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# Press Release

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# New Precision Medicine Data on DS-8201 in HER2-Expressing Breast Cancer Revealed at 2017 American Society of Clinical Oncology (ASCO) Annual Meeting

- Preliminary results from phase 1 study demonstrate a 46.7 percent overall response rate and 100 percent disease control rate with smart chemotherapy DS-8201 in a subgroup analysis of HER2-expressing metastatic breast cancer pre-treated with T-DM1 and pertuzumab
- DS-8201 demonstrated a favorable safety profile and also showed promising antitumor activity in HER2-expressing metastatic gastric cancer previously-treated with trastuzumab
- Phase 2 clinical studies currently being planned to evaluate DS-8201 in HER2-expressing metastatic breast and gastric cancer

**Tokyo, Japan, Parsippany, NJ, and Munich, Germany – (June 5, 2017)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced smart chemotherapy DS-8201 demonstrated a favorable safety profile and promising antitumor activity in patients with HER2-expressing tumors, including pre-treated metastatic breast and gastric cancer. These data were highlighted as part of a Clinical Science Symposium at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

Preliminary results from the dose expansion part of the phase 1 study of DS-8201 in a subgroup analysis of HER2-expressing metastatic breast cancer patients pre-treated with ado-trastuzumab emtansine (T-DM1) and pertuzumab demonstrated a 46.7 percent overall response rate (14 of 30 patients) and a 100 percent disease control rate (30 of 30 patients) to date. An overall response rate of 45.7 percent (16 of 35 patients) and disease control rate of 100 percent (35 of 35 patients) was observed in patients pre-treated with only T-DM1.

Antibody drug conjugates (ADCs) are a type of targeted cancer medicine that deliver cytotoxic chemotherapy ("payload") directly to cancer cells via a linker attached to a monoclonal antibody that binds to a specific target expressed on cancer cells. 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 (DXd) payload by a tetrapeptide linker designed to deliver enhanced cancer cell destruction upon release inside the cell and reduce systemic exposure to the cytotoxic payload (or chemotherapy).

"The significant tumor shrinkage and sustained tumor control that was demonstrated by DS-8201 is impressive and further confirms the initial antitumor activity shown in the dose escalation part of this study," said Toshihiko Doi, MD, PhD, Department of Experimental Therapeutics, National Cancer Center Hospital East, and study investigator. "These data suggest that DS-8201 may be a promising potential

treatment for patients with HER2-expressing metastatic breast cancer whose tumors are no longer controlled with available treatment options like T-DM1 and pertuzumab."

Thirty-nine of 50 patients with HER2-expressing metastatic breast cancer are continuing to receive treatment. To date, median progression free survival has reached 45.4 weeks (95 percent CI: 32.1, NA). Eleven patients have discontinued treatment due to adverse events (3 patients), progressive disease (6 patients) and other reasons (2 patients).

"These results demonstrate that the smart delivery of chemotherapy by DS-8201 to cancer cells may be effective and safe in treating tumors that express HER2," said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. "Based on these results, we are accelerating the development of DS-8201 and our ADC technology seeking to bring a unique precision medicine to patients and physicians who have exhausted current treatment options."

**About the DS-8201 Phase 1 Study**

DS-8201 is currently being evaluated in an open-label two-part phase 1 dosing study 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 (MTD). No dose limiting toxicity was seen administering DS-8201 up to 8.0 mg/kg every three weeks and the maximum tolerated dose was not reached.

In the dose expansion part of the study, DS-8201 is given in one of two doses (5.4 mg/kg and 6.4 mg/kg) to patients in one of four cohorts: patients with ado-trastuzumab emtansine (T-DM1)-treated HER2-positive breast cancer; patients with trastuzumab-treated HER2-positive gastric cancer or gastroesophageal junction adenocarcinoma; patients with HER2 low-expressing breast cancer; and patients with other HER2-expressing solid malignant tumors. Patient enrollment in the two breast cancer cohorts is ongoing in the U.S. and Japan. For more information about the study, please visit ClinicalTrials.gov.

A total of 134 patients have been treated to date in both the dose escalation (24 patients) and dose expansion (110 patients) parts of the study. The most common any-grade adverse events observed in the study to date included nausea (66.9 percent), decreased appetite (57.9 percent), vomiting (36.8 percent) and decreased platelet count (34.6 percent). Grade 4 adverse events included decreased platelet count (3.8 percent), decreased neutrophil count (3.0 percent), anemia (1.5 percent), and decreased white blood cell count (1.5 percent).

Preliminary results in the overall population of HER-expressing solid tumors demonstrated an overall response rate of 40.2 percent (39 of 97 patients) with a disease control rate of 91.8 percent. In the cohort enrolling patients with trastuzumab-treated HER2-positive gastric or gastroesophageal junction adenocarcinoma, a preliminary overall response rate of 44.4 percent (16 of 36 patients) and a disease control rate of 88.9 percent (32 of 36 patients) was shown to date with DS-8201. In a sub-group of patients pre-treated with CPT-11 (irinotecan), an overall response rate of 44.4 percent (8 of 18 patients) and disease control rate of 94.4 percent (17 of 18 patients) was demonstrated to date. A total of 22 out of 39 patients are still receiving treatment with median progression free survival of 27.3 weeks (95 percent CI: 13.4, NA). Seventeen patients have discontinued treatment due to adverse events (6 patients) and progressive disease (11 patients).

**About DS-8201**

DS-8201 is the lead product in the Antibody Drug Conjugate (ADC) Franchise of the Daiichi Sankyo Cancer Enterprise. DS-8201 is currently in phase 1 clinical development for HER2-positive advanced or metastatic breast cancer and gastric cancer, HER2-low-expressing breast cancer and other HER2-expressing solid cancers. The U.S. Food and Drug Administration (FDA) granted Fast Track designation to DS-8201 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 ado-trastuzumab emtansine (T-DM1). DS-8201 has not been approved for any indication in any country.

**About Daiichi Sankyo Cancer Enterprise**

The vision of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking in order 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 our Antibody Drug Conjugate (ADC) and Acute Myeloid Leukemia (AML) Franchises, our cancer pipeline includes more than 20 small molecules, monoclonal antibodies and ADCs stemming from our powerful research engines: our 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 development include: quizartinib, an oral FLT3 inhibitor, for newly-diagnosed and relapsed/refractory AML with FLT3-ITD mutations; DS-8201, an ADC for HER2-expressing breast and gastric cancer, and other HER2-expressing solid tumors; and pexidartinib, an oral CSF-1R inhibitor, for tenosynovial giant cell tumor (TGCT), which is also being explored in a range of solid tumors in combination with the anti-PD1 immunotherapy pembrolizumab. 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 16,000 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 a 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 Parsippany, 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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