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Daiichi-Sankyo

Press Release

Datopotamab Deruxtecan Granted Breakthrough Therapy Designation in U.S. for Patients with Previously Treated Advanced EGFR-Mutated Non-Small Cell Lung Cancer

- First Breakthrough Therapy Designation for Daiichi Sankyo and AstraZeneca's datopotamab deruxtecan based on TROPION-Lung05 phase 2 trial and supported by data from TROPION-Lung01 phase 3 trial
- Twelfth Breakthrough Therapy Designation granted by FDA across Daiichi Sankyo's oncology pipeline

Tokyo and Basking Ridge, NJ – (December 9, 2024) – Datopotamab deruxtecan (Dato-DXd) has been granted Breakthrough Therapy Designation (BTD) 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) with disease progression on or after treatment with an EGFR tyrosine kinase inhibitor (TKI) and platinum-based chemotherapy.

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

The U.S. Food and Drug Administration (FDA) BTD is designed to accelerate the development and regulatory review of potential new medicines that are intended to treat serious conditions and address significant unmet medical needs. The medicine needs to have shown encouraging preliminary clinical results that demonstrate substantial improvement on a clinically significant endpoint over available medicines.

The FDA granted this BTD based on data from the TROPION-Lung05 phase 2 trial with supporting data from the TROPION-Lung01 phase 3 trial. Results from a pooled analysis of patients with previously treated EGFR-mutated NSCLC in these studies were presented this month at the European Society of Medical Oncology (ESMO) Asia 2024 Congress. This is the first BTD for datopotamab deruxtecan and the twelfth BTD across Daiichi Sankyo's oncology pipeline.

"The Breakthrough Therapy Designation granted by the FDA underscores the significant unmet need for new treatments for patients with previously treated EGFR-mutated non-small cell lung cancer who have experienced disease progression," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo.

"Datopotamab deruxtecan has the potential to play an important role in improving outcomes and we look forward to working closely with the FDA to bring this medicine to patients as quickly as possible."

"This Breakthrough Therapy Designation reinforces datopotamab deruxtecan as a promising potential therapy for patients with EGFR-mutated lung cancer who continue to face significant unmet needs following disease progression on or after initial treatments," said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology R&D, AstraZeneca. "We are proud to have long supported patients with EGFR-mutated lung cancer and look forward to the possibility of bringing another innovative treatment option to this community."

Daiichi Sankyo and AstraZeneca recently announced the submission of a new Biologics License Application for accelerated approval in the U.S. for datopotamab deruxtecan for the treatment of adult patients with locally advanced or metastatic EGFR-mutated NSCLC who have received prior systemic therapies, including an EGFR-directed therapy.

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 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.

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.

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 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.

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, triple negative breast cancer 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 AstraZeenca 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 DXd 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, 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.

Datopotamab deruxtecan, 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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