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Press Release

Trastuzumab Deruxtecan Type II Variation Application Validated by EMA for the Treatment of HER2 Positive Advanced Gastric Cancer

- Application based on DESTINY-Gastric01 and DESTINY-Gastric02 phase 2 trials

Tokyo, Munich– (November 3, 2021) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that the European Medicines Agency (EMA) has validated the Type II Variation Application for trastuzumab deruxtecan, a HER2 directed antibody drug conjugate (ADC) being jointly developed by Daiichi Sankyo and AstraZeneca (LSE/STO/Nasdaq: AZN), for the treatment of adult patients with locally advanced or metastatic HER2 positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen.

Validation confirms that the application is complete and commences the scientific review process by the EMA's Committee for Medicinal Products for Human Use (CHMP). This application is based on the positive results from the DESTINY-Gastric01 pivotal phase 2 trial published in *The New England Journal of Medicine* and the DESTINY-Gastric02 phase 2 trial recently presented at the 2021 European Society for Medical Oncology (ESMO) Congress.

"After progression on initial therapy, patients with HER2 positive advanced gastric cancer are faced with limited options in Europe, so there is a significant unmet need for new therapeutic options," said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. "We look forward to working with the EMA on its review of this application and to potentially bring trastuzumab deruxtecan to physicians and patients in Europe, as it offers the potential to provide an important new treatment option to patients with locally advanced or metastatic HER2 positive gastric or GEJ adenocarcinoma who have received a prior anti-HER2-based regimen."

About HER2 Positive Gastric Cancer

Gastric (stomach) cancer is the fifth most common cancer worldwide and the fourth highest leading cause of cancer mortality, with a five-year global survival rate of 5% to 10% for advanced or metastatic disease.[1,2,3] There were approximately one million new cases of gastric cancer and 768,000 deaths reported worldwide in 2020.[4] In Europe, approximately 136,000 cases of gastric cancer are diagnosed annually, and Eastern Europe has the second highest incidence of gastric cancer worldwide after Eastern Asia.[3,4] Gastric cancer is the sixth

leading cause of cancer death in Europe, and is typically diagnosed in the advanced stage but even when diagnosed in earlier stages of the disease the survival rate remains modest.[3,5,6,7]

Approximately one in five gastric cancers are HER2 positive.[8,9] HER2 is a tyrosine kinase receptor growth promoting protein expressed on the surface of many types of tumors including breast, gastric, lung and colorectal cancers.[9] HER2 overexpression may be associated with a specific HER2 gene alteration known as HER2 amplification.[9]

Recommended first-line treatment for HER2 positive advanced or metastatic gastric cancer is combination chemotherapy plus trastuzumab, an anti-HER2 medicine, which has been shown to improve survival outcomes when added to chemotherapy.[10] For patients with metastatic gastric cancer that progress following initial treatment with a trastuzumab-based regimen, treatment options are limited, and in many regions in the world there are no additional HER2 directed medicines available.[1,5, 11]

About DESTINY-Gastric01

DESTINY-Gastric01 is a pivotal, randomized, open-label, multi-center phase 2 trial assessing the safety and efficacy of trastuzumab deruxtecan (6.4 mg/kg) in patients from Japan and South Korea with HER2 positive (defined as IHC3+ or IHC2+/ISH+) advanced gastric cancer or gastroesophageal junction adenocarcinoma who have progressed on two or more prior treatment regimens including fluoropyrimidine (5-FU), platinum chemotherapy and trastuzumab. Patients were randomized 2:1 to receive trastuzumab deruxtecan or physician's choice of chemotherapy (paclitaxel or irinotecan monotherapy). The primary endpoint of DESTINY-Gastric01 is objective response rate (ORR). Secondary endpoints include overall survival (OS), progression-free survival (PFS), duration of response (DoR), disease control rate and time to treatment failure as well as pharmacokinetic and safety endpoints. DESTINY-Gastric01 enrolled 189 patients at multiple sites in Japan and South Korea. For more information about the trial, visit ClinicalTrials.gov.

