

Press Release

Datopotamab Deruxtecan Granted Priority Review in the U.S. for Patients with Previously Treated Advanced EGFR-Mutated Non-Small Cell Lung Cancer

- Application based on TROPION-Lung05 phase 2 trial and supported by data from TROPION-Lung01 phase 3 and TROPION-PanTumor01 phase 1 trials

Tokyo and Basking Ridge, NJ – (January 13, 2025) – Daiichi Sankyo (TSE: 4568) and AstraZeneca’s (LSE/STO/Nasdaq: AZN) Biologics License Application (BLA) for datopotamab deruxtecan (Dato-DXd) has been accepted and granted Priority Review in the U.S. for the treatment of adult patients with locally advanced or metastatic epidermal growth factor receptor-mutated (EGFR-mutated) non-small cell lung cancer (NSCLC) who have received prior systemic therapies, including an EGFR-directed therapy.

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

The U.S. Food and Drug Administration (FDA) grants Priority Review to applications for medicines that, if approved, would offer significant improvements over available options by demonstrating safety or efficacy improvements, preventing serious conditions or enhancing patient compliance. The Prescription Drug User Fee Act (PDUFA) date, the FDA action date for its regulatory decision, is July 12, 2025. Datopotamab deruxtecan was previously [granted](#) Breakthrough Therapy Designation (BTD) by the FDA for this patient population.

The BLA and BTD are based on data from the [TROPION-Lung05](#) phase 2 trial and supported by data from the [TROPION-Lung01](#) phase 3 trial. In addition, the BLA is supported by the [TROPION-PanTumor01](#) phase 1 trial. In a pooled analysis of patients with previously treated advanced or metastatic EGFR-mutated NSCLC in the TROPION-Lung05 and TROPION-Lung01 trials [presented](#) at the European Society for Medical Oncology (ESMO) Asia 2024 Congress, datopotamab deruxtecan demonstrated clinically meaningful tumor response. The safety profile of datopotamab deruxtecan was consistent with previous reports from the TROPION-Lung05 and TROPION-Lung01 trials, with no new safety concerns identified.

“Treating advanced EGFR-mutated non-small cell lung cancer presents a significant challenge due to the limited efficacy of available treatments once the disease has progressed following front-line therapies,

including the use of an EGFR tyrosine kinase inhibitor,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “If approved, datopotamab deruxtecan could become the first TROP2 directed antibody drug conjugate for lung cancer, providing a promising option for patients.”

“Acquired resistance to front-line therapies and, ultimately, disease progression are unfortunate realities for most patients with advanced EGFR-mutated non-small cell lung cancer,” said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology R&D, AstraZeneca. “This Priority Review, and the previously granted Breakthrough Therapy Designation, recognize the potential for datopotamab deruxtecan to provide a much-needed option to patients whose disease has become resistant to current treatments.”

Daiichi Sankyo and AstraZeneca are evaluating datopotamab deruxtecan alone and in novel combinations as treatment for patients with NSCLC in seven phase 3 trials including the [TROPION-Lung14](#) and [TROPION-Lung15](#) trials of datopotamab deruxtecan alone and with osimertinib, AstraZeneca’s EGFR tyrosine kinase inhibitor (TKI), as treatment for patients with advanced or metastatic EGFR-mutated nonsquamous NSCLC.

About TROPION-Lung05

[TROPION-Lung05](#) is a global, multicenter, single-arm, open-label phase 2 trial evaluating the efficacy and safety of datopotamab deruxtecan in patients with locally advanced or metastatic NSCLC with actionable genomic alterations who have progressed on at least one TKI (with or without other systemic therapies) and on or after one regimen of platinum-based chemotherapy. Patients receiving up to four prior lines of treatment with tumors with one or more genomic alterations including EGFR, ALK, ROS1, NTRK, BRAF, RET or MET were eligible for the trial.

The primary trial endpoint of TROPION-Lung05 is objective response rate (ORR) as assessed by blinded independent central review (BICR). Secondary efficacy endpoints include duration of response (DoR), disease control rate (DCR), clinical benefit rate, progression-free survival (PFS), time to response (TTR), overall survival (OS) and safety.

TROPION-Lung05 enrolled 137 patients globally in Asia, Europe and North America. For more information visit [ClinicalTrials.gov](https://clinicaltrials.gov).

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

About TROPION-Lung01

TROPION-Lung01 is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan 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 approximately 600 patients in Asia, Europe, North America, Oceania and South America. For more information visit [ClinicalTrials.gov](https://clinicaltrials.gov).

Primary PFS results and interim OS results from TROPION-Lung01 were [presented](#) at the 2023 ESMO (#ESMO23) Congress. Final OS results were [presented](#) at IASLC 2024 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer (#WCLC24) and simultaneously published in the *Journal of Clinical Oncology* in September 2024.

