

Press Release

Daiichi Sankyo Presents Updated Data for DS-8201 in Patients with HER2-Expressing Breast Cancer at San Antonio Breast Cancer Symposium

- Updated analysis from an ongoing phase 1 study of DS-8201 demonstrated a confirmed overall response rate of 61.4 percent and disease control rate of 94.7 percent in patients with HER2-positive metastatic breast cancer pre-treated with ado-trastuzumab emtansine (T-DM1)
- Preliminary results from the same study of DS-8201 demonstrated a confirmed overall response rate of 31.6 percent and disease control rate of 84.2 percent in an analysis of heavily pretreated patients with HER2 low-expressing metastatic breast cancer
- Pivotal phase 2 DESTINY-Breast01 study of DS-8201 is currently enrolling patients with HER2-positive metastatic breast cancer resistant and refractory to T-DM1

Tokyo, Basking Ridge, NJ, and Munich – (December 7, 2017) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that updated safety and efficacy data from two subgroups of patients with metastatic breast cancer from an ongoing phase 1 study of DS-8201, an investigational HER2-targeting antibody drug conjugate (ADC), were presented during a Spotlight Poster Discussion session at the 2017 San Antonio Breast Cancer Symposium.

Updated preliminary results in a subgroup analysis of 57 efficacy evaluable patients with HER2-positive metastatic breast cancer pre-treated with ado-trastuzumab emtansine (T-DM1) showed that DS-8201 demonstrated a confirmed overall response rate of 61.4 percent (35 of 57 patients) and a disease control rate of 94.7 percent (54 of 57 patients). Among 50 of these patients who also were pre-treated with pertuzumab, DS-8201 demonstrated a confirmed overall response rate of 62 percent (31 of 50 patients) and a disease control rate of 94 percent (47 of 50 patients). In 39 efficacy evaluable HER2-positive patients with hormone-receptor positive disease, DS-8201 demonstrated an overall response rate of 56.4 percent (22 of 39 patients) and disease control rate of 92.3 percent (36 of 39 patients). The majority of patients with HER2-positive metastatic breast cancer were continuing to receive treatment at the time of data cut-off. Preliminary estimates of median progression free survival have reached 10.4 months.

Additionally, preliminary results in another subgroup showed that DS-8201 demonstrated a confirmed overall response rate of 31.6 percent (6 of 19 patients) and a disease control rate of 84.2 percent (16 of 19 patients) in 19 efficacy evaluable patients with heavily pretreated HER2 low-expressing breast cancer (defined as IHC2+/ISH- or IHC 1+). In 16 of these patients also classified with hormone-receptor positive disease, DS-8201 demonstrated an overall response rate of 31.3 percent (5 of 16 patients) and a disease control rate of 87.5 percent (14 of 16 patients). Most patients with HER2 low-expressing breast cancer were

continuing to receive treatment at the time of data cut-off. Median progression free survival has not yet been reached.

“These updated data in HER2-positive metastatic breast cancer are exciting in that DS-8201 is showing potential in treating patients who have progressed on several other HER2-targeting agents,” said Shanu Modi, MD, Breast Medical Oncologist, Memorial Sloan Kettering Cancer Center and study investigator. “Additionally, the results seen in patients with HER2 low-expressing breast cancer are compelling and could challenge how we define HER2-positive breast cancer with regards to ADC therapy. Clearly, further study of DS-8201 is warranted in both these types of HER2-expressing breast cancer.”

“These data add to the growing evidence that underscore the potential of our smart chemotherapy DS-8201 to treat HER2-expressing breast cancer,” said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. “While we already have advanced DS-8201 into a pivotal phase 2 trial for HER2-positive metastatic breast cancer, we are exploring next steps for the development of DS-8201 in HER2 low-expressing breast cancer.”

Combined preliminary safety data for both HER2 low-expressing and HER2-positive breast cancer subgroups were reported. The most common adverse events (>30 percent any grade) included nausea (73.0 percent), decreased appetite (55.7 percent), alopecia (40.0 percent), vomiting (39.1 percent), anemia (34.8 percent), diarrhea (33.9 percent) and constipation (30.4 percent). Grade 3 adverse events occurring in >10 percent of patients included decreased neutrophil count (10.4 percent) and decreased white blood cell count (10.4 percent). Grade 4 adverse events included decreased neutrophil count (4.3 percent), decreased platelet count (2.6 percent) and anemia (0.9 percent). Two cases of potential Grade 5 pneumonitis have been reported and will be assessed by an interstitial lung disease (ILD) adjudication committee.

Unmet Need in HER2-Expressing Metastatic Breast Cancer

About one in five breast 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 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 IHC test results are reported as: 0, IHC1+, IHC2+ or IHC3+.¹ A finding of IHC3+ is considered HER2-positive.¹ A finding of IHC2+ is borderline and typically is confirmed by a positive FISH test.¹

Several unmet needs remain today in HER2-expressing metastatic breast cancer. Many 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-DM1.² Additionally, there are no anti-HER2 therapies indicated for HER2 low-expressing tumors (IHC2+/FISH- or IHC1+).

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. In the dose expansion part of the phase 1 study, DS-8201 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. 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](https://clinicaltrials.gov).

About DS-8201

DS-8201 is the lead product in the 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 phase 2 clinical development for HER2-positive unresectable and/or metastatic breast cancer resistant or refractory to T-DM1 ([DESTINY-Breast01](#)), 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 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 or 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 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.

Contact

Jennifer Brennan

Daiichi Sankyo, Inc.

jbrennan2@dsi.com

+1 908 992 6631 (office)

+1 201 709 9309 (mobile)

References

1. American Cancer Society. Breast Cancer Overview. 2016.
2. NCCN Guidelines. Breast Cancer. Version 2.2017.