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Press Release

Daiichi Sankyo Presents Late-Breaking Phase 1 Data for Novel Investigational HER2-Targeting Antibody Drug Conjugate DS-8201a in T-DM1 Pre-Treated Breast Cancer at the ESMO 2016 Congress

- *Results of first of two-part phase 1 study demonstrate that DS-8201a was well-tolerated with no dose-limiting toxicities*
- *Overall preliminary efficacy results report an objective response rate of 35 percent and a disease control rate of 90 percent in HER2 expressing breast and gastric cancer patients*
- *In a subgroup analysis, preliminary efficacy results report an objective response rate of 42 percent and a disease control rate of 92 percent in T-DM1 treated HER2+ breast cancer*
- *Daiichi Sankyo will be advancing DS-8201a to the second part of the phase 1 study examing the safety and efficacy of DS-8201a in four different HER2 expressing cohorts*

Tokyo, Japan, Parsippany, NJ, and Munich, Germany – (October 9, 2016) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced safety and preliminary efficacy data from a phase 1 study of DS-8201a, a novel investigational HER2-targeting antibody drug conjugate, which suggest that it was well-tolerated with no dose-limiting toxicities. These results, from the dose escalation part of a two-part phase 1 study of DS-8201a, will be presented today during a late-breaking poster discussion session at the ESMO 2016 Congress, the annual meeting of the European Society for Medical Oncology (ESMO).

DS-8201a is an investigational antibody drug conjugate comprised of a humanized anti-HER2 antibody attached by a peptide linker to a novel topoisomerase I inhibitor (DXd) payload, utilizing Daiichi Sankyo's proprietary payload and linker-payload technology.

Preliminary overall efficacy results in 20 evaluable patients demonstrated an objective response rate of 35 percent (seven partial responses) and disease control rate of 90 percent, including 12 patients previously treated with ado-trastuzumab emtansine (T-DM1) and five patients with HER2 low expression (IHC2+/FISH- or IHC1+). In 15 patients with HER2+ disease defined as IHC3+ or IHC2+/FISH+, the disease control rate was 100 percent. Seventeen patients are still on treatment, and five of the first 10 patients have been under active treatment (0.8 to 6.4 mg/kg) for more than 24 weeks. Median progression free survival has not been reached.

"Despite recent advances in treating HER2+ breast and gastric cancer, there still remains a large unmet need for patients with HER2+ disease whose tumors are no longer controlled by currently approved targeted HER2 treatments or for tumors that express low HER2," said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. "These preliminary results are compelling and warrant further clinical evaluation of DS-8201a in several different patient populations expressing HER2."

"The components that make up DS-8201a are unique from any other antibody drug conjugate currently in clinical development and may explain the clinical activity observed at such an early phase of development," said José Baselga, MD, PhD, Physician-in-Chief and Chief Medical Officer at Memorial Sloan Kettering Cancer Center, New York, NY. "While the results of this study provide important preliminary proof-of-concept for the novel mechanism of action of DS-8201a, additional research will be needed to further confirm these findings."

A total of 22 patients (16 breast cancer, 5 gastric cancer, 1 gastroesphageal junction adenocarcinoma) were treated in the dose escalation part of the study. The maximum tolerated dose was not reached (0.8-8.0 mg/kg given every three weeks) and there have been no dose-limiting toxicities at pharmacologically-active exposure and a favorable pharmacokinetic profile. Seven grade 3 adverse events were seen in three patients (1 hypokalemia, 1 anemia, 1 neutrophil count decreased, 2 lymphocyte count decrease, 1 ALP increase and 1 cholangitis). Most common adverse events were mild or moderate gastrointestinal and hematological events.

HER2+ Breast Cancer Subgroup Analyses

A total of 18 patients enrolled in the study received one or more prior anti-HER2 therapies (18 received trastuzumab, 13 ado-trastuzumab emtansine, 5 pertuzumab, 4 lapatinib). In 12 evaluable HER2+ breast cancer patients previously treated with ado-tratuzumab emtansine (T-DM1), the objective response rate was 42 percent with a disease control rate of 92 percent.

