoR was 6.5 months (95% CI: 4.2-8.4).

The safety profile of *Datroway* was evaluated in a pooled analysis of 125 patients in the TROPION-Lung05, TROPION-Lung01 and TROPION-PanTumor01 trials. The safety profile observed across these trials was consistent with the known profile of this medicine with no new safety concerns identified.

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.

AstraZeneca and Daiichi Sankyo are evaluating *Datroway* alone and with *Tagrisso* (osimertinib) in other advanced or metastatic *EGFR*-mutated NSCLC settings in the TROPION-Lung14 and TROPION-Lung15 Phase III trials.

Financial considerations
Following approval in the US, an amount of 45 million is due from AstraZeneca to Daiichi Sankyo as a milestone payment for the locally advanced or metastatic *EGFR*-mutated NSCLC indication. Sales of *Datroway* in the US are recognized by Daiichi Sankyo. For further details on the financial arrangements, please consult the collaboration agreement from July 2020.

Notes

Advanced non-small cell lung cancer

Nearly 2.5 million lung cancer cases were diagnosed globally in 2022.[1] Lung cancer is broadly split into small or non-small cell lung cancer, the latter accounting for about 87% of cases.[2] Approximately 10 to 15% of patients with NSCLC in the US and Europe, and 30 to 40% of patients in Asia have an *EGFR* mutation.[3,4] The majority of *EGFR* mutations occur in tumours of nonsquamous histology.[5] TROP2 is a protein broadly expressed in the majority of NSCLC tumours.[6]

For patients with tumours that have an *EGFR* mutation, the established 1st-line treatment in the metastatic setting includes *EGFR*-directed therapy with or without platinum-based chemotherapy.[7] While these therapies have improved outcomes in earlier lines of treatment, most patients eventually experience disease progression and receive subsequent therapies.[8-11]

TROPION-Lung05

TROPION-Lung05 is a global, multicentre, single-arm, open-label Phase II trial evaluating the efficacy and safety of *Datroway* in patients with locally advanced or metastatic NSCLC with actionable genomic alterations who have progressed on at least one *EGFR*-directed therapy and platinum-based chemotherapy. Patients receiving up to four prior lines of treatment with tumours with one or more genomic alterations including *EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *RET* or *MET* were eligible for the trial.

The primary endpoint of TROPION-Lung05 is ORR as assessed by BICR. Secondary efficacy endpoints include DoR, disease control rate (DCR), clinical benefit rate, PFS, time to response (TTR), OS and safety. TROPION-Lung05 enrolled 137 patients globally in Asia, Europe and North America. For more information, visit ClinicalTrials.gov.

Primary results from TROPION-Lung05 were published in the *Journal of Clinical Oncology* in January 2025.

TROPION-Lung01

TROPION-Lung01 is a global, randomised, multicentre, open-label Phase III trial evaluating the efficacy and safety of *Datroway* versus docetaxel in adult patients with locally advanced or metastatic NSCLC with and without actionable genomic alterations who require systemic therapy following prior treatment. Patients with actionable genomic alterations were previously treated with an approved targeted therapy and platinum-based chemotherapy. Patients without known actionable genomic alterations were previously treated, concurrently or sequentially, with platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor.

The dual primary endpoints of TROPION-Lung01 are PFS as assessed by BICR and OS. Key secondary endpoints include investigator-assessed PFS, ORR, DoR, TTR, and DCR as assessed by both BICR and investigator, and safety. TROPION-Lung01 enrolled 590 patients in Asia, Europe, North America, Oceania and South America. For more information visit ClinicalTrials.gov.

Primary results from TROPION-Lung01, as presented at the ESMO 2023 Congress, showed *Datroway* demonstrated a statistically significant improvement in PFS over docetaxel. OS results were presented at the IASLC 2024 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer and simultaneously published in the *Journal of Clinical Oncology* in September 2024.

TROPION-PanTumor01

TROPION-PanTumor01 is a first-in-human, open-label, two-part, multicentre Phase I trial evaluating the safety and preliminary efficacy of *Datroway* in patients with advanced solid tumours that have relapsed or are refractory to standard treatment or for which no standard treatment is available. The dose escalation portion of the trial enrolled patients with NSCLC to assess the safety and tolerability of *Datroway* to determine the recommended dose for expansion (6mg/kg). The dose expansion part of TROPION-PanTumor01 enrolled several different cohorts including patients with NSCLC, triple-negative breast cancer (TNBC), HR-positive, HER2-negative breast cancer, small cell lung cancer, urothelial, gastric, pancreatic, castration resistant prostate and oesophageal cancer.

Safety endpoints include dose-limiting toxicities and serious adverse events. Efficacy endpoints include ORR, DoR, TTR, PFS and OS. Pharmacokinetic, biomarker and immunogenicity endpoints also are being evaluated. TROPION-PanTumor01 enrolled 890 patients in Asia and North 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 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 is approved in more than 30 countries 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 the 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 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* is approved in Russia for the same population.

***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 HR-positive, HER2-negative breast cancer. The programme includes eight 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* 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 lung cancer

AstraZeneca is working to bring patients with lung cancer closer to cure through the detection and treatment of early-stage disease, while also pushing the boundaries of science to improve outcomes in the resistant and advanced settings. By defining new therapeutic targets and investigating innovative approaches, the Company aims to match medicines to the patients who can benefit most.

The Company's comprehensive portfolio includes leading lung cancer medicines and the next wave of innovations,

including *Tagrisso* and *Iressa* (gefitinib); *Imfinzi* and *Imjudo*; *Enhertu* (trastuzumab deruxtecan) and *Datroway* in collaboration Daiichi Sankyo; *Orpathys* (savolitinib) in collaboration with HUTCHMED; as well as a pipeline of potential new medicines and combinations across diverse mechanisms of action.

AstraZeneca is a founding member of the Lung Ambition Alliance, a global coalition working to accelerate innovation and deliver meaningful improvements for people with lung cancer, including and beyond treatment.

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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