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Daiichi-Sankyo

Press Release

Datopotamab Deruxtecan Biologics License Application Accepted in the U.S. for Patients with Previously Treated Advanced Nonsquamous Non-Small Cell Lung Cancer

- Application based on results from the TROPION-Lung01 phase 3 trial
- If approved, Daiichi Sankyo and AstraZeneca's datopotamab deruxtecan may be the first TROP2 directed antibody drug conjugate for patients with lung cancer

Tokyo and Basking Ridge, NJ – (February 19, 2024) – Daiichi Sankyo (TSE: 4568) and AstraZeneca's (LSE/STO/Nasdaq: AZN) Biologics License Application (BLA) for datopotamab deruxtecan (Dato-DXd) has been accepted in the U.S. for the treatment of adult patients with locally advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) who have received prior systemic therapy.

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

The Prescription Drug User Fee Act (PDUFA) date, the U.S. Food and Drug Administration (FDA) action date for its regulatory decision, is December 20, 2024.

The BLA is based on results from the pivotal TROPION-Lung01 phase 3 trial presented at a Presidential Symposium at the European Society for Medical Oncology (#ESMO23) 2023 Congress. In the trial, datopotamab deruxtecan demonstrated a statistically significant improvement for the dual primary endpoint of progression-free survival (PFS) compared to docetaxel, the current standard of care, in patients with locally advanced or metastatic NSCLC treated with at least one prior line of therapy. For the dual primary endpoint of overall survival (OS), interim results numerically favored datopotamab deruxtecan over docetaxel in the overall population, however, results did not reach statistical significance at the time of data cut-off. In patients with nonsquamous NSCLC, datopotamab deruxtecan showed a clinically meaningful PFS benefit and a numerically favorable OS trend. The trial is ongoing and OS will be assessed at final analysis. The safety profile of datopotamab deruxtecan was consistent with that observed in other ongoing trials with no new safety concerns identified.

"Today's news is an important step forward in our goal of creating new standards of care that have the potential to transform the treatment of patients with non-small cell lung cancer," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "We are encouraged by the FDA's acceptance of the BLA as we

endeavor to make datopotamab deruxtecan the first TROP2 directed antibody drug conjugate approved to treat patients with nonsquamous non-small cell lung cancer after disease progression on prior systemic therapy. We look forward to working closely with the FDA to bring datopotamab deruxtecan to patients."

"Datopotamab deruxtecan has the potential to offer patients with previously treated advanced nonsquamous non-small cell lung cancer an effective and tolerable alternative to conventional chemotherapy," said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology R&D, AstraZeneca. "With regulatory discussions ongoing around the world and a parallel submission underway in the U.S. in breast cancer, this is only the beginning of our efforts to make this novel treatment available to patients as quickly as possible."

A parallel BLA for datopotamab deruxtecan based on results from the pivotal TROPION-Breast01 phase 3 trial is pending acceptance in the U.S. for the treatment of adult patients with metastatic hormone receptor (HR) positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer. Additional regulatory submissions for datopotamab deruxtecan in lung and breast cancer are underway globally.

About TROPION-Lung01

TROPION-Lung01 is an ongoing global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan versus docetaxel in patients with locally advanced or metastatic NSCLC with and without actionable genomic alterations previously treated with at least one prior line of therapy. Patients with actionable genomic alterations were previously 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 in Asia, Europe, North America and South America. For more information visit ClinicalTrials.gov.

About Advanced Non-Small Cell Lung Cancer

Nearly 250,000 lung cancer cases were diagnosed in the U.S. in 2023.[1] NSCLC is the most common type of lung cancer, accounting for about 80% of cases.[1] Approximately 70% and 30% of NSCLC tumors are of nonsquamous or squamous histology, respectively.[2] While immunotherapy and targeted therapies have improved outcomes in the first-line setting, most patients eventually experience disease progression and receive chemotherapy.[3,4,5] For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC, despite limited effectiveness and known side effects.[3,4,5]

TROP2 is a protein broadly expressed in the majority of NSCLC tumors.[6] There is currently no TROP2 directed ADC approved for the treatment of lung cancer.[7,8]

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.

A comprehensive development program called TROPION is underway globally with more than 14 trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple cancers, including NSCLC, triple negative breast cancer and HR positive, HER2 negative breast cancer. Beyond the TROPION program, datopotamab deruxtecan also is being evaluated in novel combinations in several ongoing trials.

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 (Dato-DXd) 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 DXd ADC Portfolio of Daiichi Sankyo

The DXd ADC portfolio of Daiichi Sankyo currently consists of six ADCs in clinical development across multiple types of cancer. ENHERTU, a HER2 directed ADC, and datopotamab deruxtecan, a TROP2 directed ADC, 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, N.J. USA. DS-3939, a TA-MUC1 directed ADC, is being developed by Daiichi Sankyo.

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, raludotatug deruxtecan and DS-3939 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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