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Daiichi-Sankyo

Press Release

Datopotamab Deruxtecan Showed Clinically Meaningful Overall Survival Improvement Versus Chemotherapy in Patients with Advanced Nonsquamous Non-Small Cell Lung Cancer in TROPION-Lung01 Phase 3 Trial

- In the overall trial population, survival results numerically favored Daiichi Sankyo and AstraZeneca's datopotamab deruxtecan but did not reach statistical significance
- TROPION-Lung01 previously met the dual primary endpoint of progression-free survival in the overall trial population
- Results support applications currently under review by regulatory authorities globally including the U.S. and EU

Tokyo and Basking Ridge, NJ – (May 27, 2024) – Topline overall survival (OS) results from the TROPION-Lung01 phase 3 trial, which previously met the dual primary endpoint of progression-free survival (PFS), numerically favored datopotamab deruxtecan (Dato-DXd) compared to docetaxel in the overall trial population of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) treated with at least one prior line of therapy. Survival results did not reach statistical significance in the overall trial population. In the pre-specified subgroup of patients with nonsquamous NSCLC, datopotamab deruxtecan showed a clinically meaningful improvement in OS compared to docetaxel, the current standard of care chemotherapy.

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

The final analysis of OS builds on the positive PFS results presented at the European Society for Medical Oncology (#ESMO23) 2023 Congress which showed datopotamab deruxtecan demonstrated a statistically significant improvement in PFS in the overall trial population and a clinically meaningful PFS benefit in patients with nonsquamous NSCLC. In TROPION-Lung01, patient enrollment by tumor histology was balanced across treatment arms and consistent with real world incidence with approximately 75% of patients having nonsquamous NSCLC.[1,2]

The safety profile of datopotamab deruxtecan in TROPION-Lung01 was consistent with the previous analysis, including fewer dose reductions or discontinuations due to adverse events compared to docetaxel and with no new safety concerns identified. No new interstitial lung disease events of any grade were adjudicated as drug-related.

"The improvement in overall survival seen with datopotamab deruxtecan coupled with the previously reported clinically meaningful progression-free survival, more than doubling of overall response and prolonged duration of response compared to docetaxel suggest that this TROP2 directed antibody drug conjugate could potentially become an important new treatment for patients with nonsquamous non-small cell lung cancer in this advanced metastatic setting," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "These data will support our ongoing discussions with regulatory authorities globally to potentially bring datopotamab deruxtecan to patients as quickly as possible and mark another step forward in creating new standards of care for patients with cancer."

"Datopotamab deruxtecan is the only investigational therapy to show a clinically meaningful survival improvement in patients with previously treated nonsquamous non-small cell lung cancer versus docetaxel, which has long been unsurpassed in this post-targeted treatment and post-immunotherapy setting," said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology R&D, AstraZeneca. "These results reinforce the potential for datopotamab deruxtecan to replace conventional chemotherapy in this late-line setting and underscore our confidence in ongoing trials evaluating this therapy in first-line lung cancer."

The data will be presented at an upcoming medical meeting and will support regulatory applications currently under review globally, including the U.S. and EU for the treatment of adult patients with locally advanced or metastatic nonsquamous NSCLC who have received prior systemic therapy.

About TROPION-Lung01

TROPION-Lung01 is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan (6.0mg/kg) versus docetaxel (75mg/m^2) 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 platinum-based chemotherapy and an approved targeted therapy. Patients without known actionable genomic alterations were previously treated, either in combination 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, Oceania and South America. For more information visit ClinicalTrials.gov.

About Advanced Non-Small Cell Lung Cancer

Nearly 2.5 million lung cancer cases were diagnosed globally in 2022.[3] NSCLC is the most common type of lung cancer, accounting for about 80% of cases.[4] Approximately 75% and 25% of NSCLC tumors are of nonsquamous or squamous histology, respectively.[1] While immunotherapy and targeted therapies have improved outcomes in the first-line setting, most patients eventually experience disease progression and receive chemotherapy.[5,6,7] For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC, despite limited effectiveness and known side effects.[5,6,7]

TROP2 is a protein broadly expressed in the majority of NSCLC tumors.[8] There is currently no TROP2 directed ADC approved for the treatment of lung cancer.[9,10]

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 negative breast cancer.

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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