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Press Release

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Daiichi Sankyo Announces [Fam-] Trastuzumab Deruxtecan Demonstrated Clinically Meaningful Response in Patients with Refractory HER2 Positive Metastatic Breast Cancer, a Population with High Unmet Need

- Pivotal phase 2 DESTINY-Breast01 trial met primary endpoint, supporting global regulatory submission plan to start in first half of fiscal year 2019

Tokyo, Munich, and Basking Ridge, NJ – (May 8, 2019) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca today announced positive topline results for the pivotal phase 2 DESTINY-Breast01 trial of [fam-] trastuzumab deruxtecan (DS-8201). The HER2 targeting antibody drug conjugate (ADC) was evaluated in patients with HER2 positive unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine (T-DM1).

The response rate in DESTINY-Breast01, as assessed by an independent review committee, confirms in a heavily-pretreated global patient population the unprecedented clinical activity in the recently published phase 1 trial. The safety and tolerability profile of [fam-] trastuzumab deruxtecan was also consistent with previous experience. These results are expected to support planned global regulatory submissions, including the Biologics License Application with the U.S. Food and Drug Administration (FDA) anticipated in the first half of fiscal year 2019.

DESTINY-Breast01 is a pivotal phase 2, open-label, global, multicenter, two-part trial of [fam-] trastuzumab deruxtecan. The optimal dose of 5.4 mg/kg was previously identified in part one of the trial. Today's results from part two evaluated the efficacy and safety of that dose in patients who have failed or discontinued previous treatment with T-DM1.

"These results confirm our commitment to pursue accelerated regulatory pathways in HER2 positive metastatic breast cancer with [fam-] trastuzumab deruxtecan," said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. "We are more dedicated than ever to our comprehensive and ambitious development strategy evaluating the potential across a spectrum of HER2 expressing cancers including breast, gastric, lung and colorectal."

"We are encouraged to see positive data from [fam-] trastuzumab deruxtecan, with the DESTINY-Breast01 trial now reinforcing what earlier data have shown," said José Baselga, Executive Vice President and President R&D Oncology, AstraZeneca. "We believe this antibody drug conjugate has the

potential to redefine the treatment of patients with HER2 expressing cancers, and we are eager to bring it as quickly as possible to patients with refractory HER2 positive breast cancer who continue to have high unmet medical need."

[Fam-] trastuzumab deruxtecan has been granted U.S. FDA Breakthrough Therapy Designation and Fast Track Designation for HER2 positive patients in the advanced or refractory breast cancer setting. A recent publication in *The Lancet Oncology* reported long-term phase 1 safety and preliminary efficacy results in HER2 positive metastatic breast cancer. This investigational agent is currently in development for the treatment of multiple HER2 expressing cancers, including in patients with HER2 low expression.

Daiichi Sankyo and AstraZeneca plan to present the data from DESTINY-Breast01 at an upcoming medical meeting.

About HER2

HER2 is a tyrosine kinase receptor growth-promoting protein found on the surface of some cancer cells that is associated with aggressive disease and poorer prognosis in breast cancer patients.[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). IHC test results are reported as: 0, IHC 1+, IHC 2+, or IHC 3+.[1] A finding of IHC 3+ and/or FISH amplification is considered positive.[1] There are currently no targeted therapies for HER2 FISH negative, IHC 2+ or IHC 1+ tumors.

Unmet Need in HER2 Positive Breast Cancer

Approximately one in five breast cancers are HER2 positive.[2] Several unmet treatment needs remain today in HER2 positive metastatic breast cancer. Many HER2 positive breast cancers eventually advance to the point where no currently approved HER2 targeting medicine continues to control the disease;[3] after treatment with trastuzumab, pertuzumab, and T-DM1, optimal treatment is less clearly defined, and choices may be limited.[4]

About DESTINY-Breast01

DESTINY-Breast01 is a pivotal phase 2, open-label, global, multicenter, two-part trial evaluating the safety and efficacy of [fam-] trastuzumab deruxtecan in patients with HER2 positive unresectable and/or metastatic breast cancer previously treated with T-DM1. The primary endpoint of the trial is objective response rate. Secondary objectives include duration of response, disease control rate, clinical benefit rate, progression-free survival and overall survival.

The first part of the trial includes a pharmacokinetic stage and a dose-finding stage to identify the recommended dose of [fam-] trastuzumab deruxtecan to be evaluated in the second part of the trial. The second part enrolled patients into one of two cohorts: patients resistant or refractory to T-DM1 (part 2a)

and patients who discontinued treatment with T-DM1 for reasons other than resistant or refractory disease (part 2b). Enrollment into DESTINY-Breast01 was completed in September 2018 with 253 patients at more than 100 sites across North America, Europe, Japan and other countries in Asia.

The safety and tolerability profile of [fam-] trastuzumab deruxtecan in DESTINY-Breast01 was consistent with the recently published phase 1 trial, in which the most common adverse events (≥30 percent, any grade) included nausea, decreased appetite, vomiting, alopecia, fatigue, anemia, diarrhea, and constipation. Cases of drug-related pneumonitis, including grade 5 events, have also been reported in the clinical development program.

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 and the most advanced program in AstraZeneca's ADC Scientific platform. 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 DXd 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, including five pivotal trials in HER2 expressing breast and gastric cancers, including in breast cancer patients with HER2 low expression. [Fam-] trastuzumab deruxtecan is also in phase 2 development for HER2 expressing advanced colorectal cancer and metastatic non-squamous HER2 overexpressing or HER2 mutated NSCLC, and phase 1 development in combination with nivolumab for HER2 expressing metastatic breast and bladder cancers.

[Fam-] trastuzumab deruxtecan was granted Breakthrough Therapy Designation in 2017 by the U.S. FDA 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. Fast Track Designation was also granted in the U.S. for the treatment of HER2 positive unresectable and/or metastatic breast cancer in patients who have progressed after prior treatment with HER2 targeted medicines, including T-DM1. 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.

[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 the Collaboration between Daiichi Sankyo and AstraZeneca

In March 2019, Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize [fam-] trastuzumab deruxtecan as a medicine worldwide, except in Japan where Daiichi Sankyo will maintain exclusive rights. Daiichi Sankyo will be solely responsible for manufacturing and supply.

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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References:
[1] American Cancer Society (ACS) Breast Cancer Overview 2018
[2] Goddard KAB et al. Public Health Genomics. 2012. 15;1-10.
[3] de Melo Gagliato D, et al. Oncotarget. 2017. 7,39: 64431-46.
[4] NCCN Guidelines. Breast Cancer. Version 3.2018. October 25, 2018.