Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

Press Release

DS-6000 Suggests Early Clinical Activity in Patients with Advanced Ovarian Cancer or Renal Cell Carcinoma

- Initial dose escalation results from first-in-human phase 1 trial of DS-6000, Daiichi Sankyo's fifth DXd ADC in clinical development, featured in oral presentation at ASCO
- Dose expansion phase currently enrolling patients with ovarian cancer and renal cell carcinoma

Tokyo, Munich, Basking Ridge, NJ and Nashville, Tenn – (June 7, 2022) – Daiichi Sankyo (TSE: 4568) and Sarah Cannon Research Institute (Sarah Cannon) announced that initial results from the first-in-human phase 1 study of DS-6000, a CDH6 directed DXd antibody drug conjugate (ADC), suggest early clinical activity in patients with advanced ovarian cancer or renal cell carcinoma with disease progression following standard of care treatment. The data were presented today in an oral session (Abstract #3002) at the American Society of Clinical Oncology (#ASCO22) Annual Meeting.

Patients with advanced ovarian cancer or renal cell carcinoma may have disease progression after initial treatments and there is a need for new therapeutic approaches for recurrent disease, as five-year survival rates in the U.S. are low at 30% and 15%, respectively.[1,2,3,4] The CDH6 protein is significantly overexpressed in ovarian cancer and renal cell carcinoma and has been identified as a promising therapeutic target.[5,6]

Preliminary safety and efficacy results of DS-6000 were reported from the dose escalation part of the phase 1 trial in 30 heavily pretreated patients, including 21 patients with advanced ovarian cancer, one of which was missing a primary diagnosis of ovarian cancer, and nine patients with renal cell carcinoma.

The safety and tolerability of DS-6000 was evaluated at increasing dose levels from 1.6 mg/kg to 9.6 mg/kg with two dose-limiting toxicities observed at the 9.6 mg/kg dose (grade 3 febrile neutropenia and grade 4 thrombocytopenia). The most common treatment-related emergent adverse events (TEAEs) (≥ 10% of patients) reported were nausea (60.0%), fatigue (56.7%), vomiting (30.0%), neutrophil count decrease (23.3%), decreased appetite (20.0%), and diarrhea (13.3%). Grade ≥ 3 TEAEs occurred in seven patients (23.3%), the most common of which were neutrophil count decrease (16.7%), anemia (6.7%) and febrile neutropenia (6.7%). One patient experienced grade 2 pneumonitis at the 9.6 mg/kg dose that led to treatment discontinuation.

Preliminary efficacy results in 20 evaluable patients included six partial responses (PRs) in patients with ovarian cancer (n=5) and renal cell carcinoma (n=1). Four PRs were confirmed and two are awaiting confirmation. Stable disease was reported in 12 patients with platinum-resistant ovarian cancer. Eight CA-125 responses were observed in 17 evaluable patients with ovarian cancer, based on the Gynecologic Cancer Intergroup (GCIG) criteria.

"These initial results from the first-in-human trial of DS-6000 suggest early signals of safety and efficacy in patients with advanced renal cell or ovarian cancer with disease progression following multiple standard treatments," said Erika Hamilton, MD, Director, Breast Cancer and Gynecologic Cancer Research, Sarah Cannon Research Institute at Tennessee Oncology, Nashville, Tennessee. "Based on these data, enrollment is underway in the dose expansion phase of the trial to further evaluate safety and efficacy of DS-6000 in patients with platinum-resistant ovarian cancer or clear cell renal cell carcinoma."

All patients enrolled in the study (n=30) had received a median of three prior lines of systemic therapies (range, 1-12), including four (range, 1-12) for patients with ovarian cancer and two (range, 1-6) for patients with renal cell carcinoma. Seventeen of the 20 patients with ovarian cancer had platinum-resistant disease. As of the data cut-off on February 25, 2022, 17 patients (56.7%) were still being treated with DS-6000 including 12 patients with ovarian cancer and five patients with renal cell carcinoma.

"Despite recent additions to the treatment landscapes for recurrent ovarian and renal cell cancer, continued innovation is needed to improve outcomes for these patients. We have combined our DXd ADC technology with a promising therapeutic target, CDH6, with the aim to develop a new class of therapy for patients with cancer," said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. "We are encouraged by these preliminary data, which suggest that DS-6000 may have the potential to serve as a new type of targeted therapy option for patients with advanced renal cell or ovarian tumors, including platinum-resistant ovarian cancer, and further evaluation is ongoing in the dose expansion part of the trial."

About the Phase 1 Study

The two-part, multicenter, open-label, first-in-human phase 1 trial is evaluating the safety and efficacy of DS-6000 in adult patients with advanced ovarian cancer and renal cell carcinoma resistant or refractory to standard of care therapy. Patients with ovarian cancer need to be previously treated with platinum-based chemotherapy and a taxane.

The first part of the study (dose escalation) is assessing the safety and tolerability of increasing doses of DS-6000 to determine the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE). The second part of the study (dose expansion) will further evaluate the safety and efficacy of DS-6000 at the RDE of 8.0 mg/kg in patients with advanced ovarian cancer and in patients with advanced renal cell carcinoma.

