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Press Release

Ifinatamab Deruxtecan Continues to Demonstrate Durable Responses in Patients with Advanced Small Cell Lung Cancer in Early Trial

- Encouraging objective response rate of 52.4% was seen with ifinatamab deruxtecan in heavily pretreated patients
- IDeate-01 phase 2 trial currently enrolling patients with extensive-stage small cell lung cancer

Tokyo and Basking Ridge, NJ – (September 10, 2023) – Updated results from a subgroup analysis of a phase 1/2 trial showed that ifinatamab deruxtecan (I-DXd) continues to demonstrate durable responses in patients with heavily pretreated advanced small cell lung cancer (SCLC). These data were presented today during an oral presentation (OA05.05) at the 2023 World Conference on Lung Cancer (#WCLC23) hosted by the International Association for the Study of Lung Cancer.

Ifinatamab deruxtecan is a specifically engineered potential first-in-class B7-H3 directed antibody drug conjugate (ADC) designed using Daiichi Sankyo's (TSE: 4568) proprietary DXd ADC technology.

Lung cancer is the second most common cancer worldwide and SCLC represents about 15% of all cases.[1,2] Approximately 65% of all SCLC tumors have a moderate-to-high expression of B7-H3, which is associated with disease progression and lower survival.[2,3,4]

A confirmed objective response rate (ORR) of 52.4% (95% CI: 29.8-74.3) was observed in 21 patients with advanced SCLC receiving ifinatamab deruxtecan (6.4 to 16.0 mg/kg) in the dose escalation part of the phase 1/2 trial. One complete response (CR) and 10 partial responses (PRs) were seen. A median duration of response (DOR) of 5.9 months (95% CI: 2.8-7.5) was observed. Median progression-free survival (PFS) was 5.6 months (95% CI: 3.9-8.1) and median overall survival (OS) was 12.2 months (95% CI: 6.4-NA) as of data cutoff of January 31, 2023.

Tumor reduction seen with ifinatamab deruxtecan was observed across a broad range of B7-H3 protein expression levels and no apparent trend of correlation between clinical efficacy parameters and B7-H3 protein expression was observed.

"With limited effective treatment options beyond traditional chemotherapy and immunotherapy, small cell lung cancer can be difficult to treat," said Melissa Johnson, MD, Director, Lung Cancer Research, Sarah Cannon Research Institute. "The high response rate, along with the fact that all patients except one experienced a reduction in tumor size with ifinatamab deruxtecan, is promising."

The safety profile of ifinatamab deruxtecan in patients with SCLC was consistent with previous reports in the overall population of this phase 1/2 trial. Grade 3 or higher treatment-emergent adverse events (TEAEs) occurred in 36.4% of patients. The most common (>20%) TEAEs occurring in patients were nausea (59.1%), fatigue (50.0%), anemia (27.3%), vomiting (27.3%) and decreased appetite (22.7%). There was one grade 2 event confirmed to be treatment-related interstitial lung disease (ILD) or pneumonitis as determined by an independent adjudication committee. There was one grade 5 event of COVID-19 pneumonia that was determined not to be treatment related.

"In addition to the response rate seen with ifinatamab deruxtecan, we are further encouraged by the median overall survival seen in these patients at approximately one year," said Mark Rutstein, MD, Global Head, Oncology Clinical Development, Daiichi Sankyo. "Additional evaluation of this B7-H3 directed antibody drug conjugate is underway in our ongoing phase 2 trial in patients with previously treated extensive-stage small cell lung cancer and we look forward to learning these results."

In the subset of patients with SCLC, two patients (9.1%) had brain metastases at baseline. Patients were heavily pretreated receiving a median of two prior lines of systemic therapy in the locally advanced/ metastatic setting (range, 1-7), including platinum-based chemotherapy (100%), immunotherapy (81.8%), taxane chemotherapy (22.7%) and irinotecan or topotecan chemotherapy (22.7%). The median duration of follow up was 11.7 months (95% CI: 4.63-12.88) and two patients remain on treatment with ifinatamab deruxtecan.

