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Press Release

DS-9606 Shows Promising Preliminary Clinical Activity in Patients with Advanced Solid Tumors

- First presentation of clinical data from Daiichi Sankyo's second ADC platform
- Patient enrollment into dose escalation continues to determine recommended dose of DS-9606 for dose expansion

Tokyo and Basking Ridge, NJ – (September 15, 2024) – Initial results from dose escalation in the first-in-human phase 1 trial of DS-9606 suggest early promising clinical activity in patients with advanced solid tumors known to express Claudin-6 (CLDN6). These data were presented today during a Proffered Paper session (610O) at the 2024 European Society for Medical Oncology (#ESMO24).

DS-9606 is an investigational CLDN6 directed, modified pyrrolobenzodiazepine (PBD) antibody drug conjugate (ADC) from Daiichi Sankyo's (TSE: 4568) second antibody drug conjugate (ADC) platform.

CLDN6 is expressed in several tumor types including endometrial, ovarian and gastric cancers, germ cell tumors (GCT) and non-small cell lung cancer (NSCLC), and can be associated with poor prognosis, making CLDN6 a promising therapeutic target.[1-6]

Preliminary safety and efficacy results of DS-9606 were reported from the dose escalation part of the phase 1 trial in 53 heavily pretreated patients, including 19 with ovarian, 11 with GCT, seven with gastric/esophageal, seven with NSCLC, five with pancreatic, two with breast and two with endometrial cancer. Patients received a median of four prior therapies (range, 1- 9).

The safety and tolerability of DS-9606 were evaluated at increasing dose levels from 0.016 mg/kg to 0.225 mg/kg with no dose-limiting toxicities observed and no treatment withdrawals due to treatment-related adverse events. The most common treatment emergent adverse events (TEAEs) of any grade in ≥7.5% of patients were nausea (18.9%), fatigue (18.9%), anemia (17.0%), abdominal pain (15.1%), constipation (13.2%), vomiting (13.2%), diarrhea (11.3%), pyrexia (9.4%), weight loss (9.4%), decreased appetite (9.4%), arthralgia (9.4%), cough (9.4%), sinusitis (7.5%), dyspnea (7.5%) and pleural effusion (7.5%). Grade 3 or higher TEAEs occurred in 30.2% of patients (n=16) and included anemia (3.8%), abdominal pain (3.8%), pleural effusion (3.8%), constipation (1.9%), vomiting (1.9%) and diarrhea (1.9%). When grouped, skin-associated events (17%) were also identified as common TEAEs with the

majority being grade 1 except for one grade 2 (skin hyperpigmentation) and one grade 3 (rash) event, which resulted in a dose reduction for each patient.

Preliminary efficacy results were observed in doses greater than or equal to 0.072 mg/kg (except 0.190 mg/kg due to immature data) and included four confirmed objective responses including two responses observed in patients with GCT and one response each in patients with gastric/esophageal cancer and NSCLC. Of seven evaluable patients with GCT, the two patients with confirmed objective response remained on treatment for more than six months and five had a greater than or equal to 90% reduction in alpha-fetoprotein and human chorionic gonadotropin tumor markers. Twenty one of the 53 patients are still receiving treatment with DS-9606 as of data cutoff of June 14, 2024.

“These initial results of DS-9606 are encouraging, particularly those observed in germ cell tumors which are known to express CLDN6 and where the majority of patients experienced a reduction in tumor markers,” said Manish R. Patel, MD, Director of Drug Development, Florida Cancer Specialists and Sarah Cannon Research Institute. “Enrollment continues into the study in order to determine the recommended dose for expansion and better understand how advanced solid tumors may respond to DS-9606.”

“While these results provide preliminary proof-of-concept for DS-9606, further clinical evaluation is warranted across different tumor types that are known to express CLDN6,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “We continue to apply our science and technology expertise to DS-9606, which has been developed from our second antibody drug conjugate platform in order to create potentially new and innovative treatments for certain patients with cancer.”

About the Phase 1 Trial

The multicenter, open-label, first-in-human phase 1 trial is evaluating the safety, tolerability and efficacy of DS-9606 in adult patients with advanced solid tumors that are known to express CLDN6.

The dose escalation part of the study is assessing the safety and tolerability of increasing doses of DS-9606 to determine the maximum tolerated dose and/or the recommended dose for expansion. Dose expansion will follow to further evaluate the safety and tolerability as well as efficacy of DS-9606 at the recommended dose in patients with advanced solid tumors in cohorts that will be determined based on data obtained in dose escalation.

The study will evaluate safety and efficacy endpoints, including objective response rate, duration of response and progression-free survival per investigator assessment. Pharmacokinetic and immunogenicity endpoints will also be evaluated.

The phase 1 trial is currently enrolling patients in Europe and North America. For more information, please visit ClinicalTrials.gov.

About Claudin-6 (CLDN6)

Claudin-6 (CLDN6), a member of the claudin family, is a gene that encodes a protein that plays an important role in cell production and differentiation.[7,8] CLDN6 is expressed in several tumor types including endometrial, ovarian and gastric cancers, GCT and NSCLC, and can be associated with poor prognosis, making CLDN6 a promising therapeutic target.[1-6]

About DS-9606

DS-9606 is an investigational CLDN6 directed, modified PBD ADC. Designed using Daiichi Sankyo's second ADC technology platform, DS-9606 consists of a humanized CLDN6 monoclonal antibody, developed in collaboration with Tokyo University of Pharmacy and Life Sciences, attached to a modified PBD payload. DS-9606 is being evaluated in a phase 1 clinical trial in several advanced solid tumors that are known to express CLDN6.

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 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 needs. For more information, please visit www.daiichisankyo.com.

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