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Press Release

Daiichi Sankyo Presents Long-Term Phase 1 Results of Antibody Drug Conjugate DS-8201 in Patients with HER2-Expressing Breast, Gastric and Other Solid Cancers at 2018 American Society of Clinical Oncology (ASCO) Annual Meeting

- Updated subgroup analysis in 34 heavily pretreated patients with HER2-low-expressing metastatic breast cancer demonstrated a 50.0 percent confirmed overall response rate and an 85.3 percent disease control rate with DS-8201
- A 54.5 percent confirmed overall response rate and a 93.9 percent disease control rate was demonstrated with DS-8201 in updated subgroup analysis of patients with HER2-positive metastatic breast cancer pretreated with ado-trastuzumab emtansine (T-DM1) (as well as trastuzumab and pertuzumab in the majority of cases)
- Confirmed responses and disease control also were observed with investigational DS-8201 in HER2-expressing gastric cancer and other solid tumors including colorectal and non-small cell lung cancer
- Broad and comprehensive program is underway to accelerate development of DS-8201 including two pivotal phase 2 trials in metastatic breast cancer (DESTINY-Breast01) and gastric cancer (DESTINY-Gastric01) with plans proceeding to initiate phase 3 studies in HER2-positive and HER2-low-expressing metastatic breast cancer

Tokyo, Basking Ridge, NJ, and Munich – (June 1, 2018) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that long-term phase 1 safety and efficacy data for DS-8201, an investigational HER2-targeting antibody drug conjugate (ADC), in 241 heavily pretreated patients with HER2-expressing breast, gastric and other solid cancers who received recommended expansion doses of 5.4 mg/kg or 6.4 mg/kg, will be presented today during an Oral Abstract Session at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL (Abstract 2501; 2:57 – 3:09 PM CDT).

Updated preliminary results in a subgroup analysis of 34 patients with heavily pretreated HER2-low-expressing metastatic breast cancer (defined as IHC 2+/ISH- or IHC 1+/ISH- tumors) showed that DS-8201 demonstrated a confirmed overall response rate of 50.0 percent (17/34 patients) and a disease control rate of 85.3 percent (29/34 patients). Preliminary estimates of median duration of response have reached 11 months (95 percent CI: NA) and median progression-free survival has reached 12.9 months (95 percent CI: NA). A total of 14 patients (41.2 percent) were continuing to receive treatment at the time of data cutoff, which was April 18, 2018.

“HER2-targeted treatments historically have not been effective in treating metastatic breast cancer with low levels of HER2 expression,” said Hiroji Iwata, MD, PhD, Vice Director and Chief of Breast Oncology at Aichi Cancer Center Hospital, Nagoya, Japan. “While these results of DS-8201 in the HER2-low-expressing subgroup need to be further confirmed in a larger clinical setting, the preliminary data are intriguing in that

we may need to begin rethinking how we approach HER2 as a cell surface target for precision medicine treatment in metastatic breast cancer."

In an updated preliminary subgroup analysis in 99 efficacy evaluable patients with HER2-positive metastatic breast cancer pretreated with ado-trastuzumab emtansine (T-DM1) (as well as trastuzumab and pertuzumab in the majority of cases), DS-8201 demonstrated a confirmed overall response rate of 54.5 percent (54/99 patients) and a disease control rate of 93.9 percent (93/99 patients). Median duration of response and median progression-free survival have not yet been reached. Out of 111 patients with HER2-positive metastatic breast cancer who received at least one dose of DS-8201, 65 (55.1 percent) were continuing to receive treatment at the time of data cut off.

Updated overall safety data across all subgroups of the phase 1 study were reported. The most common adverse events (>30 percent, any Grade), included nausea (68.9 percent), decreased appetite (55.6 percent), alopecia (36.1 percent), vomiting (34.9 percent) and anemia (32.0 percent). Grade 3 adverse events occurring in ≥10 percent of patients included decreased neutrophil count (15.4 percent), anemia (14.9 percent), decreased white blood cell count (12.4 percent) and decreased platelet count (10.4 percent). Twenty-three patients (9.5 percent) discontinued treatment due to adverse events, which included ten (10) Grade 5 adverse events: pneumonitis (4), disease progression (2), interstitial lung disease (ILD) (1), ileus (1), pneumonia aspiration (1) and pneumonia (1). All reported or suspected cases of ILD or pneumonitis currently are under review by an independent ILD adjudication committee.

