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Press Release

Datopotamab Deruxtecan Showed Median Overall Survival of 14.6 Months in Patients with Advanced Nonsquamous Non-Small Cell Lung Cancer in TROPION-Lung01 Phase 3 Trial

- TROPION-Lung01, evaluating Daiichi Sankyo and AstraZeneca's datopotamab deruxtecan versus chemotherapy, previously met the dual primary endpoint of progression-free survival in the overall trial population
- Presidential Symposium for NeoCOAST-2 demonstrates potential for datopotamab deruxtecan plus durvalumab and chemotherapy in neoadjuvant early-stage non-small cell lung cancer

Tokyo and Basking Ridge, NJ – (September 9, 2024) – Detailed results from the TROPION-Lung01 phase 3 trial showed a clinically meaningful trend toward improving overall survival (OS) with datopotamab deruxtecan (Dato-DXd) compared to docetaxel, the current standard of care chemotherapy, in adult patients with locally advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) treated with at least one prior line of therapy. Results will be presented today during an oral presentation (OA08.03) at the 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*.

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).

In the overall trial population, OS results numerically favored datopotamab deruxtecan compared to docetaxel (median OS 12.9 versus 11.8 months) but did not reach statistical significance (hazard ratio [HR] =0.94; 95% confidence interval [CI]: 0.78-1.14; p=0.530). In the pre-specified subgroup of patients with nonsquamous NSCLC, datopotamab deruxtecan showed a 2.3 month improvement in OS compared to docetaxel (14.6 months versus 12.3 months; HR=0.84; 95% CI: 0.68-1.05). In patients with nonsquamous NSCLC, OS improvement was observed regardless of the presence of actionable genomic alterations. In patients with squamous NSCLC, datopotamab deruxtecan did not show an OS improvement, consistent with the previous analysis.

“Despite many efforts to surpass docetaxel with novel approaches in previously treated advanced or metastatic non-small cell lung cancer, patients only survive for about one year,” said Jacob Sands, MD, Dana-Farber Cancer Institute, Medical Oncology and investigator in the trial. “For datopotamab deruxtecan to show a statistically significant improvement in progression-free survival along with improved response rate, duration of response and an overall survival improvement numerically consistent with progression-free survival is clinically meaningful for patients with nonsquamous lung cancer.”

The safety profile of datopotamab deruxtecan in TROPION-Lung01 was consistent with the previous analysis including lower rates of dose reduction (20% vs. 30%) and discontinuation (8% vs. 12%) due to adverse events compared to docetaxel. The median treatment duration for datopotamab deruxtecan was 4.2 months versus 2.8 months for docetaxel. Grade 3 or higher treatment-related adverse events (TRAEs) occurred in 26% and 42% of patients in the datopotamab deruxtecan and docetaxel arms, respectively. The most common grade 3 or higher TRAEs for datopotamab deruxtecan versus docetaxel were neutropenia (1% vs. 23%), leukopenia (0% vs. 13%), stomatitis (7% vs. 1%), anemia (4% vs. 4%), interstitial lung disease (ILD) (4% vs. 1%) and asthenia (3% vs. 2%). No new ILD events of any grade were adjudicated as drug-related since the previous analysis.

This final analysis of OS builds on the positive progression-free survival (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. The OS data have been shared with health authorities currently reviewing applications for this indication.

“For patients with nonsquamous non-small cell lung cancer, disease progression is common, making this patient population difficult to treat,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “The data from TROPION-Lung01 demonstrate the potential of datopotamab deruxtecan in this setting and support our comprehensive development program where we also are evaluating this TROP2 directed antibody drug conjugate as part of combination strategies in earlier treatment settings of non-small cell lung cancer.”

“TROPION-Lung01 showed a clinically meaningful trend towards improving the survival of patients with advanced or metastatic nonsquamous non-small cell lung cancer, building on the previously reported progression-free survival data,” said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology R&D, AstraZeneca. “Together with the data we have presented for the potential TROP2-QCS

biomarker and from NeoCOAST-2 in early-stage disease, these results underscore our confidence in the important role datopotamab deruxtecan can play across segments and settings of non-small cell lung cancer."

In TROPION-Lung01, patient enrollment by tumor histology was balanced across treatment arms and consistent with real world incidence with approximately 75% of enrolled patients having nonsquamous NSCLC.[1,2] In the datopotamab deruxtecan arm, patients were previously treated with platinum containing therapy (99%), anti-PD-1/PD-L1 therapy (88%) or targeted therapy (15%). In the docetaxel arm, patients were previously treated with platinum containing therapy (100%), anti-PD-1/PD-L1 therapy (88%) or targeted therapy (16%). In both arms, 17% of patients had tumors expressing actionable genomic alterations, such as epidermal growth factor receptor mutations.

