

## Press Release

# Daiichi Sankyo Presents Updated Data for DS-8201 in Patients with HER2-Expressing Gastric Cancer at ASCO 2018 Gastrointestinal Cancers Symposium

- Updated analysis from ongoing phase 1 study of DS-8201 demonstrated a confirmed overall response rate of 45.5 percent and a disease control rate of 81.8 percent in 44 evaluable patients with HER2-expressing gastric cancer previously treated with trastuzumab and chemotherapy
- Preliminary subgroup analysis of patients previously treated with CPT-11 (irinotecan) showed similar response rates to the overall study population, which may suggest an absence of relevant cross-resistance to smart chemotherapy delivery to tumor cells by the ADC construct of DS-8201
- Pivotal phase 2 DESTINY-Gastric01 study of DS-8201 is currently enrolling patients in Japan with HER2-positive advanced gastric cancer resistant or refractory to trastuzumab

**Tokyo, Basking Ridge, NJ, and Munich – (January 18, 2018)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that updated phase 1 safety and efficacy data for DS-8201, an investigational HER2-targeting antibody drug conjugate (ADC), in a subgroup of patients with HER2-expressing gastric cancer previously treated with trastuzumab and chemotherapy were presented during a poster session at the 2018 American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium in San Francisco, California.

Updated preliminary subgroup analysis results in 44 of 45 efficacy evaluable patients with HER2-expressing gastric cancer or gastroesophageal junction adenocarcinoma previously treated with trastuzumab and chemotherapy showed that DS-8201 demonstrated a confirmed overall response rate of 45.5 percent (20 of 44 patients) and a disease control rate of 81.8 percent (36 of 44 patients). Median duration of response was 7.0 months (95 percent CI: NR). The Kaplan-Meier estimate of median progression-free survival was 5.8 months (95 percent CI: 3.0, 8.3). A total of 17 out of 44 patients were continuing to receive treatment at the time of data cut-off.

“Gastric cancer can be difficult to treat due to its molecular complexity, and currently there are no HER2-targeted therapies or antibody drug conjugates approved for HER2-positive advanced gastric cancer that progresses following treatment with trastuzumab,” said Toshihiko Doi, MD, PhD, Department of Experimental Therapeutics, National Cancer Center Hospital East. “These phase 1 results are encouraging and demonstrate the importance of continuing to study the potential of DS-8201 in treating HER2-positive gastric cancer. The pivotal phase 2 study is currently underway.”

A subgroup analysis of 23 patients previously treated with CPT-11 (irinotecan) showed that DS-8201 demonstrated a confirmed overall response rate of 43.5 percent (10 of 23 patients) and a disease control rate of 82.6 percent (19 of 23 patients). Median duration of response was 6.9 months (95 percent CI: NR). The Kaplan-Meier estimate of median progression-free survival for this subgroup of patients was 4.1 months (95 percent CI: 2.5, 8.3).

“These data from patients with HER2-positive gastric cancer who have failed HER2-targeted therapy combined with chemotherapy, and for many who also failed irinotecan as a systemic chemotherapy suggest that the ADC technology of DS-8201 appears able to deliver on what it was specifically researched and innovated for: a smart chemotherapy approach to tumors expressing some degree of HER2 receptors, regardless of prior treatment with a topoisomerase I inhibitor,” said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. “A comprehensive translational research effort is planned and underway to further understand the biological basis for the observed activity, including the role of tumor heterogeneity and HER2 expression, the mechanisms of resistance that may have contributed to failing prior lines of treatment, and factors more directly related to the unique pharmacological profile of DS-8201.”

Updated preliminary safety data for this subgroup of trastuzumab-treated HER2-expressing gastric cancer patients were also reported. The most common adverse events (>30 percent, any grade) included nausea (71.1 percent), decreased appetite (64.4 percent), platelet count decreased (33.3 percent), white blood cell count decreased (33.3 percent) and constipation (31.1 percent). Grade 3 adverse events occurring in >10 percent of patients included anemia (24.4 percent), neutrophil count decreased (15.6 percent), platelet count decreased (13.3 percent) and white blood cell count decreased (11.1 percent). Grade 4 adverse events included platelet count decreased (4.4 percent), white blood cell count decreased (4.4 percent) and neutrophil count decreased (4.4 percent). Three patients discontinued treatment due to treatment-emergent adverse events (pneumonia, decreased appetite, and pneumonitis). Two potential cases of interstitial lung disease (ILD) were reported by the investigators (one grade 1 and one grade 3) in gastric cancer subjects and together with all reported or suspected ILD cases are being assessed by an independent ILD adjudication committee. These include two cases of potential Grade 5 pneumonitis previously reported in the breast cancer cohorts.

Based on these phase 1 data, patients are currently being enrolled in the pivotal, phase 2 open-label DESTINY-Gastric01 study investigating the safety and efficacy of DS-8201 in patients with HER2-positive advanced gastric cancer or gastroesophageal junction adenocarcinoma (defined as IHC3+ or IHC2+/ISH+)

who have progressed on two prior regimens including fluoropyrimidine agent, platinum agent and trastuzumab. For more information about this study, visit [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).

### **Unmet Need in Gastric Cancer**

Gastric cancer is the fifth most common cancer worldwide, with nearly one million new cases reported in 2012.<sup>1</sup> Approximately one in five gastric cancers overexpress HER2, a tyrosine kinase receptor growth-promoting protein found on the surface of some cancer cells.<sup>2</sup> HER2-expressing gastric cancer 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.<sup>3</sup> 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*.<sup>4</sup>

In the dose expansion part of the phase 1 study, DS-8201 is given to patients with HER2-positive advanced or metastatic breast cancer or gastric cancer, HER2 low-expressing breast cancer or 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](http://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 ado-trastuzumab emtansine (T-DM1) ([DESTINY-](#)

[Breast01](#)), pivotal phase 2 development for HER2-positive advanced gastric cancer resistant or refractory to trastuzumab ([DESTINY-Gastric01](#)), and phase 1 development for other HER2-expressing advanced/unresectable or metastatic solid tumors.

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 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 vision 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 Franchise, 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 CSF-1R inhibitor, for tenosynovial giant cell tumor (TGCT). For more information, please visit: [www.DSCancerEnterprise.com](http://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](http://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](http://www.dsi.com).

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