"These updated results further support our broad and comprehensive development program underway exploring the potential of DS-8201 in HER2-low-expressing breast cancer, which represents about half of all breast cancers, as well as in HER2-positive metastatic breast cancer, where unmet treatment needs remain," said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. "Our pivotal phase 2 trial in HER2-positive metastatic breast cancer is underway, and we are planning phase 3 trials in HER2-low-expressing and HER2-positive metastatic breast cancer in order to determine whether the smart delivery of chemotherapy with DS-8201 may be an effective treatment option against breast tumors that express varying levels of HER2 as a cell surface antigen. A similar biological paradigm is being tested in our other ongoing phase 2 studies of DS-8201 in gastric and colorectal cancer."

HER2-Expressing Gastric Cancer and Other Solid Cancer Subgroup Analyses

Updated preliminary results of two additional subgroup analyses were reported in addition to the two breast cancer subgroups. In the subgroup of 44 patients with HER2-expressing (defined as IHC 3+ or IHC 2+/

ISH-) gastric cancer or gastroesophageal junction adenocarcinoma previously treated with trastuzumab and chemotherapy, DS-8201 demonstrated a confirmed overall response rate of 43.2 percent (19/44 patients) and a disease control rate of 79.5 percent (35/44 patients). Preliminary estimates of median duration of response has reached 7.0 months (95 percent CI: NA) and median progression-free survival has reached 5.6 months (95 percent CI: 3.0, 8.3).

In an updated preliminary analysis in 31 evaluable patients with other HER2-expressing solid tumors such as colorectal and non-small cell lung cancer, DS-8201 demonstrated a confirmed overall response rate of 38.7 percent (12/31 patients) and a disease control rate of 83.9 percent (26/31 patients). Preliminary estimates of median duration of response has reached 12.9 months (95 percent CI: 2.8, 12.9) and median progression-free survival has reached 12.1 months (95% CI: 2.7, 14.1).

Unmet Need in HER2-Expressing Breast and Gastric Cancer

About one in five breast and gastric cancers overexpress HER2, a tyrosine kinase receptor growth-promoting protein found on the surface of some cancer cells, which is associated with aggressive disease.[1,2] To be considered HER2-positive, tumor cancer cells are usually tested by one of two methods: immunohistochemistry (IHC) or fluorescent in situ hybridization (FISH).[1,3] IHC test results are reported as: 0, IHC 1+, IHC 2+ or IHC 3+.[1,3] A finding of IHC 3+ is considered HER2-positive.[1,3] A finding of IHC 2+ is borderline and typically is confirmed by a positive FISH test.[1,3]

Several unmet needs remain today in HER2-expressing metastatic breast cancer. Many HER2-positive tumors advance to the point where no currently approved HER2-targeting treatment continues to control the disease, and there is no current standard of care for HER2-positive tumors after treatment with trastuzumab, pertuzumab and T-DM1.[4] Additionally, there are no anti-HER2 therapies indicated for HER2 low-expressing tumors (IHC 2+/FISH- or IHC 1+).

HER2-expressing gastric cancer also is an area of unmet medical need as advances in the treatment of the disease have been limited, largely due to its genetic complexity and heterogeneity.[5] Currently, there are no approved HER2-targeting therapy options for patients with HER2-positive advanced gastric cancer after treatment with trastuzumab.

