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Daiichi-Sankyo

Press Release

TROPION-Lung07 Phase 3 Trial Initiated to Evaluate Datopotamab Deruxtecan in Combination with Pembrolizumab in Patients with Previously Untreated Metastatic Non-Small Cell Lung Cancer

Tokyo and Basking Ridge, NJ – January 30, 2023 – Daiichi Sankyo (TSE: 4568) today announced that the first patient has been dosed in the global, randomized TROPION-Lung07 phase 3 trial evaluating datopotamab deruxtecan (Dato-DXd) in combination with pembrolizumab with or without platinum chemotherapy, in patients with previously untreated advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) with PD-L1 expression less than 50% (TPS<50%) and without actionable genomic alterations.

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

Among patients with NSCLC, nearly half are diagnosed at an advanced stage and generally have a poor prognosis.[1,2,3] While first-line treatment with pembrolizumab or other checkpoint inhibitors, with or without chemotherapy, has improved outcomes in patients with NSCLC without actionable genomic alterations, disease progression still occurs in the majority of patients.[4,5]

“Metastatic non-squamous non-small cell lung cancer remains a challenge because the majority of patients experience disease progression following their initial treatment, underscoring the need for more effective treatment options in the first-line setting,” said Mark Rutstein, MD, Global Head, Oncology Clinical Development, Daiichi Sankyo. “The TROPION-Lung07 trial will assess the potential of the combination of datopotamab deruxtecan and pembrolizumab with and without chemotherapy, to evaluate whether this combination may be a more effective standard treatment option than the current standard of care for patients in the first-line setting.”

“The combination of datopotamab deruxtecan with a checkpoint inhibitor with or without chemotherapy, has shown increased activity and a manageable safety profile in early trials, including TROPION-Lung02,” said Cristian Massacesi, MD, Chief Medical Officer and Oncology Chief Development Officer, AstraZeneca. “With this initiation, TROPION-Lung07 becomes the third phase 3 trial in our evaluation of

these investigational combinations for the first-line treatment of patients with non-small cell lung cancer, across PD-L1 segments and tumor histologies."

TROPION-Lung07 is the third clinical trial collaboration and supply agreement between Daiichi Sankyo and AstraZeneca with a subsidiary of Merck & Co., Inc., Rahway, NJ., USA to evaluate the combination of datopotamab deruxtecan and pembrolizumab. Previous clinical trial collaboration agreements were entered in October 2021 for the TROPION-Lung08 phase 3 trial and May 2020 for the TROPION-Lung02 phase 1b trial.

About TROPION-Lung07

TROPION-Lung07 is a global, randomized, open-label, phase 3 trial assessing the efficacy and safety of datopotamab deruxtecan in combination with pembrolizumab with or without platinum chemotherapy compared with pembrolizumab and platinum chemotherapy in patients with previously untreated, advanced or metastatic non-squamous NSCLC with less than 50% programmed death-ligand (PD-L1) expression (tumor proportion score [TPS] < 50%) and without actionable genomic alterations. Eligible participants in the three-arm study will be randomized in a 1:1:1 ratio to the following intervention arms: Arm A (datopotamab deruxtecan [6 mg/kg] plus pembrolizumab 200 mg IV plus platinum chemotherapy every three weeks), Arm B (datopotamab deruxtecan [6 mg/kg] plus pembrolizumab 200 mg IV every three weeks), and Arm C (pembrolizumab 200 mg IV plus pemetrexed [500 mg/m^2] plus platinum chemotherapy every three weeks).

The primary endpoints of TROPION-Lung07 are progression-free survival (PFS) as assessed by blinded independent central review and overall survival. Secondary endpoints include objective response rate, duration of response, time to response, disease control rate as assessed by both investigator and blinded independent central review, PFS as assessed by investigator, PFS2 and safety.

TROPION-Lung07 will enroll approximately 975 patients at sites in North America, South America, Europe, Asia and Oceania. For more information visit ClinicalTrials.gov.

About Non-Small Cell Lung Cancer Without Actionable Genomic Alterations

Lung cancer is the second most common cancer and the leading cause of cancer-related mortality worldwide.[1] NSCLC is diagnosed at an advanced stage in nearly 50% of patients and often has a poor prognosis with worsening outcomes after each line of subsequent therapy. [6,7,8]

While the introduction of targeted therapies and checkpoint inhibitors in recent years have improved outcomes for patients with advanced NSCLC, the majority of tumors do not have known actionable

genomic alterations.[7,8,9,10] The current standard of care in the first-line treatment of patients with advanced NSCLC without actionable genomic alterations consists of checkpoint inhibitors with or without platinum-based chemotherapy based on PD-L1 expression. While these therapies may improve survival, at least 40% to 60% of patients experience disease progression, underscoring the need for new therapeutic approaches and options.[11,12,13,14]

TROP2 (trophoblast cell-surface antigen 2) is a transmembrane glycoprotein that is widely expressed in several types of tumors, including NSCLC.[15,16,17,18] TROP2 is expressed across all lung cancer subtypes with the highest expression seen in the majority of adenocarcinoma and squamous cell carcinoma (the most common forms of NSCLC).[19] No TROP2 directed therapies are currently approved for the treatment of patients with NSCLC.[19,20,21]

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 the three 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 10 trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple tumors including NSCLC, triple negative breast cancer and HR positive, HER2 low or negative breast cancer. Trials in combination with other anticancer treatments are also underway.

About the Daiichi Sankyo and AstraZeneca Collaboration

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize datopotamab deruxtecan in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights. Daiichi Sankyo is responsible for the manufacturing and supply of 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 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 DS-6000 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 dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose "to contribute to the enrichment of quality of life around the world." In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases with high unmet medical needs. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 16,000 employees around the world draw upon a rich legacy of innovation to realize our 2030 Vision to become an "Innovative Global Healthcare Company Contributing to the Sustainable Development of Society." For more information, please visit: www.daiichisankyo.com.

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