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Press Release

Daiichi Sankyo Presents Updated Results of [Fam-] Trastuzumab Deruxtecan (DS-8201) in Patients with HER2 Expressing Advanced Colorectal Cancer at 2018 European Society for Medical Oncology (ESMO) Congress

- Updated analysis from ongoing phase 1 study of [fam-] trastuzumab deruxtecan (DS-8201) demonstrated a confirmed overall response rate of 15.8 percent and a disease control rate of 84.2 percent in 19 evaluable patients with heavily pretreated colorectal cancer with varying levels of HER2 expression
- Currently no HER2 targeting therapy is approved for patients with HER2 expressing colorectal cancer
- A global phase 2 study is currently enrolling patients with HER2 expressing colorectal cancer, part of a broad development program evaluating [fam-] trastuzumab deruxtecan across multiple types of HER2 expressing tumors

Tokyo, Munich, and Basking Ridge, NJ – (October 21, 2018) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that updated phase 1 safety and efficacy data for [fam-] trastuzumab deruxtecan, an investigational HER2 targeting antibody drug conjugate (ADC), were presented for a subgroup of patients with heavily pretreated HER2 expressing colorectal cancer at the 2018 European Society for Medical Oncology (ESMO) Congress in Munich, Germany.

An updated subgroup analysis in 19 evaluable patients with heavily pretreated HER2 expressing (defined as IHC ≥1+ or amplified) colorectal cancer receiving a recommended expansion dose of 6.4 mg/kg showed that [fam-] trastuzumab deruxtecan demonstrated a confirmed overall response rate of 15.8 percent (3 of 19 patients) and a disease control rate of 84.2 percent (16 of 19 patients). Median duration of response has not been reached and median progression-free survival was 3.9 months (95 percent CI: 2.1, 8.3) for this subgroup of patients. These patients had tumors with varying degrees of HER2 expression based on central IHC assessment of archival tissue, including six patients with HER2 IHC of zero (0). Tumor shrinkage primarily was observed in tumors with higher levels of HER2 IHC.

“We are encouraged by these preliminary results with [fam-] trastuzumab deruxtecan, particularly given the unmet medical need for patients with HER2 expressing colorectal cancer that has progressed on one or more prior therapies,” said Takayuki Yoshino, MD, PhD, Director of Gastroenterology and Gastrointestinal Oncology at National Cancer Center Hospital East, Kashiwa, Japan, a study investigator. “These initial findings support further evaluation of [fam-] trastuzumab deruxtecan in this specific type of colorectal cancer.”

“There are no therapies specifically approved for patients with HER2 expressing colorectal cancer, and continued study of [fam-] trastuzumab deruxtecan will provide a better understanding of the potential

role of a HER2 targeting antibody drug conjugate in these patients," said Gilles Gallant, BPharm, PhD, Vice President, DS-8201 Global Team Leader, Oncology Research and Development, Daiichi Sankyo. "Patient enrollment is underway into our global phase 2 study evaluating safety and efficacy of [fam-] trastuzumab deruxtecan in patients with HER2 expressing advanced colorectal cancer."

Updated overall safety data as of August 10, 2018 across all subgroups of the ongoing phase 1 study with [fam-] trastuzumab deruxtecan in various HER2 expressing cancers were also reported at ESMO. Among 259 patients who received at least one dose of [fam-] trastuzumab deruxtecan 5.4 or 6.4 mg/kg in Part 1 or Part 2 of the study (regardless of tumor type), the most common adverse events (≥30 percent, any Grade) included nausea (74.1 percent), decreased appetite (56.8 percent;) vomiting (43.6 percent), anemia (37.8 percent), alopecia (37.5 percent), fatigue (34.0 percent), diarrhea (33.6 percent) and constipation (32.8 percent). A total of 54.1 percent of patients experienced a ≥ Grade 3 adverse event and 22.8 percent had a serious adverse event, including 4.6 percent of patients who experienced an adverse event that led to death. As previously presented, five cases of Grade 5 interstitial lung disease (ILD)/pneumonitis were reported by the investigators for the overall population of the phase 1 study, none of which was observed in patients with colorectal cancer. Any reported cases of ILD/pneumonitis in the [fam-] trastuzumab deruxtecan clinical development program are evaluated by an independent adjudication committee.