"It is impressive that DS-8201a showed activity in these patients since many were heavily pre-treated with more than one HER2-targeting agent including T-DM1, and some with very substantial tumor load or large tumors," said Kenji Tamura, MD, PhD, Chairman, Department of Breast and Medical Oncology, National Cancer Center Hospital, Tokyo, Japan and lead investigator of the study. "This finding will be further evaluated in the second part of this study where one cohort will include only advanced breast cancer patients previously treated with T-DM1."

About DS-8201a

Pre-clinical models have demonstrated that DS-8201a has a unique mechanism of action (MOA) where it selectively binds to the HER2 receptor on a tumor cell surface, triggering an antibody-dependent cell cytotoxic (ADCC) response.[1] DS-8201a is then internalized via endocytosis (transportation into cells by an energy-using process) and the intracellular lysosomal enzymes break down the peptide to release the DXd payload, which then inhibits topoisomerase I activity, causing DNA damage and cell death.[1]

The linker-payload combination of DS-8201a allows for a higher drug-to-antibody ratio (DAR) of about 8 compared to a DAR of about 3.5 seen with ado-trastuzumab emtansine (T-DM1).[1] The higher DAR of DS-8201a may help target low expressing HER2 tumors by supplying more payload per antibody to a tumor.[1]

About the DS-8201a Phase 1 Study

DS-8201a, given as an intravenous infusion every three weeks, is currently being evaluated in an open-label two-part phase 1 study in patients with advanced/unresectable or metastatic breast cancer, gastric or gastroesophageal junction adenocarcinoma, or other solid tumors that is/are refractory to or intolerable with standard treatment or for which no standard treatment is available.

The primary objective of part 1 of the study (dose escalation) is to assess the safety and tolerability of DS-8201a and determine the maximum tolerated dose (MTD). Secondary objectives include evaluating the pharmacokinetics, efficacy and human anti-human antibody (HAHA) against DS-8201a.

The second part (dose expansion) of the ongoing phase 1 clinical trial is enrolling patients in Japan and the United States into one of four cohorts: patients with HER2+ breast cancer previously treated with T-DM1; patients with HER2+ gastric or gastroesophageal junction adenocarcinoma previously treated with trastuzumab; patients with HER2 low expressing breast cancer; and patients with other solid cancers that express HER2. For more information about the study visit ClinicalTrials.gov.

Unmet Need in HER2+ Metastatic Breast Cancer

HER2 (known as human epidermal growth factor receptor 2) is a tyrosine kinase receptor growth-promoting protein found on the surface of some cancer cells.[2] About one in five breast cancers overexpress the *HER2/neu* gene, which causes these cancers to grow more aggressively.[2] To be considered HER2+, cancer cells are tested by one of two methods: immunohistochemistry (IHC) or fluorescent in situ hybridization (FISH).[2] IHC test results are reported as: 0, IHC1+, IHC2+ or IHC3+. A finding of IHC3+ is considered HER2+.[2] A finding of IHC2+ is borderline and typically is confirmed by a positive FISH test.[2]

Several unmet needs remain today in HER2+ metastatic breast cancer. Many tumors advance to the point where no currently approved HER2-targeted treatment continues to control the disease.[3] Additionally, there are no existing options indicated for HER2 low expressing tumors (IHC2+/FISH- or IHC1+) as well as HER2 heterogeneously expressing tumors (tumors with some tumor cells having high HER2 expression and some having low HER2 expression), which generally have poor prognosis.[1,4]

About Daiichi Sankyo Cancer Enterprise

The vision of Daiichi Sankyo Cancer Enterprise is to push beyond traditional thinking to align world-class science to create innovative treatments for patients with cancer. The oncology pipeline of Daiichi Sankyo continues to grow and currently includes more than 20 small molecules and monoclonal antibodies with novel targets in both solid and hematological cancers. Compounds in phase 3 development include: quizartinib, an oral FLT3-ITD inhibitor, for newly-diagnosed and relapsed/refractory FLT3-ITD+ acute myeloid leukemia (AML); pexidartinib, an oral CSF-1R inhibitor, for tenosynovial giant cell tumor (TGCT), also known as pigmented villonodular synovitis (PVNS) and giant cell tumor of the tendon sheath (GCT-TS), which also is being investigated in combination with anti-PD1 immunotherapy, pembrolizumab, in a range of solid tumors;

and tivantinib, an oral MET inhibitor, for second-line treatment in patients with MET-high hepatocellular carcinoma in partnership with ArQule, Inc.

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 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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