

## Press Release

# Datopotamab Deruxtecan Met Dual Primary Endpoint of Progression-Free Survival in Patients with Advanced Non Small Cell Lung Cancer in TROPION-Lung01 Phase 3 Trial

- First phase 3 results for Daiichi Sankyo and AstraZeneca's TROP2 directed ADC demonstrated statistically significant improvement in progression-free survival versus standard chemotherapy in previously treated locally advanced or metastatic disease
- Trial will continue to assess the dual primary endpoint of overall survival

**Tokyo and Basking Ridge, NJ – (July 3, 2023)** – Topline results from the [TROPION-Lung01](#) phase 3 trial showed datopotamab deruxtecan (Dato-DXd) demonstrated a statistically significant improvement for the dual primary endpoint of progression-free survival (PFS) compared to docetaxel, the current standard of care chemotherapy, in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) treated with at least one prior therapy.

Datopotamab deruxtecan is a specifically engineered TROP2 directed DXd antibody drug conjugate (ADC) being jointly developed by Daiichi Sankyo (TSE: 4568) and AstraZeneca (LSE/STO/Nasdaq: AZN).

For the dual primary endpoint of overall survival (OS), the data were not mature and an early trend was observed in favor of datopotamab deruxtecan versus docetaxel that did not meet the pre-specified threshold for statistical significance at this interim analysis. The trial will continue as planned to assess OS with greater maturity. The investigators and participants will remain blinded to the results.

The safety profile of datopotamab deruxtecan was consistent with previous clinical trials with no new safety signals identified. All grade interstitial lung disease (ILD) was generally consistent with prior clinical trials, with the majority being low grade. Some grade 5 events were observed.

More than one million people worldwide are diagnosed with advanced NSCLC each year.<sup>1,2</sup> While immunotherapy and targeted therapies have improved outcomes in the first-line metastatic setting, most patients eventually experience disease progression and receive chemotherapy.<sup>3,4,5</sup> For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC in the absence of other treatment options and despite limited effectiveness and known side effects.<sup>3,4,5</sup> TROP2 is a protein highly expressed in a large majority of lung cancers.<sup>6</sup> There are currently no TROP2 directed ADCs approved for the treatment of patients with lung cancer.<sup>7,8</sup>

“We are encouraged by the statistically significant results of the dual primary endpoint of progression-free survival seen with datopotamab deruxtecan and look forward to the final overall survival analysis,” said Ken Takeshita, MD, Global Head, Oncology R&D, Daiichi Sankyo. “We plan to share these data with regulatory authorities to discuss next steps.”

“With TROPION-Lung01, we met the dual primary endpoint of progression-free survival, challenging the entrenched standard of care in a previously treated and unselected patient population that has long deserved an alternative to chemotherapy,” said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology R&D, AstraZeneca. “These first phase 3 trial results from the datopotamab deruxtecan clinical program provide compelling evidence for the potential role this TROP2 directed antibody drug conjugate can play in treating patients with lung cancer.”

TROPION-Lung01 enrolled patients with and without actionable genomic alterations, such as EGFR and ALK. Patients with actionable genomic alterations were previously treated with platinum-based chemotherapy and an approved targeted therapy. Patients without actionable genomic alterations were previously treated, concurrently or sequentially, with platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor.

Detailed results from the TROPION-Lung01 trial will be presented at an upcoming medical meeting and will be shared with regulatory authorities.

### **About TROPION-Lung01**

[TROPION-Lung01](#) is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan (6.0 mg/kg Q3W) versus docetaxel (75 mg/m<sup>2</sup> Q3W) in patients with locally advanced or metastatic NSCLC with and without actionable genomic alterations previously treated with at least one prior therapy. Patients with actionable genomic alterations were treated with platinum-based chemotherapy and an approved targeted therapy. 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 blinded independent central review (BICR) and OS. Key secondary endpoints include investigator-assessed PFS, objective response rate, duration of response, time to response, disease control rate as assessed by both BICR and investigator, and safety.

TROPION-Lung01 enrolled approximately 600 patients at sites in Asia, Europe, North America and South America. For more information visit [ClinicalTrials.gov](https://clinicaltrials.gov).

## **About Non-Small Cell Lung Cancer**

More than one million people worldwide are diagnosed with advanced NSCLC each year.<sup>1,2</sup> While immunotherapy and targeted therapies have improved outcomes in the first-line metastatic setting, most patients eventually experience disease progression and receive chemotherapy.<sup>3,4,5</sup> For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC in the absence of other treatment options and despite limited effectiveness and known side effects.<sup>3,4,5</sup> TROP2 is a protein highly expressed in a large majority of lung cancers.<sup>6</sup> There are currently no TROP2 directed ADCs approved for the treatment of patients with lung cancer.<sup>7,8</sup>

## **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 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 five lead 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, via tetrapeptide-based cleavable linkers.

A comprehensive development program called TROPION is underway globally with more than 12 trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple tumors, including NSCLC, triple negative breast cancer and hormone receptor positive, HER2 low or negative breast cancer. Beyond the TROPION program, datopotamab deruxtecan also is being evaluated in novel combinations in several ongoing trials.

In NSCLC, the TROPION-Lung07, TROPION-Lung08 and AVANZAR phase 3 trials are evaluating datopotamab deruxtecan and immune checkpoint inhibitor combinations as potential first-line treatment options for patients with advanced or metastatic disease, a strategy informed by the results of two early trials. AstraZeneca also is researching a potential diagnostic test to help identify patients most likely to benefit from treatment with datopotamab deruxtecan.

## About the DXd ADC Portfolio of Daiichi Sankyo

The DXd ADC portfolio of Daiichi Sankyo currently consists of five ADCs in clinical development across multiple types of cancer. The company's clinical trial stage DXd ADCs include ENHERTU, a HER2 directed ADC and datopotamab deruxtecan (Dato-DXd), a TROP2 directed ADC, which are being jointly developed and commercialized globally with AstraZeneca; and patritumab deruxtecan (HER3-DXd), a HER3 directed ADC. Two additional ADCs including ifinatamab deruxtecan (I-DXd; DS-7300), a B7-H3 directed ADC, and raludotatug deruxtecan (R-DXd; DS-6000), a CDH6 directed ADC, are being developed through a strategic early-stage research collaboration with Sarah Cannon Research Institute.

Designed using Daiichi Sankyo's proprietary DXd ADC technology to target and deliver a cytotoxic payload inside cancer cells that express a specific cell surface antigen, 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.

Datopotamab deruxtecan, ifinatamab deruxtecan, patritumab deruxtecan and raludotatug deruxtecan 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](http://www.daiichisankyo.com).

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## References

<sup>1</sup> Siegel R, et al. *CA Cancer J Clin*. 2021;71:7-33.

<sup>2</sup> World Health Organization. International Agency for Research on Cancer. *Lung Fact Sheet*. Accessed June 2023.

<sup>3</sup> Chen R, et al. *J Hematol Oncol*. 2020;13(1):58.

<sup>4</sup> Majeed U, et al. *J Hematol Oncol*. 2021;14(1):108.

<sup>5</sup> Pircher, A, et al. *Anticancer Research*. 2013;33(9):3831-3836.

<sup>6</sup> Mito R, et al. *Pathol Int*. 2020;70(5):287-294.

<sup>7</sup> Rodríguez-Abreau D et al. *Ann Onc*. 2021 Jul;32(7): 881-895.

<sup>8</sup> American Cancer Society. [Targeted Drug Therapy for Non-Small Cell Lung Cancer](#). Accessed June 2023.