Unmet Need in Colorectal Cancer

Colorectal cancer is the third most common cancer worldwide. In 2012, there were approximately 1.36 million new cases diagnosed and 690,000 deaths worldwide.[1] Approximately 25 percent of patients have metastatic disease at diagnosis, meaning the disease has spread to distant organs, and about 50 percent of patients with colorectal cancer will eventually develop metastases.[2] Prognosis for these patients remains poor.[3]

An increase in the number of approved targeted therapies for advanced colorectal cancer over the past decade has helped improve outcomes for some patients, however efficacy and tolerability of second and third-line treatments remain limited.[4,5,6,7,8] Approximately 3 percent of colorectal cancers overexpress the HER2 protein, which is a well-established therapeutic target in breast and gastric cancer.[4] In addition, research indicates that HER2 amplification may be associated with resistance to anti-epidermal growth factor receptor (EGFR)-targeted therapy and shorter survival.[9,10] Currently, no approved HER2 targeting therapies exist for patients with colorectal cancer.

About the [Fam-] Trastuzumab Deruxtecan Phase 1 Study

An open-label, two-part phase 1 study is currently evaluating [fam-] trastuzumab deruxtecan 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 this study was to assess the safety and tolerability of [fam-] trastuzumab deruxtecan and determine the maximum tolerated dose. Data from this part of the study were published in the *Lancet Oncology*.[11]

In the dose expansion part of the phase 1 study, [fam-] trastuzumab deruxtecan is given in one of two doses (5.4 mg/kg and 6.4 mg/kg) to patients with HER2 positive advanced or metastatic breast cancer and gastric cancer, HER2 low expressing breast cancer and other HER2 expressing solid tumors including colorectal cancer. Overall, 292 patients have been enrolled into this phase 1 study of [fam-] trastuzumab deruxtecan. For more information about the study, visit ClinicalTrials.gov.

About [Fam-] Trastuzumab Deruxtecan

[Fam-] trastuzumab deruxtecan (DS-8201; [fam-] trastuzumab deruxtecan in U.S. only; trastuzumab deruxtecan in other regions of world) 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, [fam-] trastuzumab deruxtecan is 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.

A broad and comprehensive development program with [fam-] trastuzumab deruxtecan is underway in North America, Europe and Asia. [Fam-] trastuzumab deruxtecan is in phase 3 development versus ado-trastuzumab emtansine (T-DM1) (DESTINY-Breast03) and versus investigator's choice post T-DM1 (DESTINY-Breast02) for HER2 positive metastatic breast cancer; pivotal phase 2 clinical development for HER2 positive metastatic breast cancer resistant or refractory to T-DM1 (DESTINY-Breast01); pivotal phase 2 development for HER2 positive advanced gastric cancer resistant or refractory to trastuzumab (DESTINY-Gastric01); phase 2 development for HER2 expressing advanced colorectal cancer; phase 2 development for metastatic non-squamous HER2 overexpressing or HER2 mutated NSCLC; and, phase 1 development in combination with nivolumab for HER2 expressing metastatic breast and bladder cancer.

[Fam-] trastuzumab deruxtecan 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 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). [Fam-] trastuzumab deruxtecan has received SAKIGAKE Designation for

the treatment of HER2 positive advanced gastric or gastroesophageal junction cancer by the Japan Ministry of Health, Labour and Welfare (MHLW).

[Fam-] trastuzumab deruxtecan 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: [fam-] trastuzumab deruxtecan, 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 *FLT3*-ITD acute myeloid leukemia (AML); 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.

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