

Press Release

DS-7300 Continues to Show Promising Durable Response in Patients with Several Types of Advanced Cancer

- Extended follow-up data from phase 1/2 trial of DS-7300 in patients with metastatic lung, prostate or esophageal cancer to be featured in Proffered Paper session at ESMO

Tokyo, Basking Ridge, NJ and Nashville, Tenn -- (September 10, 2022) – Daiichi Sankyo (TSE: 4568) and Sarah Cannon Research Institute (SCRI) announced that extended follow-up data from a [phase 1/2 trial](#) of DS-7300, a specifically designed potential first-in-class B7-H3 directed DXd antibody drug conjugate (ADC), continues to show promising durable tumor response in patients with several types of heavily pretreated cancers including lung, prostate or esophageal cancer. These data were presented today in a Proffered Paper session (Abstract #453O) at the European Society of Medical Oncology (#ESMO22) Congress.

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.^{1,2,3,4,5,6}

A response rate of 32% (95% CI: 24-41) was observed with 38 responses (33 confirmed; 28%; 95% CI: 20-37) in 118 patients with various solid tumors including small cell lung cancer (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 (HNSCC) or endometrial cancer receiving doses of DS-7300 ranging from 4.8 mg/kg to 16.0 mg/kg.

“These results represent important progress in the development of DS-7300, which is continuing to show promising durable efficacy in patients with several different types of advanced cancers, including lung, prostate or esophageal cancer,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “Based on these results, we are evaluating next steps for the clinical development of DS-7300 beyond the phase 2 trial recently initiated in patients with extensive-stage small cell lung cancer.”

Lung Cancer Subset Efficacy Analyses

In two subsets of patients with advanced lung cancer, response rates of 58% (95% CI: 33-80) and 40% (95% CI: 5-85) were observed in patients with SCLC (n=19) and squamous NSCLC (n=5), respectively. Eleven

responses (10 confirmed; 53%; 95% CI: 29-76) were seen in patients with SCLC and two confirmed responses (40%; 95% CI: 5-85) were seen in patients with squamous NSCLC. Median duration of response (DOR) was 5.5 months (95% CI: 2.8-NR) in patients with SCLC and 4.3 months (95% CI: 3.1-NR) in patients with squamous NSCLC. Median follow-up was 4.9 months (95% CI: 3.3-8.8) in patients with SCLC and 1.7 months (95% CI: 0.3-5.2) in patients with squamous NSCLC.

“All lung cancer patients except for one with squamous non-small cell lung cancer experienced a reduction in tumor size with DS-7300, which is potentially promising for patients looking beyond standard chemotherapy and immunotherapy options,” said Melissa L. Johnson, MD, Director, Lung Cancer Research, Sarah Cannon Research Institute at Tennessee Oncology. “We are eager to confirm the encouraging efficacy and safety results in patients with small cell lung cancer in an ongoing phase 2 trial currently enrolling patients with extensive-stage disease.”

Prostate Subset Efficacy Analysis

A response rate of 33% (95% CI: 21-47) was observed in a subset of patients in the dose escalation and expansion cohorts with metastatic CRPC (n=54). Eighteen responses (15 confirmed; 28%; 95% CI: 17-42) were seen in patients with metastatic CRPC and median DOR was 4.4 months (95% CI: 2.7-NR). Median follow-up was 9.3 months (95% CI: 7.5-10.6). For metastatic CRPC, 46% of patients had baseline liver metastases of which 40% of patients had a response.

Esophageal Subset Efficacy Analysis

A response rate of 23% (95% CI: 8-45) was observed in a subset of patients in the dose escalation and expansion cohorts with ESCC (n=22). Five responses (four confirmed; 18%; 95% CI: 5-40) were seen in patients with ESCC and median DOR was 2.8 months (95% CI: 2.6-NR). Median follow-up was 7.7 months (95% CI: 3.3-10.9).

Overall Safety

The safety and tolerability of DS-7300 was consistent with that previously reported from the trial. The most common treatment emergent adverse events (TEAEs) reported in >10% of all patients (n=147) were nausea (63%), anemia (33%), infusion-related reaction (32%), decreased appetite (31%), fatigue (30%), vomiting (30%), diarrhea (16%), pyrexia (16%), constipation (14%), chills (13%) and dehydration (11%). Grade \geq 3 TEAEs occurred in 66 patients (45%), the most common of which were anemia (19%), neutropenia (4%), nausea (3%), pneumonia (3%) and decreased neutrophil count (3%). Two grade 1 and four grade 2 treatment-related interstitial lung disease (ILD)/pneumonitis events were reported at the 12.0 mg/kg dose and one grade 5 ILD event previously reported at the 16.0 mg/kg dose, which was discontinued due to safety

concerns. These ILD events were adjudicated as drug-related by an independent adjudication committee. Two ILD/pneumonitis events are currently pending adjudication. Treatment discontinuations due to TEAEs occurred in 8% of patients.

