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# Press Release

# Daiichi Sankyo Initiates Pivotal Phase 3 Trial of [Fam-] Trastuzumab Deruxtecan (DS-8201) in HER2 Low Metastatic Breast Cancer

- DESTINY-Breast04 to evaluate [fam-] trastuzumab deruxtecan (DS-8201) versus investigator's choice in HER2 low, unresectable and/or metastatic breast cancer previously treated with standard chemotherapy
- No anti-HER2 therapies are currently approved for HER2 low expressing breast cancer, which represents over 40 percent of all breast cancers
- There are now three phase 3 studies underway with [fam-] trastuzumab deruxtecan in HER2 expressing metastatic breast cancer, part of the broad global development program in multiple HER2 expressing tumors

**Tokyo, Munich, and Basking Ridge, NJ – (January 14, 2019)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that the first patient has been dosed in DESTINY-Breast04, a global pivotal phase 3 study evaluating the safety and efficacy of [fam-] trastuzumab deruxtecan (DS-8201), an investigational HER2 targeting antibody drug conjugate (ADC), in patients with HER2 low, unresectable and/or metastatic breast cancer previously treated with standard chemotherapy.

Over 40 percent of all breast cancers express low levels of HER2 as a cell surface antigen (IHC 2+/ISH- or IHC 1+), but no anti-HER2 therapies are currently approved for these low expressing tumors.[1,2] In current clinical practice, these patients are classified and treated according to guidelines for HER2 negative breast cancer and according to the hormone receptor (HR) status.[2] Many patients eventually progress on current treatments to a point where limited options are available.[1] For HER2 negative, HR positive breast cancer, guidelines recommend endocrine therapy plus a cyclin-dependent kinase (CDK) 4/6 inhibitor, and, if tumors become resistant, physician's choice of single-agent chemotherapies is recommended.[2] For HER2 negative, HR negative breast cancer ("triple negative"), treatment is typically with physician's choice of single-agent chemotherapies.[1]

"DESTINY-Breast04 has been initiated based on preliminary phase 1 study results to determine whether [fam-] trastuzumab deruxtecan could serve as a targeted therapy option for patients with HER2 low metastatic breast cancer that progresses after standard chemotherapy, regardless of HR status," said Gilles Gallant, BPharm, PhD, Vice President, DS-8201 Global Team Leader, Oncology Research and Development, Daiichi Sankyo. "HER2 targeting agents have improved survival rates for HER2 positive breast cancer, but none have been approved in HER2 low expressing tumors. DESTINY-Breast04, our third phase 3 breast cancer trial with [fam-] trastuzumab deruxtecan, has potential to define a new patient population for HER2 targeted treatment."

**About DESTINY-Breast04**

DESTINY-Breast04 is a randomized, active-controlled, open-label, multicenter, two-arm, global phase 3 trial designed to compare the safety and efficacy of [fam-] trastuzumab deruxtecan versus investigator's choice (capecitabine, eribulin, gemcitabine, paclitaxel, or nab-paclitaxel) in patients with HER2 low, unresectable and/or metastatic breast cancer previously treated with one to two prior lines of chemotherapy. Patients will be confirmed as low HER2 expression (defined as IHC 2+/ISH- or IHC 1+) through evaluation at a central laboratory.

The primary efficacy endpoint of DESTINY-Breast04 is progression-free survival based on blinded independent central review. Secondary efficacy endpoints include progression-free survival based on investigator assessment, overall survival, objective response rate and duration of response. Safety endpoints include serious adverse events, treatment-emergent adverse events and adverse events of special interest. Health economics and outcomes research endpoints as well as pharmacokinetic and biomarker endpoints will also be measured.

DESTINY-Breast04 will enroll up to 540 patients at approximately 160 sites in regions including, but not limited to, North America, Western Europe, and Asia. For more information about the study, visit ClinicalTrials.gov.

**Unmet Need in HER2 Low Expressing Breast Cancer**

Breast cancer is the most common cancer and the most common cause of cancer mortality among women worldwide.[3] There were approximately 1.67 million new cases of breast cancer diagnosed in 2012.[3] Appromixately one in five breast cancers (20 percent) are HER2 positive (IHC 3+ or IHC 2+/ISH+).[4] 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.[5,6] A number of HER2 targeting therapies are approved to treat HER2 positive metastatic breast cancer and have improved survival rates.[7] The remaining 80 percent of breast cancers are classified as HER2 negative; however, over 40 percent still express some level of HER2 as a cell surface antigen and as measured by immunohistochemistry (IHC).[1] No anti-HER2 agents are indicated for these low expressing tumors, which may be defined as IHC 2+/ISH- or IHC 1+.[2]

**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. 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, [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. In addition to DESTINY-Breast04, [fam-] trastuzumab deruxtecan is in phase 3 development versus ado-trastuzumab emtansine (T-DM1) (DESTINY-Breast03) and versus investigator's choice post T-DM1 (DESTINY-Breast02) for HER2 positive metastatic breast cancer; pivotal phase 2 development for HER2 positive metastatic breast cancer resistant or refractory to T-DM1 (DESTINY-Breast01); pivotal phase 2 development for HER2 positive advanced gastric cancer resistant or refractory to trastuzumab (DESTINY-Gastric01); phase 2 development for HER2 expressing advanced colorectal cancer; phase 2 development for metastatic non-squamous HER2 overexpressing or HER2 mutated NSCLC; and, phase 1 development in combination with nivolumab for HER2 expressing metastatic breast and bladder cancer.

[Fam-] trastuzumab deruxtecan 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 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). [Fam-] 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 (MHLW).

[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 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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