The primary objective of the dose escalation part of the study is to assess the safety and tolerability of increasing doses of DS-6000 to determine the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) in patients with advanced ovarian tumors or renal cell carcinoma. The primary objective of the second part of the study (dose expansion) is to further evaluate the safety and efficacy of DS-6000 at the RDE in two cohorts including patients with advanced renal cell carcinoma in Cohort 1 and patients with advanced ovarian cancer in Cohort 2. The study will evaluate safety endpoints including dose-limiting toxicities and adverse events and efficacy endpoints including objective response rate, duration of response, disease control rate, clinical benefit rate, time to response and progression-free survival. Pharmacokinetic and exploratory biomarker endpoints also will be assessed.

A total of approximately 102 patients are expected to be enrolled in this study at multiple sites in the U.S. For more information, please visit Clinicaltrials.gov.

About CDH6

CDH6 (human cadherin-6) is a cadherin family protein overexpressed in several cancers, particularly ovarian tumors and renal cell carcinoma.[5] Overexpression of CDH6 is associated with tumor growth and proliferation and is correlated with poor prognosis in patients with renal cell carcinoma.[5] No CDH6 directed cancer therapies are currently approved for treatment of any cancer.

About Ovarian Cancer and Renal Cell Carcinoma

Approximately 314,000 women were diagnosed with ovarian cancer worldwide in 2020 and more than 207,000 died from the disease.[7] The five-year survival rate for patients in the U.S. with advanced ovarian cancer is 30%.[3] More than 70% of patients diagnosed with stage III or IV ovarian cancer will have a recurrence of their disease within the first five years following standard treatment with platinum chemotherapy-based regimens.[8] For patients who develop resistance to platinum-based chemotherapy, treatment options are especially limited.[8]

Renal cell carcinoma accounts for approximately 90% of all kidney cancer.[9] Approximately 431,000 people were diagnosed with kidney cancer worldwide in 2020 and more than 179,000 people died from the disease.[7] The five-year survival rate for patients in the U.S. with advanced renal cell carcinoma is 15%.[4] Patients with advanced or metastatic renal cell cancer may progress after first-line treatment with immune checkpoint inhibitor-based regimens and have limited treatment options as disease progression continues.[10]

The introduction of targeted treatments and immunotherapies in recent years has increased options and improved survival outcomes for some patients with ovarian cancer or renal cell carcinoma, but new therapeutic approaches and options are needed for tumors that progress on available medicines.[10,11]

About DS-6000

DS-6000 is an investigational potential first-in-class CDH6 directed ADC and one of five ADCs in clinical development in the oncology pipeline of Daiichi Sankyo. Designed using Daiichi Sankyo's proprietary DXd ADC technology, DS-6000 is comprised of a humanized anti-CDH6 IgG1 monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

Daiichi Sankyo is developing DS-6000 through a strategic collaboration with Sarah Cannon Research Institute with study operational oversight and delivery provided through Sarah Cannon's early phase oncology clinical research organization, Sarah Cannon Development Innovations in Nashville, TN.

DS-6000 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 580 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.

Media Contacts:

Global/US:
Sarah McGovern
Daiichi Sankyo, Inc.
smcgovern@dsi.com
+1 908 821 7376 (mobile)

Japan:
Masashi Kawase
Daiichi Sankyo Co., Ltd.
kawase.masashi.a2@daiichisankyo.co.jp
+81 3 6225 1126 (office)

EU:
Simone Jendsch-Dowe
Daiichi Sankyo Europe GmbH
simone.dowe@daiichi-sankyo.eu
+49 89 7808437 (office)
+49 176 11780822 (mobile)

Sarah Cannon:
Samantha Maxwell
Director, Marketing and Communications
samantha.maxwell@SarahCannon.com
615.922.9180 (mobile)

Investor Relations Contact:
DaiichiSankyoIR@daiichisankyo.co.jp

References:

[1] Pignata ASCO Educational Book 40 (April 2, 2020) 187-196.
[2] Lisio A et al. *Int J Mol Sci* 2019; 20(4).
[3] SEER Cancer Stat Facts: Ovarian Cancer. Data from SEER 18 2011–2017.
[4] SEER Cancer Stat Facts: Kidney and Renal Pelvis Cancer. Data from SEER 12 2012–2018.
[5] Bartolomé RA, et al. *Mol Oncol.* 2021 Jul;15(7):1849-1865.
[6] Bialucha CU, et al. *Cancer Discov* 2017;(9): 1–16.
[7] Global Cancer Observatory. Population Fact Sheet. Updated November 2020. Accessed January 2021.
[8] du Bois, et al. *Cancer.* 2009 Mar 15;115(6):1234-44.
[9] Patel HV, et al. *Curr Opin Oncol.* 2020; 32:240–249.
[10] Tenold M et al. ASCO Educational Book 40 (2020) 187-196.
[11] Kurnit K et al. *Obstetrics and Gynecology* (2021); 137(1): 108-121.