Press Release

DS-3939 Shows Promising Preliminary Clinical Activity in Patients with Advanced Solid Tumors in Phase 1/2 Trial

- First presentation of clinical data from the sixth DXd antibody drug conjugate from the oncology pipeline of Daiichi Sankyo
- Early results support continued development of DS-3939, a potential first-in-class TA-MUC1 directed antibody drug conjugate

Tokyo and Basking Ridge, NJ – (October 19, 2025) – Initial results from the dose escalation part of the first-in-human phase 1/2 trial of DS-3939 demonstrated promising clinical activity in patients with previously treated advanced solid tumors refractory to standard treatment. These data were presented today during a proffered paper session (917O) at the 2025 European Society for Medical Oncology (#ESMO25).

DS-3939 is a specifically engineered, potential first-in-class tumor-associated mucin-1 (TA-MUC1) directed DXd antibody drug conjugate (ADC) discovered and being developed by Daiichi Sankyo (TSE: 4568).

TA-MUC1 is a tumor-specific transmembrane glycoprotein that is overexpressed in most human epithelial cancers, making it a promising target for cancer therapy.[1, 2] Currently, there are no TA-MUC1 directed medicines approved for any type of cancer.

Preliminary safety and efficacy results of DS-3939 were reported from the dose escalation part of the phase 1/2 trial in 64 patients with advanced solid tumors, including 16 with non-small cell lung cancer (NSCLC), 12 with pancreatic ductal adenocarcinoma, nine with urothelial carcinoma, eight with ovarian cancer, seven with biliary tract cancer, seven with colorectal cancer and five with breast cancer.

Patients in the dose escalation phase of the study (n=64) received a median of three prior therapies (range, 1-17) for locally advanced/metastatic disease, including more than one-third receiving prior topoisomerase I inhibitor treatment (n=24; 37.5%). As of the data cut-off on August 1, 2025, 15 patients (23.4%) were still being treated with DS-3939.

The safety and tolerability of DS-3939 was evaluated at increasing dose levels from 1.0 mg/kg to 10.0 mg/kg. The most common treatment-emergent adverse events (TEAEs) of any grade in ≥20% of patients were nausea (60.9%), vomiting (35.9%), fatigue (28.1%), anemia (26.6%), constipation (26.6%), decreased

appetite (23.4%), diarrhea (23.4%) and decreased neutrophil count (23.4%). Grade 3 or higher TEAEs occurred in 46.9% of patients (n=30) and the most common (>2%) included decreased neutrophil count (15.6%), anemia (10.9%), pneumonitis (4.7%) and decreased platelet count (3.1%). There were three dose-limited toxicities observed, including one grade 3 anemia needing transfusion (4.0 mg/kg dose), one grade 3 abdominal pain (6.0 mg/kg dose) and one grade 4 decreased platelet count (8.0 mg/kg dose). All grade adjudicated as treatment-related interstitial lung disease (ILD)/pneumonitis occurred in 10.9% (n=7) of patients. The majority of ILD events were low grade (grade 2 [n=6 or 9.4%]) with one grade 3 (n=1 or 1.6%) event as determined by an independent adjudication committee. Following the data cut-off of August 1, 2025, two ILD events were adjudicated as grade 5 and two additional ILD events are pending adjudication.

Preliminary efficacy results were reported across dose levels from 1.0 mg/kg to 10.0 mg/kg of DS-3939. One confirmed complete response was observed in a patient with ovarian cancer and 10 confirmed partial responses were seen in patients with ovarian cancer (n=5), NSCLC (n=4) and breast cancer (n=1). Thirty-nine cases of stable disease were observed in patients with NSCLC (n=11), urothelial carcinoma (n=8), pancreatic ductal adenocarcinoma (n=6), colorectal cancer (n=5), biliary tract cancer (n=4), breast cancer (n=3) and ovarian cancer (n=2) after a median follow-up of 8.8 months (range, 0.6-22.9).

“These initial results are encouraging for patients with advanced solid tumors where treatment options remain limited once standard therapies are no longer effective,” said Manish R. Patel, MD, Director of Drug Development, Florida Cancer Specialists and Sarah Cannon Research Institute. “Enrollment continues into the dose expansion part of the trial to help us better understand the potential role DS-3939 may play in treating numerous types of advanced solid tumors.”

“These first-in-human results offer preliminary evidence that targeting the novel tumor antigen TA-MUC1 may be a promising treatment approach for multiple types of cancer,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “Additionally, these results represent the sixth antibody drug conjugate from the pipeline of Daiichi Sankyo with encouraging early phase data further demonstrating the portability of our DXd antibody drug conjugate technology to new tumor targets.”

About the Phase 1/2 Trial

The two-part, multicenter, open-label, first-in-human phase 1/2 trial is assessing the safety and efficacy of DS-3939 in patients with locally advanced, metastatic or unresectable solid tumors not amenable to standard of care treatment for each tumor type.

The first part of the trial (dose escalation) assessed the safety and tolerability of increasing doses of DS-3939 to determine the maximum tolerated dose and/or the recommended doses for expansion (RDEs) in patients with locally advanced, metastatic or unresectable solid tumors.

The second part of the trial (dose expansion) consists of multiple expansion cohorts to assess the safety and efficacy of DS-3939. The trial will evaluate safety endpoints, including dose-limiting toxicities and adverse events, and efficacy endpoints, including objective response rate, disease control rate, duration of response, time to response, progression-free survival and overall survival. Pharmacokinetic and biomarker endpoints also will be assessed.

The trial is ongoing and enrolling patients across multiple tumor types at sites globally, including Asia, Europe and North America. For more information, please visit ClinicalTrials.gov.

About TA-MUC1

TA-MUC1, a tumor-specific transmembrane glycoprotein, is a molecular target that is expressed across a broad range of solid tumors, but has limited expression in normal human tissues.[1] Based on the overexpression of TA-MUC1 in solid tumors, it is an attractive target for cancer therapy.[2] Currently, there are no TA-MUC1 directed therapies approved for any type of cancer.

About DS-3939

DS-3939 is an investigational, potential first-in-class TA-MUC1 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, DS-3939 is one of six DXd ADCs in the oncology pipeline of Daiichi Sankyo. DS-3939 is comprised of a humanized anti-TA-MUC1 antibody, attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

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 DATROWAY®, a TROP-2 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 & Co., Inc, Rahway, NJ, USA. 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.

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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