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Press Release

TROPION-Lung05 Phase 2 Trial of Datopotamab Deruxtecan Initiated in Patients with Advanced or Metastatic NSCLC with Actionable Genomic Alterations

Tokyo, Munich and Basking Ridge, NJ – (December 14, 2020) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca today announced the initiation of TROPION-Lung05, a global phase 2 trial of datopotamab deruxtecan (Dato-DXd; DS-1062), a TROP2 directed antibody drug conjugate (ADC), in patients with advanced or metastatic non-small cell lung cancer (NSCLC) with actionable genomic alterations previously treated with kinase inhibitor therapy and platinum-based chemotherapy with or without immunotherapy.

Targeted therapy with tyrosine kinase inhibitors (TKIs) is recommended as first-line or in subsequent lines of treatment in patients with advanced or metastatic NSCLC that tests positive for certain genomic alterations as TKIs offer improved response rates or survival compared to traditional chemotherapy.[1] However, once a patient develops acquired resistance to TKIs, treatment options become more limited.[1,2]

TROP2 expression has been associated with poor overall and disease-free survival in several types of solid tumors. TROP2 expression has been observed in the majority of adenocarcinoma and squamous cell carcinoma NSCLC.[3,4,5] There are no TROP2 directed therapies or ADCs currently approved for the treatment of NSCLC.

“Following preliminary findings of durable responses observed in TROPION-PanTumor01, the ongoing phase 1 trial of datopotamab deruxtecan in non-small cell lung cancer, we will evaluate whether targeting TROP2 with our DXd ADC technology could be a new treatment strategy for patients with previously treated advanced or metastatic non-small cell lung cancer with actionable genomic alterations,” said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo.

“Many patients with NSCLC will ultimately develop resistance to available targeted therapies, and treatment options for advanced NSCLC are limited,” said Cristian Massacesi, Senior Vice President, Head of Late Stage Development Oncology R&D, AstraZeneca. “TROPION-Lung05 provides an opportunity to evaluate datopotamab deruxtecan, a targeted ADC approach with promise in this patient population.”

About TROPION-Lung05

The global, multicenter, single-arm, open-label phase 2 study will evaluate the efficacy and safety of datopotamab deruxtecan (6.0 mg/kg) in patients with advanced or metastatic NSCLC with actionable genomic alterations with progression on or after at least one tyrosine kinase inhibitor and at least one regimen of platinum-based chemotherapy (with or without other systemic therapies). Patients with one or more genomic alterations including EGFR, ALK, ROS1, NTRK, BRAF, RET, or MET exon 14 skipping who received up to four prior lines of treatment are eligible for the study.

The primary trial endpoint is overall response rate as assessed by blinded independent central review. Secondary efficacy endpoints include duration of response, best percentage change in the sum of diameters of measurable tumors, disease control rate, clinical benefit rate, progression-free survival, time to response, objective response rate and overall survival. Safety endpoints include treatment emergent adverse events and other safety parameters. Pharmacokinetic and immunogenicity endpoints also will be evaluated.

The study will enroll patients at multiple sites in North America, Europe and Asia. For more information visit Clinicaltrials.gov.

About Non-Small Cell Lung Cancer (NSCLC)

Lung cancer is the most common cancer and the leading cause of cancer mortality worldwide; there were an estimated 2.1 million new cases of lung cancer in 2018 and 1.8 million deaths.[6] NSCLC accounts for 80 to 85 percent of all lung cancers.[7]

The majority of patients with advanced NSCLC traditionally received platinum-based chemotherapy as first-line treatment.[8] The introduction of targeted therapies and immune checkpoint inhibitors in the past two decades has created new options and shifted treatment to a more personalized approach.[8]

A number of targeted tyrosine kinase inhibitors, which offer improved survival rates over traditional chemotherapy regimens, are approved for treatment of NSCLC with specific genomic alterations.[1] The most common alterations for which kinase inhibitors are approved are EGFR (approximately 10 to 35% frequency) and ALK rearrangement (approximately 3 to 7%). All patients eventually develop resistance to available therapies.[2]

About TROP2

TROP2 (trophoblast cell-surface antigen 2) is a transmembrane glycoprotein that is overexpressed in many cancers.[9] TROP2 expression has been associated with poor overall and disease-free survival in several types of solid tumors. TROP2 expression has been observed in up to 64% of adenocarcinoma and up to 75% of squamous cell carcinoma NSCLC.[3,4,5] There are no TROP2 directed therapies or ADCs currently approved for the treatment of NSCLC.

About Datopotamab Deruxtecan (Dato-DXd; DS-1062)

Datopotamab deruxtecan (Dato-DXd; DS-1062) is one of three lead DXd antibody drug conjugates (ADCs) in the oncology pipeline of Daiichi Sankyo.

ADCs are targeted cancer medicines that deliver cytotoxic chemotherapy ("payload") to cancer cells via a linker attached to a monoclonal antibody that binds to a specific target expressed on cancer cells. Designed using Daiichi Sankyo's proprietary DXd ADC technology, datopotamab deruxtecan is comprised of a humanized anti-TROP2 IgG1[3] monoclonal antibody attached to a topoisomerase I inhibitor payload, an exatecan derivative, via a tetrapeptide-based cleavable linker with a drug-to-antibody ratio (DAR) of four.

TROPION is the broad and comprehensive clinical development program to evaluate the efficacy and safety of datopotamab deruxtecan across multiple TROP2 cancers as both a monotherapy and in combination with other anticancer treatments. In addition to TROPION-Lung05, datopotamab deruxtecan is currently being evaluated in a number of clinical trials, including TROPION-Lung01, a phase 3 study in patients with advanced or metastatic non-small cell lung cancer (NSCLC) without actionable genomic alterations and TROPION-PanTumor01, a phase 1 study in patients with advanced solid tumors that have progressed on standard treatments or for whom no standard treatment is available, which has completed enrollment of patients into a unresectable advanced NSCLC cohort and is currently enrolling patients into a triple negative breast cancer (TNBC) cohort.

Datopotamab deruxtecan is an investigational agent that has not been approved for any indication in any country. Safety and efficacy have not been established.

About the Collaboration between Daiichi Sankyo and AstraZeneca

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize trastuzumab deruxtecan (a HER2 directed ADC) in March 2019, and datopotamab deruxtecan (a TROP2 directed ADC) in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights. Daiichi Sankyo is responsible for manufacturing and supply of trastuzumab deruxtecan and datopotamab deruxtecan.

About Daiichi Sankyo Cancer Enterprise

The mission of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. Anchored by our DXd antibody drug conjugate (ADC) technology, our powerful research engines include biologics, medicinal chemistry, modality and other research laboratories in

Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley, CA. For more information, please visit: www.DSCancerEnterprise.com.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical therapies to improve standards of care and address diversified, unmet medical needs of people globally by leveraging our world-class science and technology. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for cardiovascular diseases, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo is primarily focused on providing novel therapies in oncology, as well as other research areas centered around rare diseases and immune disorders. For more information, please visit: www.daiichisankyo.com.

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