

Press Release

[Fam-] Trastuzumab Deruxtecan (DS-8201) Granted FDA Priority Review for Treatment of Patients with HER2 Positive Metastatic Breast Cancer

Tokyo, Munich and Basking Ridge, NJ – (October 17, 2019) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca today announced that the U.S. Food and Drug Administration (FDA) has accepted for review the Biologics License Application (BLA) for [fam-] trastuzumab deruxtecan (DS-8201) and granted Priority Review.

The Prescription Drug User Fee Act (PDUFA) date for [fam-] trastuzumab deruxtecan, an investigational HER2 targeting antibody drug conjugate (ADC), for the treatment of patients with HER2 positive metastatic breast cancer is set for the first quarter of fiscal year 2020.

“We are pleased that the FDA has accepted the application and granted Priority Review as we believe [fam-] trastuzumab deruxtecan has the potential to redefine the treatment of patients with HER2 positive metastatic breast cancer,” said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. “Following the recent regulatory submission in Japan, we look forward to working closely with regulatory authorities to bring [fam-] trastuzumab deruxtecan to patients in the U.S. and Japan as soon as possible.”

“[Fam-] trastuzumab deruxtecan has the potential to transform the treatment landscape for patients with HER2 positive metastatic breast cancer who have limited treatment options,” said José Baselga, MD, PhD, Executive Vice President, Research & Development Oncology, AstraZeneca. “The priority review draws on the strength and consistency of results seen in phase 1 and phase 2 trials and is an important step on the journey to deliver this potential new medicine to patients.”

[Fam-] trastuzumab deruxtecan was previously granted U.S. FDA Breakthrough Therapy Designation and Fast Track designation. The BLA is based on the combination of data from the phase 1 trial published in *The Lancet Oncology*,¹ and the pivotal phase 2 DESTINY-Breast01 trial. The response rate observed in DESTINY-Breast01, as assessed by an independent review committee, validated the clinical activity observed in the phase 1 trial. Detailed data from DESTINY-Breast01 will be presented at the forthcoming San Antonio Breast Cancer Symposium in December.

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

About HER2 Positive Breast Cancer

Approximately one in five breast cancers are HER2 positive.^{2,3} Despite recent improvements and approvals of new medicines, there remains significant clinical needs for patients with advanced HER2 positive metastatic breast cancer.^{4,5} This disease remains incurable with patients eventually progressing after available treatment.^{4,5} Additionally, there are currently no approved HER2 targeted medicines for HER2 FISH negative, IHC 2+ or IHC 1+ tumors.

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 trastuzumab emtansine. The primary endpoint of the trial is objective response rate, as determined by independent central review. Secondary objectives include, duration of response, disease control rate, clinical benefit rate, progression-free survival, and overall survival. 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 phase 1 trial data published in *The Lancet Oncology*, 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 interstitial lung disease (ILD) and 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 comprehensive development program is underway in North America, Europe and Asia, including five pivotal trials in HER2 expressing metastatic breast and gastric cancers, including a trial in patients with metastatic breast cancer and low levels of HER2 expression. Phase 2 trials are underway for HER2 expressing advanced colorectal cancer as well as metastatic non-squamous HER2 overexpressing or HER2 mutated non-small cell lung cancer. Trials in combination with other anticancer treatments, such as immunotherapy, also are underway.

Regulatory submission of [fam-] trastuzumab deruxtecan was recently made to Japan's Ministry of Health, Labour and Welfare (MHLW) for the treatment of HER2 positive breast cancer. It also has received SAKIGAKE designation for the treatment of advanced HER2 positive gastric or gastroesophageal junction cancer by Japan's 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 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 potential new medicine worldwide, except in Japan where Daiichi Sankyo will maintain exclusive rights. Daiichi Sankyo will be solely responsible for the 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 pipeline, 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/immunoncology and small molecules in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley, CA. For more information, please visit: www.DSCancerEnterprise.com.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical therapies to improve standards of care and address diversified, unmet medical needs of people globally by leveraging our world-class science and technology. With more than 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 cardiovascular diseases, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo is primarily focused on providing novel therapies in oncology, as well as other research areas centered around rare diseases and immune disorders. For more information, please visit: www.daiichisankyo.com.

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³ Sledge G, *et al.* Past, Present, and Future Challenges in Breast Cancer Treatment. *J Clin Oncol.* 2014;32(19):1979-1986.

⁴ de Melo Gagliato D, *et al.* Mechanisms of Resistance and Sensitivity to Anti-HER2 Therapies in HER2+ Breast Cancer. *Oncotarget.* 2016;7(39):64431-46.

⁵ National Comprehensive Cancer Network (NCCN). NCCN Guidelines. Breast Cancer. Available at <https://nccn.org>. Accessed August 2019.