About TROPION-PanTumor01

TROPION-PanTumor01 is a first-in-human, open-label, two-part, multicenter phase 1 trial evaluating the safety and preliminary efficacy of datopotamab deruxtecan in patients with advanced solid tumors 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 datopotamab deruxtecan to determine the recommended dose for expansion (6 mg/kg). The dose expansion part of TROPION-PanTumor01 enrolled several different cohorts including patients with NSCLC, triple negative breast cancer (TNBC), HR positive, HER2 low or negative breast cancer, small cell lung cancer, urothelial, gastric, pancreatic, castration resistant prostate and esophageal 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 approximately 900 patients in Asia and North America. For more information visit [ClinicalTrials.gov](https://clinicaltrials.gov).

About 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 80% of cases.² Approximately 10% to 15% of patients with NSCLC in the U.S. and Europe, and 30% to 40% of patients in Asia have an EGFR mutation.^{3,4} The majority of EGFR mutations occur in tumors of nonsquamous histology.⁵

For patients with tumors that have an EGFR mutation, the established first-line treatment in the metastatic setting is an EGFR TKI.⁶ While EGFR TKIs have improved outcomes in the first-line setting, most patients eventually experience disease progression and receive subsequent therapies, such as chemotherapy.^{7,8,9,10}

TROP2 is a protein broadly expressed in the majority of NSCLC tumors.¹¹ There is currently no TROP2 directed ADC approved for the treatment of lung cancer.^{6,12}

About Datopotamab Deruxtecan (Dato-DXd)

Datopotamab deruxtecan (Dato-DXd) is an investigational TROP2 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, datopotamab deruxtecan is one of six DXd ADCs in the oncology pipeline of Daiichi Sankyo, and one of the most advanced programs in AstraZeneca's ADC scientific platform. Datopotamab deruxtecan is comprised of a humanized 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.

Datopotamab deruxtecan is approved in Japan under the brand name DATROWAY[®] for the treatment of adult patients with HR positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) unresectable or recurrent breast cancer after prior chemotherapy based on the results of the [TROPION-Breast01](#) trial. Datopotamab deruxtecan is an investigational medicine in all countries outside of Japan.

About the Datopotamab Deruxtecan Clinical Development Program

A comprehensive global clinical development program is underway with more than 20 trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple cancers, including NSCLC, TNBC and HR positive, HER2 low or negative breast cancer. The program includes seven phase 3 trials in lung cancer and five phase 3 trials in breast cancer evaluating datopotamab deruxtecan as a monotherapy and in combination with other anticancer treatments in various settings.

About the Daiichi Sankyo and AstraZeneca Collaboration

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize ENHERTU[®] in [March 2019](#) and datopotamab deruxtecan 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 datopotamab deruxtecan.

About the ADC Portfolio of Daiichi Sankyo

The Daiichi Sankyo ADC portfolio consists of seven ADCs in clinical development crafted from two distinct ADC technology platforms discovered in-house by Daiichi Sankyo.

The ADC platform furthest in clinical development is Daiichi Sankyo's DXd ADC Technology where each ADC consists of a monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers. The DXd ADC portfolio currently consists of ENHERTU, a HER2 directed ADC, and datopotamab deruxtecan (Dato-DXd), a TROP2 directed ADC, which are being jointly developed and commercialized globally with AstraZeneca.

Patritumab deruxtecan (HER3-DXd), a HER3 directed ADC, ifinatamab deruxtecan (I-DXd), a B7-H3 directed ADC, and raludotatug deruxtecan (R-DXd), a CDH6 directed ADC, are being jointly developed and commercialized globally with Merck & Co., Inc, Rahway, NJ, USA. DS-3939, a TA-MUC1 directed ADC, is being developed by Daiichi Sankyo.

The second Daiichi Sankyo ADC platform consists of a monoclonal antibody attached to a modified pyrrolobenzodiazepine (PBD) payload. DS-9606, a CLDN6 directed PBD ADC, is the first of several planned ADCs in clinical development utilizing this platform.

Ifinatamab deruxtecan, patritumab deruxtecan, raludotatug deruxtecan, DS-3939 and DS-9606 are investigational medicines that have not been approved for any indication in any country. Safety and efficacy have not been established.

About Daiichi Sankyo

Daiichi Sankyo is an innovative global healthcare company contributing to the sustainable development of society that discovers, develops and delivers new standards of care to enrich the quality of life around the world. With more than 120 years of experience, Daiichi Sankyo leverages its world-class science and technology to create new modalities and innovative medicines for people with cancer, cardiovascular and other diseases with high unmet medical need. For more information, please visit www.daiichisankyo.com.

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