About DESTINY-Gastric02

DESTINY-Gastric02 is an open-label, single-arm, phase 2 trial in Western patients evaluating the safety and efficacy of trastuzumab deruxtecan (6.4 mg/kg) in patients with HER2 positive metastatic and/or unresectable gastric or GEJ adenocarcinoma with disease progression on or after a trastuzumab-containing regimen. The primary endpoint of DESTINY-Gastric02 is confirmed ORR based on independent central review. Secondary endpoints include PFS, OS, DoR and safety. DESTINY-Gastric02 enrolled 79 patients at multiple sites in North America and Europe. For more information about the trial, visit ClinicalTrials.gov.

About Trastuzumab Deruxtecan

Trastuzumab deruxtecan (fam-trastuzumab deruxtecan-nxki in the U.S. only) is a HER2 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC technology, trastuzumab deruxtecan is the lead

ADC in the oncology portfolio of Daiichi Sankyo and the most advanced program in AstraZeneca's ADC scientific platform. Trastuzumab deruxtecan consists of a HER2 monoclonal antibody attached to a topoisomerase I inhibitor payload, an exatecan derivative, via a stable tetrapeptide-based cleavable linker.

Trastuzumab deruxtecan (5.4 mg/kg) is approved in more than 30 countries for the treatment of adult patients with unresectable or metastatic HER2 positive breast cancer who have received two or more prior anti-HER2 based regimens based on the results from the DESTINY-Breast01 trial.

Trastuzumab deruxtecan (6.4 mg/kg) is approved in Israel, Japan, Singapore and U.S. for the treatment of adult patients with locally advanced or metastatic HER2 positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen based on the results from the DESTINY-Gastric01 trial.

About the Trastuzumab Deruxtecan Clinical Development Program

A comprehensive global development program is underway evaluating the efficacy and safety of trastuzumab deruxtecan monotherapy across multiple HER2 targetable cancers including breast, gastric, lung and colorectal cancers. Trials in combination with other anticancer treatments, such as immunotherapy, are also underway.

Trastuzumab deruxtecan was highlighted in the Clinical Cancer Advances 2021 report as one of two significant advancements in the "ASCO Clinical Advance of the Year: Molecular Profiling Driving Progress in GI Cancers," based on data from both the DESTINY-Gastric01 and DESTINY-CRC01 trials, as well as one of the targeted therapy advances of the year in non-small cell lung cancer (NSCLC) based on the interim results of the *HER2* mutated cohort of the DESTINY-Lung01 trial.

Trastuzumab deruxtecan recently received its fourth Breakthrough Therapy Designation (BTD) in the U.S., which was for the treatment of adult patients with unresectable or metastatic HER2 positive breast cancer who have received one or more prior anti-HER2-based regimens.

About the Daiichi Sankyo and AstraZeneca Collaboration

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize trastuzumab deruxtecan in March 2019 and datopotamab deruxtecan (Dato-DXd) in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights for each ADC. Daiichi Sankyo is responsible for the manufacturing and supply of trastuzumab deruxtecan and datopotamab deruxtecan.

About Daiichi Sankyo in Oncology

The oncology portfolio of Daiichi Sankyo is powered by our team of world-class scientists that push beyond traditional thinking to create transformative medicines for people with cancer. Anchored by our DXd antibody drug conjugate (ADC) technology, our research engines include biologics, medicinal chemistry, modality and other research laboratories in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in the U.S. We also work alongside leading academic and business collaborators to further advance the understanding of cancer as Daiichi Sankyo builds towards our ambitious goal of becoming a global leader in oncology by 2025.

About Daiichi Sankyo

Daiichi Sankyo is dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose "to contribute to the enrichment of quality of life around the world." In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases with high unmet medical needs. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 16,000 employees around the world draw upon a rich legacy of innovation to realize our 2030 Vision to become an "Innovative Global Healthcare Company Contributing to the Sustainable Development of Society." For more information, please visit: www.daiichisankyo.com.

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