

## Press Release

# Daiichi Sankyo Confirms Plans to Accelerate BLA Submission to U.S. FDA for [Fam-] Trastuzumab Deruxtecan (DS-8201) in HER2 Positive Metastatic Breast Cancer Post T-DM1

- BLA submission to U.S. FDA for [fam-] trastuzumab deruxtecan in HER2 positive metastatic breast cancer previously treated with T-DM1 to be accelerated to first half of fiscal year 2019
- Data from pivotal phase 2 DESTINY-Breast01 study, which will be presented at upcoming medical meeting, to form basis of BLA submission
- [Fam-] trastuzumab deruxtecan has been granted U.S. FDA 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

**Tokyo, Munich, and Basking Ridge, NJ – (March 28, 2019)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced plans to accelerate filing of the Biologics License Application (BLA) with the U.S. Food and Drug Administration (FDA) for [fam-] trastuzumab deruxtecan (DS-8201), an investigational HER2 targeting antibody drug conjugate (ADC), in patients with HER2 positive metastatic breast cancer previously treated with ado trastuzumab emtansine (T-DM1). Submission of the application, which was originally planned for 2020, is now scheduled for the first half of fiscal year 2019.

“We are pleased to confirm the acceleration of the [fam-] trastuzumab deruxtecan clinical development program for this potential indication in patients with HER2 positive metastatic breast cancer pretreated with T-DM1 ahead of schedule,” said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. “Simultaneously, we are committed to our aggressive development strategy evaluating the potential of [fam-] trastuzumab deruxtecan across a spectrum of HER2 expressing cancers including breast, gastric, lung and colorectal.”

[Fam-] trastuzumab deruxtecan has been granted U.S. FDA Breakthrough Therapy 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. The initial BLA submission of [fam-] trastuzumab deruxtecan will be based on results from the pivotal phase 2 [DESTINY-Breast01](#) study, which will be presented at an upcoming medical conference. Final determination of exact timing of the BLA submission of [fam-] trastuzumab deruxtecan will be based on the outcome of a pre-BLA meeting with the FDA.

## **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).

Enrollment into DESTINY-Breast01 was completed in September 2018, with approximately 230 patients at more than 100 sites in North America, Europe, Japan and other countries in Asia. For more information about this study, visit [ClinicalTrials.gov](https://clinicaltrials.gov).

## **Unmet Need in HER2 Positive Breast Cancer**

Breast cancer is the most common cancer and the most common cause of cancer mortality in women worldwide; there were an estimated 2.1 million new cases of female breast cancer diagnosed in 2018.<sup>1</sup> Approximately one in five breast cancers (20 percent) are HER2 positive (IHC3+ or IHC2+/ISH+).<sup>2,3</sup> 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.<sup>4,5</sup> To be considered HER2 positive, tumor cancer cells are usually tested first by immunohistochemistry (IHC) and reported as: 0, IHC 1+, IHC 2+ or IHC 3+. A finding of IHC 3+ is considered HER2 positive, and a finding of IHC 2+ is borderline and typically is confirmed by a positive fluorescent in situ hybridization (FISH) test.<sup>3,4</sup>

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 therapy continues to control the disease, and there is no established standard of care after treatment with trastuzumab, pertuzumab and T-DM1.<sup>6</sup>

## **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 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 studies. [Fam-] trastuzumab deruxtecan is in pivotal phase 3 development in previously treated HER2 low expressing metastatic breast cancer versus investigator's choice ([DESTINY-Breast04](#)); phase 3 development in HER2 positive metastatic breast cancer versus ado-trastuzumab emtansine (T-DM1) ([DESTINY-Breast03](#)); and phase 3 development in HER2 positive metastatic breast cancer versus investigator's choice post T-DM1 ([DESTINY-Breast02](#)). [Fam-] trastuzumab deruxtecan also is in pivotal phase 2 clinical 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 patients with HER2 positive unresectable and/or metastatic breast cancer 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](http://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](http://www.daiichisankyo.com).

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### References

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<sup>1</sup> Bray F. et al. Global Cancer Statistics 2018. *CA Cancer J Clin.* 2018;68:394–424

<sup>2</sup> Sledge, et al. *J Clin Oncol.* 2014; 32:1-8.

<sup>3</sup> American Cancer Society. Tests for Stomach Cancer. 2018.

<sup>4</sup> American Cancer Society (ACS) Breast Cancer Overview 2018

<sup>5</sup> Tandon et al. *J Clin Oncol.* 1989; 7: 1120–8.

<sup>6</sup> NCCN Guidelines. Breast Cancer. Version 3.2018. October 25, 2018.