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Daiichi-Sankyo

Press Release

ENHERTU® Approved in the EU for the Treatment of HER2 Positive Metastatic Breast Cancer

- Approval based on the DESTINY-Breast01 phase 2 trial which showed clinically meaningful and durable responses in patients with previously treated disease

Tokyo and Munich – (January 20, 2021) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca's ENHERTU® (trastuzumab deruxtecan) has been granted conditional approval in the European Union (EU) as a monotherapy 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.

In Europe, approximately 531,000 cases of breast cancer in women are diagnosed annually, with an estimated one in five cases being HER2 positive.[1,2,3] The impact of the disease is significant, with breast cancer responsible for more than 141,000 deaths per year in Europe.[1]

"One in five women with breast cancer have HER2 positive disease and those with previously-treated metastatic disease often progress quickly," said Professor Fabrice André, Head of Research, Department of Medical Oncology, Gustave Roussy Cancer Campus, Villejuif, France. "One of the biggest challenges in this setting has been identifying treatment strategies that produce a durable response. The DESTINY-Breast01 trial showed a breadth, depth and durability of response not previously seen in this patient population."

Approval by the European Commission of ENHERTU on January 18 was based on positive results from the single arm, pivotal phase 2 DESTINY-Breast01 trial. After a median follow-up of 20.5 months, ENHERTU showed a confirmed objective response rate of 61.4%, including a 6.5% complete response rate and a 54.9% partial response rate, and an estimated median duration of response of 20.8 months in 184 patients with HER2 positive metastatic breast cancer who had received at least two previous lines of therapy.[4] This analysis was presented at the 2020 San Antonio Breast Cancer Symposium. A previous analysis with a median of 11.1 months of follow-up was published in *The New England Journal of Medicine* in February 2020.

The safety of ENHERTU has been evaluated in a pooled analysis of 234 patients with unresectable or metastatic HER2 positive breast cancer who received at least one dose of ENHERTU 5.4 mg/kg in clinical studies. The median duration of exposure to ENHERTU was 9.8 months (range: 0.7 to 37.1 months). The

most common adverse reactions were nausea (79.9%), fatigue (60.3%), vomiting (48.7%), alopecia (46.2%), constipation (35.9%), decreased appetite (34.6%), anemia (33.8%), neutropenia (32.5%), diarrhea (30.8%), thrombocytopenia (23.1%), cough (21.4%), leukopenia (20.5%) and headache (20.1%).

Cases of interstitial lung disease (ILD) or pneumonitis were reported in 15.0% of patients. In 2.6% of patients, ILD lead to death. Patients should be advised to immediately report cough, dyspnea, fever and/or any new or worsening respiratory symptoms. Patients should be monitored for signs and symptoms of ILD or pneumonitis and those with suspected ILD or pneumonitis should be evaluated by radiographic imaging, preferably a computed tomography (CT) scan. Patients with a history of ILD or pneumonitis may be at increased risk.

"This expedited review underscores the practice-changing potential of ENHERTU for patients in the metastatic setting," said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. "ENHERTU is the first-ever new medicine to be approved for breast cancer in Europe on the basis of phase 2 single arm data, and one of the fastest accelerated assessment procedures for an application in oncology."

"ENHERTU is already transforming outcomes for patients with HER2 positive metastatic breast cancer in the U.S. and Japan, and this approval enables us to bring the benefits of this medicine to patients in the EU," said Dave Fredrickson, Executive Vice President, Oncology Business Unit, AstraZeneca. "We will continue to explore the potential of ENHERTU in this setting, as well as in earlier lines of treatment and stages of disease, with the ambition of improving the lives of patients with HER2 targetable breast cancer."

In March 2020, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) granted ENHERTU accelerated assessment for the treatment of adults with unresectable or metastatic HER2 positive breast cancer who have received two or more prior anti-HER2 based regimens.

About HER2 Positive Breast Cancer

Approximately 531,000 cases of breast cancer are diagnosed in Europe annually, with an estimated one in five cases being HER2 positive.[1,2,3] The impact of the disease is significant, with breast cancer responsible for more than 141,000 deaths per year in Europe.[1]

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. HER2 overexpression may be associated with a

specific HER2 gene alteration known as HER2 amplification and is often associated with aggressive disease and poor prognosis in breast cancer.[5]

There remain significant unmet clinical needs for patients with HER2 positive metastatic breast cancer. The disease remains incurable with patients eventually progressing after currently available treatment options.[6,7]

About DESTINY-Breast01

DESTINY-Breast01 is a pivotal phase 2, single-arm, open-label, global, multicenter, two-part trial evaluating the safety and efficacy of ENHERTU 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.

About ENHERTU

ENHERTU® (trastuzumab deruxtecan; fam-trastuzumab deruxtecan-nxki in the U.S. only) is a HER2 directed antibody drug conjugate (ADC). Designed using Daiichi Sankyo's proprietary DXd ADC technology, ENHERTU is the lead ADC in the oncology portfolio of Daiichi Sankyo 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. ENHERTU is comprised of a humanized anti-HER2 IgG1 monoclonal antibody with the same amino acid sequence as trastuzumab attached to a topoisomerase I inhibitor payload, an exatecan derivative, via a tetrapeptide-based cleavable linker.

In addition to the approval in the EU, ENHERTU (5.4 mg/kg) is approved in the U.S., under accelerated approval, and Japan, under the conditional early approval system, as a treatment for adult patients with unresectable or metastatic HER2 positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting based on the DESTINY-Breast01 trial. ENHERTU is also approved in the U.S. and Japan (6.4 mg/kg) for the treatment of patients with HER2 positive unresectable advanced or recurrent gastric cancer that has progressed after a trastuzumab-containing regimen based on the DESTINY-Gastric01 trial.

About the ENHERTU Clinical Development Program

A comprehensive development program is underway globally, with nine pivotal trials evaluating the efficacy and safety of ENHERTU monotherapy across multiple HER2 targetable cancers, including breast, gastric

and lung cancers. Trials in combination with other anticancer treatments, such as immunotherapy, are also underway.

As part of this broad development program, ENHERTU is being assessed in several ongoing phase 3 breast cancer trials, including DESTINY-Breast02, which is evaluating ENHERTU as a third line treatment for patients with HER2 positive metastatic breast cancer; DESTINY-Breast03, which is evaluating ENHERTU versus trastuzumab emtansine as a second line treatment for the same population of patients; DESTINY-Breast04, which is evaluating ENHERTU in patients with metastatic breast cancer and low expression of HER2; and DESTINY-Breast05, which is comparing ENHERTU with trastuzumab emtansine for the adjuvant treatment of patients with high-risk HER2 positive early breast cancer with residual invasive disease following neoadjuvant treatment.

In May 2020, ENHERTU received Breakthrough Therapy Designation (BTD) for the treatment of patients with metastatic non-small cell lung cancer whose tumors have a HER2 mutation and with disease progression on or after platinum-based therapy.

About the Collaboration Between Daiichi Sankyo and AstraZeneca

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize ENHERTU (a HER2 directed ADC) in March 2019, and datopotamab deruxtecan (a TROP2 directed ADC) in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights. Daiichi Sankyo is responsible for manufacturing and supply of ENHERTU and datopotamab deruxtecan.

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: https://www.daiichisankyo.com/.

ENHERTU® is a registered trademark of Daiichi Sankyo Company, Ltd.

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