Summary of TROPION-Lung01 Overall Survival Results

Overall Trial Population	**Datopotamab Deruxtecan (n=299)**	**Docetaxel (n=305)**
Median OS (months) (95% CI)[i]	12.9 months (11.0-13.9)	11.8 months (10.0-12.8)
HR (95% CI)	0.94 (0.78-1.14)	
p-value	0.530	
Pre-specified boundary (2-sided)	0.045	
Nonsquamous Histology	**Datopotamab Deruxtecan (n=234)**	**Docetaxel (n=234)**
Median OS (months) (95% CI)[i]	14.6 months (12.4-16.0)	12.3 months (10.7-14.0)
HR (95% CI)	0.84 (0.68-1.05)	
OS Probability at 12 months (%) (95% CI)	58.8% (52.0-64.9)	52.8% (45.9-59.2)
OS Probability at 24 months (%) (95% CI)	29.0% (22.8-35.5)	21.7% (16.0-28.0)
Nonsquamous Histology - with Actionable Genomic Alterations	**Datopotamab Deruxtecan (n=48)**	**Docetaxel (n=50)**
Median OS (months) (95% CI)[i]	15.6 months	9.8 months
HR (95% CI)	0.65 (0.40-1.08)	
Nonsquamous Histology - without Actionable Genomic Alterations	**Datopotamab Deruxtecan (n=186)**	**Docetaxel (n=184)**
Median OS (months) (95% CI)[i]	13.6 months	12.3 months
HR (95% CI)	0.89 (0.70-1.13)	
Squamous Histology	**Datopotamab Deruxtecan (n=65)**	**Docetaxel (n=71)**
Median OS (months) (95% CI)[i]	7.6 months (5.0-11.0)	9.4 months (7.2-12.5)
Hazard Ratio (95% CI)	1.32 (0.91-1.92)	

CI, confidence interval; HR, hazard ratio; OS, overall survival

[i]Median follow-up was 23.1 months for both the datopotamab deruxtecan and docetaxel arms

Results from an exploratory analysis of TROPION-Lung01 were featured in a WCLC Presidential Symposium (PL02.11) on September 8 which showed TROP2 as measured by AstraZeneca's proprietary computational pathology platform, quantitative continuous scoring (QCS), was predictive of clinical outcomes in patients with advanced or metastatic NSCLC treated with datopotamab deruxtecan.

Datopotamab deruxtecan plus durvalumab and chemotherapy showed promising response rates in patients with early-stage resectable NSCLC

Results from the NeoCOAST-2 phase 2 platform trial evaluating durvalumab in multiple novel combinations, before and after surgery, in patients with early-stage (stage IIA-IIIB) resectable NSCLC were featured in a WCLC Presidential Symposium (PL02.07). Preliminary results from the trial arm testing neoadjuvant durvalumab plus datopotamab deruxtecan and carboplatin demonstrated a pathological complete response (pCR) rate of 34.1% (95% CI: 20.5-49.9) and a major pathological response (mPR) rate of 65.9% (95% CI: 50.1-79.5). This was numerically higher than response rates shown by other combination regimens tested; however, the trial was not powered to make direct statistical comparisons between arms.

The safety profile of durvalumab plus datopotamab deruxtecan and carboplatin was consistent with the known safety profiles of these agents with grade 3 or higher TRAEs occurring in 18.5% of patients. Surgical rates across arms were comparable and in line with those shown in recent phase 3 trials. Daiichi Sankyo and AstraZeneca are evaluating datopotamab deruxtecan in combination with durvalumab in multiple ongoing trials.

About TROPION-Lung01

TROPION-Lung01 is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan (6.0 mg/kg) versus docetaxel (75 mg/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 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 blinded independent central review (BICR) and OS. Key secondary endpoints include investigator-assessed PFS, objective response

rate (ORR), 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 NeoCOAST-2

NeoCOAST-2 is a global, randomized, multicenter, open-label, multi-arm phase 2 platform trial evaluating the efficacy and safety of durvalumab in multiple novel combinations, before and after surgery, in patients with resectable, early-stage (stage IIA-IIIB) NSCLC.

The dual primary endpoints of NeoCOAST-2 are antitumor activity of neoadjuvant treatment assessed by pCR and the safety and tolerability of neoadjuvant and adjuvant treatment. Key secondary endpoints include event-free survival, disease-free survival and ORR as assessed by both RECIST version 1.1 and investigator, OS, tumor resection and mPR as defined by central blinded independent pathologist review.

NeoCOAST-2 will enroll approximately 490 patients in Asia, Europe and North 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.[1] NSCLC is the most common type of lung cancer, accounting for about 80% of cases.[2] Approximately 75% and 25% of NSCLC tumors are of nonsquamous or squamous histology, respectively.[3] While immunotherapy and targeted therapies have improved outcomes in the first-line metastatic setting, most patients eventually experience disease progression and receive chemotherapy.[4,5,6] For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC, despite limited effectiveness and known side effects.[4,5,6]

TROP2 is a protein broadly expressed in the majority of NSCLC tumors.[7] There is currently no TROP2 directed ADC approved for the treatment of lung cancer.[8,9]

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. 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 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 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 (Dato-DXd), 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. 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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