About the DS-8201 Phase 1 Study

The open-label, two-part phase 1 study is currently evaluating DS-8201 in patients with advanced/ unresectable or metastatic solid tumors that are refractory or intolerant to standard treatment, or for whom no standard treatment is available. The primary objective of the dose escalation phase of the study was to assess

the safety and tolerability of DS-8201 and determine the maximum tolerated dose. Data from this part of the study were published in the *Lancet Oncology*.[6]

In the dose expansion part of the phase 1 study, DS-8201 is given to patients with HER2-positive advanced or metastatic breast cancer and gastric cancer, HER2-low-expressing breast cancer and other HER2-expressing or mutant solid tumors. Patient enrollment in the two breast cancer cohorts and the HER2-expressing solid tumors cohort is ongoing in the U.S. and Japan. For more information about the study, please visit ClinicalTrials.gov.

About DS-8201

DS-8201 is the lead product in the investigational ADC Franchise of the Daiichi Sankyo Cancer Enterprise. ADCs are targeted cancer medicines that deliver cytotoxic chemotherapy ("payload") to cancer cells via a linker attached to a monoclonal antibody that binds to a specific target expressed on cancer cells. Designed using Daiichi Sankyo's proprietary ADC technology, DS-8201 is a smart chemotherapy comprised of a humanized HER2 antibody attached to a novel topoisomerase I inhibitor payload by a tetrapeptide-based linker. It is designed to target and deliver chemotherapy inside cancer cells and reduce systemic exposure to the cytotoxic payload (or chemotherapy) compared to the way chemotherapy is commonly delivered.

DS-8201 is currently in pivotal phase 2 clinical development for HER2-positive unresectable and/or metastatic breast cancer resistant or refractory to T-DM1 (DESTINY-Breast01) in North America, Europe and Asia; pivotal phase 2 development for HER2-positive advanced gastric cancer resistant or refractory to trastuzumab (DESTINY-Gastric01) in Japan and South Korea; phase 2 development for HER2-expressing advanced colorectal cancer in North America, Europe and Japan; phase 2 development for unresectable and/or metastatic non-squamous HER2-overexpressing or HER2-mutated non-small cell lung cancer (NSCLC) in North America, Europe and Japan; and phase 1 development for other HER2-expressing advanced/unresectable or metastatic solid tumors in the U.S. and Japan.

DS-8201 has been granted Breakthrough Therapy designation for the treatment of patients with HER2-positive, locally advanced or metastatic breast cancer who have been treated with trastuzumab and pertuzumab and have disease progression after ado-trastuzumab emtansine (T-DM1), and Fast Track designation for the treatment of HER2-positive unresectable and/or metastatic breast cancer in patients who have progressed after prior treatment with HER2-targeted therapies including T-DM1 by the U.S. Food and Drug Administration (FDA). DS-8201 has also been granted SAKIGAKE Designation by the Japan Ministry of Health, Labour and Welfare (MHLW) for the treatment of HER2-positive advanced gastric or gastroesophageal junction cancer.

DS-8201 is an investigational agent that has not been approved for any indication in any country. Safety and efficacy have not been established.

About Daiichi Sankyo Cancer Enterprise

The mission of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. Anchored by three pillars including our investigational Antibody Drug Conjugate Franchise, Acute Myeloid Leukemia Franchise and Breakthrough Science, we aim to deliver seven distinct new molecular entities over eight years during 2018 to 2025. Our powerful research engines include two laboratories for biologic/immuno-oncology and small molecules in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley, CA. Compounds in pivotal stage development include: DS-8201, an antibody drug conjugate (ADC) for HER2-expressing breast, gastric and other cancers; quizartinib, an oral selective FLT3 inhibitor, for newly-diagnosed and relapsed/refractory acute myeloid leukemia (AML) with *FLT3*-ITD mutations; and pexidartinib, an oral CSF1R inhibitor, for tenosynovial giant cell tumor (TGCT). For more information, please visit: www.DSCancerEnterprise.com.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for hypertension and thrombotic disorders, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo research and development is primarily focused on bringing forth novel therapies in oncology, including immuno-oncology, with additional focus on new horizon areas, such as pain management, neurodegenerative diseases, heart and kidney diseases, and other rare diseases. For more information, please visit: www.daiichisankyo.com. Daiichi Sankyo, Inc., headquartered in Basking Ridge, New Jersey, is a member of the Daiichi Sankyo Group. For more information on Daiichi Sankyo, Inc., please visit: www.dsi.com.

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