Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

Press Release

Daiichi Sankyo Initiates Two Phase 3 Trials of [Fam-] Trastuzumab Deruxtecan (DS-8201) in Patients with HER2 Positive Metastatic Breast Cancer including Head-to-Head Versus T-DM1 and Post-T-DM1 Study

- DESTINY-Breast03 to compare [fam-] trastuzumab deruxtecan (DS-8201) versus ado-trastuzumab emtansine (T-DM1) in HER2 positive, unresectable and/or metastatic breast cancer previously treated with trastuzumab and taxane
- DESTINY-Breast02 to evaluate [fam-] trastuzumab deruxtecan versus investigator's choice in HER2 positive, unresectable and/or metastatic breast cancer previously treated with standard of care HER2 therapies including T-DM1
- Enrollment into pivotal phase 2 DESTINY-Breast01 study of [fam-] trastuzumab deruxtecan in HER2 positive unresectable and/or metastatic breast cancer previously treated with T-DM1 is complete

Tokyo, Munich, and Basking Ridge, NJ– (September 25, 2018) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that the first patients have been dosed in DESTINY-Breast03 and DESTINY-Breast02, two global phase 3 studies evaluating the safety and efficacy of [fam-] trastuzumab deruxtecan (DS-8201), an investigational HER2 targeting antibody drug conjugate (ADC), in patients with previously-treated HER2 positive unresectable and/or metastatic breast cancer. DESTINY-Breast03 will be a head-to-head comparison of [fam-] trastuzumab deruxtecan versus ado-trastuzumab emtansine (T-DM1), also a HER2 targeting ADC, while DESTINY-Breast02 will assess [fam-] trastuzumab deruxtecan in patients previously treated with standard of care HER2 therapies including T-DM1.

Current treatment guidelines for patients with HER2 positive metastatic breast cancer recommend the combination of trastuzumab, pertuzumab and a taxane as first-line therapy.[1,2] For patients whose cancer progresses after initial treatment, T-DM1 is an anti-HER2 agent specifically approved for second-line therapy.[1] For cancers that progress after HER2 targeted agents trastuzumab, pertuzumab and T-DM1, there is no specific standard of care. Options for these patients are standard chemotherapy with or without continued anti-HER2 therapy and consideration of palliative care.[1]

"The DESTINY-Breast03 trial is a key element of our comprehensive development strategy to determine the potential of [fam-] trastuzumab deruxtecan as a second-line therapy in patients with HER2 positive metastatic breast cancer," said Gilles Gallant, BPharm, PhD, Vice President, DS-8201 Global Team Leader, Oncology Research and Development, Daiichi Sankyo. "DESTINY-Breast03 will also help assess whether our investigational and proprietary ADC linker and payload technology used in [fam-] trastuzumab deruxtecan demonstrates clinical relevance when compared to another HER2 targeting ADC currently approved in this setting."

Enrollment into DESTINY-Breast01, the pivotal phase 2 trial evaluating [fam-] trastuzumab deruxtecan in HER2 positive unresectable and/or metastatic breast cancer resistant or refractory to T-DM1 was completed in September 2018, with approximately 230 patients at more than 100 sites in North America, Europe, Japan and other countries in Asia.

About DESTINY-Breast03

DESTINY-Breast03 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 T-DM1 in patients with HER2 positive unresectable and/or metastatic breast cancer previously treated with trastuzumab and a taxane.

The primary efficacy endpoint of DESTINY-Breast03 is progression-free survival based on blinded independent central review. Secondary efficacy endpoints include overall survival, objective response rate, duration of response, clinical benefit rate and progression-free survival based on investigator assessment. Safety endpoints include serious adverse events, treatment-emergent adverse events and adverse events of special interest. Exploratory efficacy endpoints include duration of stable disease and time to response. Health economics and outcomes research endpoints as well as pharmacokinetic and biomarker endpoints will also be measured.

DESTINY-Breast03 will enroll approximately 500 patients at 150 study sites in North America, Asia and Europe. For more information about the study, visit ClinicalTrials.gov.

About DESTINY-Breast02

DESTINY-Breast02 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 (trastuzumab plus capecitabine or lapatinib plus capecitabine) in patients with HER2 positive unresectable and/or metastatic breast cancer previously treated with standard of care HER2 therapies including T-DM1.

The primary efficacy endpoint of DESTINY-Breast02 is progression-free survival based on blinded independent central review. Secondary efficacy endpoints include overall survival, objective response rate, duration of response, clinical benefit rate and progression-free survival based on investigator assessment. 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-Breast02 will enroll up to 600 patients at approximately 160 study sites in North America, South America, Europe and Asia. For more information about the study, visit ClinicalTrials.gov.

About DESTINY-Breast01

DESTINY-Breast01 is a pivotal phase 2, open-label, global, multicenter, two-part study 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 study 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 study 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 study. The second part of the study 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). For more information about this study, visit ClinicalTrials.gov.

Unmet Need in HER2 Positive Metastatic Breast Cancer

Breast cancer is the second most common cancer worldwide, responsible for approximately 1.67 million of 14.1 million new cases of cancer diagnosed each year.[4] Despite improving survival rates over the past 25 years, breast cancer was the fifth leading cause of cancer death overall and was the number one cause of cancer death in women in 2012.[3,4] For patients diagnosed with metastatic breast cancer, five-year survival rates are low.[5]

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.[4] Several unmet needs remain today in HER2 positive 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.[1,6]

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-Breast03 and DESTINY-Breast02 phase 3

trials, [fam-] trastuzumab deruxtecan is in pivotal phase 2 clinical development for HER2 positive metastatic breast cancer resistant or refractory to ado-trastuzumab emtansine (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 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). [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. 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. NCCN Guidelines. Breast Cancer. Version 2. 2017.
2. Baselga J, et al. N Engl J Med. 2012;366(2):109-19.
3. Ferlay J, et al. J Cancer. 2015;136(5):E359-86.
4. Sledge, et al. J Clin Oncol. 2014;32:1-8.
5. American Cancer Society. Breast Cancer Overview. 2018.
6. Cardoso F, et al. 3rd ESO-ESMO International Consensus Guidelines for Breast. 2017;31:244-259.