Summary of SCLC Subset Analysis of Phase 1/2 Trial

Efficacy Measure	**Patients with SCLC receiving doses of ifinatamab deruxtecan (between 6.4 and 16.0 mg/kg) n=21**
Confirmed ORR, % (95% CI)	52.4% (29.8-74.3)
CR, n (%)	1 (4.8%)
PR, n (%)	10 (47.6%)
DOR, median (95% CI), months	5.9 months (2.8-7.5)
PFS, median (95% CI), months	5.6 months (3.9-8.1)
OS, median (95% CI), months	12.2 months (6.4-NA)

CR, complete response; DOR, duration of response; NA, not applicable; ORR, objective response rate; OS, overall survival; PR, partial response; PFS, progression-free survival.

About the Phase 1/2 Trial

The phase 1/2 trial is the first-in-human, open-label study evaluating the safety, tolerability and preliminary activity of ifinatamab deruxtecan in adult patients with advanced/unresectable or metastatic solid tumors that are refractory or intolerable to standard treatment or for whom no standard treatment exists.

The phase 1 part of the trial (dose escalation) is assessing the safety and tolerability of increasing doses of ifinatamab deruxtecan to determine the maximum tolerated dose or recommended dose for expansion (RDE). This portion of the trial enrolled approximately 100 patients with advanced/unresectable or metastatic SCLC, squamous non-small cell lung cancer (NSCLC), metastatic castration-resistant prostate cancer (CRPC), esophageal squamous cell carcinoma (ESCC), head and neck squamous cell carcinoma, bladder cancer, sarcoma, endometrial cancer, melanoma or breast cancer.

The phase 2 part of the trial (dose expansion) is evaluating the safety, tolerability and preliminary activity of ifinatamab deruxtecan in patients with squamous NSCLC, metastatic CRPC or ESCC.

The dose escalation part of the trial is evaluating dose-limiting toxicity and safety. The dose expansion part of the trial is evaluating ORR, DOR, disease control rate, PFS, OS and safety. Pharmacokinetic endpoints, exploratory biomarker and immunogenicity endpoints also will be assessed.

Patient enrollment in the ESCC and squamous NSCLC cohorts of the dose expansion part of the trial remains underway in Asia and North America. For more information, please visit ClinicalTrials.gov.

About Small Cell Lung Cancer

Lung cancer is the second most common cancer and the leading cause of cancer-related deaths worldwide.[1] The two main types of lung cancer include NSCLC, which represents more than 80 to 85% of all cases, and SCLC, which comprises about 15% of cases.[2] The five-year survival rate is only 3% for patients diagnosed with advanced SCLC.[5]

About B7-H3

B7-H3 is a transmembrane protein that belongs to the B7 family, which also includes PD-L1.[6] B7-H3 is overexpressed in a wide range of cancer types, including lung, prostate and esophageal, and its overexpression has been shown to correlate with poor prognosis in some cancers, making B7-H3 a

promising therapeutic target.[2,4,7,8,9,10] There are no B7-H3 directed medicines approved for the treatment of any cancer.

About Ifinatamab Deruxtecan

Ifinatamab deruxtecan (I-DXd) is an investigational potential first-in-class B7-H3 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC technology, ifinatamab deruxtecan is comprised of a humanized anti-B7-H3 IgG1 monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

Ifinatamab deruxtecan is being evaluated in a global development program, which includes IDeate-01, a phase 2 monotherapy trial in patients with previously treated extensive-stage SCLC, and a phase 1/2 first-in-human trial in collaboration with Sarah Cannon Research Institute.

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 (Dato-DXd), a TROP2 directed ADC, are being jointly developed and commercialized globally with AstraZeneca. Four additional Daiichi Sankyo DXd ADCs include patritumab deruxtecan (HER3-DXd), a HER3 directed ADC, ifinatamab deruxtecan (I-DXd; DS-7300), a B7-H3 directed ADC, raludotatug deruxtecan (R-DXd; DS-6000), a CDH6 directed ADC, and DS-3939, a TA-MUC1 directed ADC.

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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