

Press Release

Second Clinical Trial Collaboration Initiated to Evaluate Datopotamab Deruxtecan in Combination with KEYTRUDA® (pembrolizumab) in Patients with Metastatic Non-Small Cell Lung Cancer

- TROPION-Lung08 phase 3 trial to evaluate the Daiichi Sankyo and AstraZeneca TROP2 directed ADC with Merck & Co., Inc., Kenilworth, NJ., USA's anti-PD-1 therapy as combination regimen for first-line metastatic NSCLC

Tokyo, Munich and Basking Ridge, NJ – (October 25, 2021) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca (LSE/STO/Nasdaq: AZN) today announced that a second clinical trial collaboration and supply agreement has been entered with a subsidiary of Merck & Co., Inc., Kenilworth, NJ., USA (known as MSD outside of the United States and Canada) to evaluate the combination of datopotamab deruxtecan (Dato-DXd), a TROP2 directed DXd antibody drug conjugate (ADC), and Merck & Co., Inc., Kenilworth, NJ., USA's anti-PD-1 therapy KEYTRUDA® (pembrolizumab).

Under the terms of the agreement between Daiichi Sankyo and Merck & Co., Inc., Kenilworth, NJ., USA, Daiichi Sankyo will lead TROPION-Lung08, a global phase 3 trial that will evaluate datopotamab deruxtecan in combination with KEYTRUDA compared to KEYTRUDA alone in treatment-naïve patients with PD-L1 high advanced or metastatic non-small cell lung cancer (NSCLC) without actionable genomic alterations, on behalf of the Daiichi Sankyo and AstraZeneca collaboration. Additional details of the agreement were not disclosed.

Current standard of care in the first-line treatment of patients with metastatic NSCLC without actionable genomic alterations is PD-L1 immunotherapy with or without platinum-based chemotherapy.¹ While these therapies can improve survival in this subtype of NSCLC, at least 40 to 60% of tumors do not respond to initial treatment and disease progression occurs, underscoring the need for new innovative treatment approaches.^{2,3,4,5}

“Entering into this second clinical trial collaboration is based on encouraging results in an ongoing phase 1b study and advances development of datopotamab deruxtecan into a phase 3 study in first-line metastatic non-small cell lung cancer,” said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head,

Oncology Development, Oncology R&D, Daiichi Sankyo. “In this specific trial, we will evaluate whether combining our TROP2 directed ADC with an anti-PD-1 therapy improves outcomes in patients with previously untreated advanced non-small cell lung cancer with no actionable genomic alterations.”

“While PD-L1 immunotherapy can improve outcomes in advanced or metastatic non-small cell lung cancer, the progression-free survival for the majority of patients is still less than one year,” said Cristian Massacesi, MD, Chief Medical Officer and Oncology Chief Development Officer, AstraZeneca. “The TROPION-Lung08 trial will evaluate whether the combination of datopotamab deruxtecan and an immune checkpoint inhibitor that targets the PD-1 pathway will improve outcomes in this setting.”

A [previous](#) clinical trial collaboration agreement was entered in May 2020 for the [TROPION-Lung02](#) phase 1b trial evaluating the safety and efficacy of datopotamab deruxtecan and KEYTRUDA with or without platinum-based chemotherapy in previously treated or treatment-naïve patients with advanced or metastatic NSCLC without actionable genomic alterations.

About TROPION-Lung08

TROPION-Lung08 is a global, open-label, randomized phase 3 trial that will evaluate the efficacy and safety of the combination of datopotamab deruxtecan and KEYTRUDA versus KEYTRUDA alone in treatment-naïve patients with PD-L1 high advanced or metastatic NSCLC without actionable genomic alterations (e.g., EGFR, ALK, ROS1, NTRK, BRAF, RET, MET or other known actionable mutations). The primary endpoints of TROPION-Lung08 are progression-free survival (PFS), as assessed by blinded independent central review (BICR), and overall survival (OS). TROPION-Lung08 is expected to enroll approximately 740 patients at multiple sites in Asia, Europe, North America, and South America.

KEYTRUDA[®] is a registered trademark of Merck Sharp & Dohme Corp, a subsidiary of Merck & Co., Inc., Kenilworth, NJ, U.S.A.

About Non-Small-Cell Lung Cancer (NSCLC)

Lung cancer is the second most common cancer and the leading cause of cancer-related mortality worldwide, with 80 to 85% classified as NSCLC.^{6,7,8} NSCLC is diagnosed at an advanced stage in more than 50% of patients and often has a poor prognosis with worsening outcomes after each line of subsequent therapy.^{9,10,11}

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.¹² Current standard of care in the first-line treatment of patients with advanced NSCLC without actionable genomic alterations is immunotherapy with or without platinum-based chemotherapy, based upon PD-L1 expression.¹ While these therapies may improve survival, at least 40 to 60% of tumors do not respond to initial treatment and disease progression occurs, underscoring the need for new innovative treatment approaches.^{2,3,4,5}

About TROP2

TROP2 (trophoblast cell-surface antigen 2) is a transmembrane glycoprotein that is widely expressed in several types of solid tumors, including NSCLC.^{13,14} Research indicates that TROP2 expression is associated with increased tumor progression and poor overall and disease free survival in several types of solid tumors.^{13,14} While TROP2 is expressed across all lung cancer subtypes, results from one NSCLC study demonstrated TROP2 expression in all adenocarcinoma cases and 92% of squamous cell carcinoma cases (the most common forms of NSCLC), while a separate study found high TROP2 expression in 64% of adenocarcinoma and 75% of squamous cell carcinoma cases.^{13,14} No TROP2 directed therapies are currently approved for the treatment of patients with NSCLC.¹⁵

About Datopotamab Deruxtecan

Datopotamab deruxtecan (Dato-DXd) is an investigational TROP2 directed antibody drug conjugate (ADC). Designed using Daiichi Sankyo's proprietary DXd ADC technology, datopotamab deruxtecan is one of 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 IgG1³ monoclonal antibody, developed in collaboration with Sapporo Medical University, attached to a topoisomerase I inhibitor payload, an exatecan derivative, via a tetrapeptide-based cleavable linker.¹⁶

A comprehensive development program called TROPION is underway globally with trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple solid tumors, including NSCLC, triple negative breast cancer (TNBC), HR positive/HER2 negative breast cancer, small cell lung cancer, urothelial, gastric and esophageal cancer. Trials in combination with other anticancer treatments, such as immunotherapy, 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.

Daiichi Sankyo in Oncology

The oncology portfolio of Daiichi Sankyo is powered by our team of world-class scientists that push beyond traditional thinking to create transformative medicines for people with cancer. Anchored by our DXd antibody drug conjugate (ADC) technology, our 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 the U.S. We also work alongside leading academic and business collaborators to further advance the understanding of cancer as Daiichi Sankyo builds towards our ambitious goal of becoming a global leader in oncology by 2025.

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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