“Prostate and esophageal cancer are two types of cancer that remain difficult to treat in advanced stages, where many patients experience repeated disease recurrence,” said Toshihiko Doi, MD, PhD, Director of Exploratory Oncology Research, Director of Clinical Trial Center and Center of Promotion of Translational Research, and Chief of Department of Experimental Therapeutics, National Cancer Center Hospital East. “Targeting the B7-H3 protein in both prostate and esophageal cancer with DS-7300 may be an encouraging treatment strategy for these patients who have limited treatment options in the metastatic setting.”

Patients enrolled in both the dose escalation and dose expansion parts of the trial across the 4.8 mg/kg to 16.0 mg/kg doses of DS-7300 received a median of five prior lines of therapies (range, 0-14). As of the data cut-off on June 30, 2022, 35 patients (24%) were still being treated with DS-7300 including eight patients (40%) with SCLC, 17 patients (23%) with metastatic CRPC, four patients (15%) with ESCC and five patients (56%) with squamous NSCLC. The expansion cohort in patients with squamous NSCLC remains open for enrollment.

About the DS-7300 Phase 1/2 Trial

This first-in-human, open-label phase 1/2 trial is evaluating the safety, tolerability and preliminary activity of DS-7300 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 DS-7300 to determine the maximum tolerated dose (MTD) or recommended dose for expansion (RDE). This portion of the trial enrolled 81 patients with advanced/unresectable or metastatic SCLC, squamous NSCLC, metastatic CRPC, ESCC, HNSCC, 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 DS-7300 at the RDE of 12.0 mg/kg 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, progression-free survival, overall survival and safety. Pharmacokinetic endpoints, exploratory biomarker and immunogenicity endpoints also will be assessed.

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

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.^{1,2,3,4,5,6} Currently, no B7-H3 directed medicines are approved for the treatment of any cancer.

About Lung, Prostate and Esophageal Cancer

Lung cancer is the second most common cancer and the leading cause of cancer-related mortality worldwide with more than 2.2 million new cases and 1.7 million deaths in 2020.⁷ 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.⁸ NSCLC is further divided into three subtypes including squamous cell carcinoma, which represents about 25% of cases and originates in squamous cells that line the inside of the airways in the lungs.⁸ More than half of patients with lung cancer are diagnosed in the metastatic stage.⁹ The five-year survival rate is only 8% and 3% for patients diagnosed with advanced NSCLC and SCLC, respectively.^{10,11}

Prostate cancer is the second most frequent cancer and the fifth leading cause of cancer death among men with an estimated 1.4 million new cases and 375,000 deaths worldwide in 2020.⁷ The five-year survival rate is only 32.3% for patients with metastatic prostate cancer.^{12,13}

Esophageal cancer is the tenth most common cancer worldwide and the sixth leading cause of cancer mortality with an estimated 604,000 new cases and 544,000 deaths reported in 2020.⁷ The majority of patients with esophageal cancer are diagnosed at advanced stage where the five-year survival rate is only 5.7%.^{14,15}

About DS-7300

DS-7300 is an investigational B7-H3 directed ADC and is one of five ADCs currently in clinical development in the oncology pipeline of Daiichi Sankyo. Designed using Daiichi Sankyo's proprietary DXd ADC technology, DS-7300 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.

In addition to the [phase 1/2 trial](#) in collaboration with Sarah Cannon Research Institute, DS-7300 also is being evaluated by Daiichi Sankyo in a [phase 2 trial](#) in patients with extensive-stage SCLC.

DS-7300 is an investigational medicine that has not been approved for any indication in any country. Safety and efficacy have not been established.

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.

About Sarah Cannon Research Institute

Sarah Cannon Research Institute is the research arm of HCA Healthcare’s Cancer Institute, Sarah Cannon. Focused on advancing therapies for patients, it is one of the world’s leading clinical research organizations conducting community-based clinical trials. A leader in drug development, Sarah Cannon has led more than 600 first-in-human clinical trials since its inception in 1993, and has been a clinical trial leader in the majority of approved cancer therapies for more than a decade. Additionally, Sarah Cannon offers management, regulatory, and other research support services for drug development and industry sponsors through its contract research organization (CRO), Sarah Cannon Development Innovations.

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