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Press Release

ENHERTU® Approved in China for Patients with HER2 Positive Metastatic Breast Cancer Treated with One or More Prior Anti-HER2-Based Regimens

- First approval for Daiichi Sankyo and AstraZeneca's ENHERTU in China
- Approval based on DESTINY-Breast03 results where ENHERTU demonstrated a 72% reduction in the risk of disease progression or death versus trastuzumab emtansine (T-DM1)

Tokyo – (February 24, 2023) – Daiichi Sankyo (TSE: 4568) and AstraZeneca's (LSE/STO/Nasdaq: AZN) ENHERTU® (trastuzumab deruxtecan) has been approved in China as a monotherapy 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.

ENHERTU is a specifically engineered HER2 directed antibody drug conjugate (ADC) being jointly developed and commercialized by Daiichi Sankyo and AstraZeneca.

In China, breast cancer is the most common cancer in women, with more than 415,000 cases diagnosed in 2020.[1] There were nearly 120,000 breast cancer deaths in China in 2020, representing approximately 18% of global breast cancer deaths.[1] Approximately one in five cases of breast cancer are considered HER2 positive.[2]

The approval by China's National Medical Products Administration (NMPA) is based on the results of the DESTINY-Breast03 phase 3 trial, where ENHERTU demonstrated a 72% reduction in the risk of disease progression or death compared to trastuzumab emtansine (T-DM1) (hazard ratio [HR] = 0.28; 95% confidence interval [CI]: 0.22-0.37; p<0.000001) in patients with HER2 positive unresectable and/or metastatic breast cancer previously treated with trastuzumab and a taxane. The median progression-free survival (PFS) for patients treated with ENHERTU was not reached (95% CI: 18.5-NE) compared to 6.8 months for T-DM1 (95% CI: 5.6-8.2) as assessed by blinded independent central review (BICR). ENHERTU was granted Breakthrough Therapy Designation and priority review in 2022 by the China NMPA for this tumor type based on these data.

"This approval marks an important day for the breast cancer community in China as patients with HER2 positive metastatic breast cancer continue to need additional treatment options," said Binghe Xu, MD, Professor and Director of the Department of Medical Oncology, Cancer Hospital and Institute Cancer

Hospital, Chinese Academy of Medical Sciences. "Despite initial treatment, patients with HER2 positive metastatic breast cancer will often experience disease progression, demonstrating the importance of early systemic disease control and the potential for ENHERTU to help eligible patients with metastatic breast cancer."

Additional results from the DESTINY-Breast03 phase 3 trial showed that confirmed objective response rate (ORR) was more than doubled in the ENHERTU arm (79.7%; n=208; 95% CI: 74.3-84.4) versus the T-DM1 arm (34.2%; n=90; 95% CI: 28.5-40.3). Complete responses (CR) were observed in 16.1% (n=42) of patients and partial responses (PR) were observed in 63.6% (n=166) of patients treated with ENHERTU compared to 8.7% (n=23) achieving CR and 25.5% (n=67) achieving PR in patients treated with T-DM1. In addition, in the secondary endpoint analysis of PFS as assessed by investigator, patients treated with ENHERTU had a median PFS of 25.1 months (95% CI: 22.1-NE) compared to 7.2 months (95% CI: 6.8-8.3) for T-DM1 (HR=0.26; 95% CI: 0.20-0.35). Overall survival (OS) was analyzed but immature at time of analysis (HR=0.55; 95% CI: 0.36-0.86). Nearly all patients treated with ENHERTU were alive at one year (94.1%; 95% CI: 90.3-96.4) compared to 85.9% of patients treated with T-DM1 (95% CI: 80.9-89.7).

"ENHERTU is extending the time before disease progression or death and helping to redefine outcomes for patients with previously treated HER2 positive metastatic breast cancer, and now physicians in China will have this important medicine as an option for their patients," said Kiminori Nagao, Head of the Asia, South and Central America (ASCA) Business Unit, Daiichi Sankyo. "With this approval, ENHERTU has the potential to become a new standard of care in China in the second line setting for patients with HER2 positive metastatic breast cancer."

"This first approval of ENHERTU in China represents a significant advance in the treatment of HER2 targetable tumors and provides the opportunity for patients with previously treated HER2 positive metastatic breast cancer to benefit from the potential of this important medicine as a second line therapy," said Dave Fredrickson, Executive Vice President, Oncology Business Unit, AstraZeneca. "The approval underscores our commitment to patients in China, where there has been an increased incidence rate of breast cancer, as we continue to explore the potential benefits of ENHERTU earlier in the treatment of HER2 directed metastatic breast cancer and across HER2 targetable cancers."

The safety profile of ENHERTU in DESTINY-Breast03 was evaluated in 257 patients with unresectable or metastatic HER2 positive breast cancer and was consistent with previous clinical trials with no new safety

concerns identified. The most common adverse events (AEs) occurring in ≥20% of patients in the ENHERTU arm were nausea (75.9%), fatigue (49.4%), vomiting (49.0%), neutropenia (42.8%), alopecia (37.0%), constipation (34.2%), anemia (32.7%), transaminases increased (31.5%), musculoskeletal pain

(31.1%), leukopenia (30.4%), decreased appetite (29.2%), diarrhea (29.2%), thrombocytopenia (25.7%), headache (21.8%) and abdominal pain (21.0%). The most common serious AEs occurring in >1% of patients were interstitial lung disease (ILD) (2.3%) and vomiting (1.9%). Discontinuation of therapy due to an adverse event occurred in 10.5% of patients treated with ENHERTU. The most frequent adverse event occurring in >2% of patients associated with permanent discontinuation was ILD (8.2%).

About DESTINY-Breast03

DESTINY-Breast03 is a global, head-to-head, randomized, open-label, pivotal phase 3 trial evaluating the efficacy and safety of ENHERTU (5.4 mg/kg) 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 PFS based on BICR. OS is a key secondary efficacy outcome measure. Other secondary endpoints include ORR, duration of response, PFS based on investigator assessment and safety. Primary results from DESTINY-Breast03 were published in *The New England Journal of Medicine* with updated PFS and OS results published in *The Lancet*.

DESTINY-Breast03 enrolled 524 patients at multiple sites in Asia, Europe, North America, Oceania and South America. For more information about the trial, visit ClinicalTrials.gov.

About HER2 Positive Breast Cancer

Breast cancer is the most common cancer and one of the leading causes of cancer-related deaths worldwide.[3] More than two million breast cancer cases were diagnosed in 2020, with nearly 685,000 deaths globally.[3] In China, breast cancer is the most common cancer in women, with more than 415,000 cases diagnosed in 2020.[1] There were nearly 120,000 breast cancer deaths in China in 2020, representing approximately 18% of global breast cancer deaths.[1] Approximately one in five cases of breast cancer are considered HER2 positive.[2]

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.[4] HER2 protein overexpression may occur as a result of *HER2* gene amplification and is often associated with aggressive disease and poor prognosis in breast cancer.[5]

Despite initial treatment with trastuzumab and a taxane, patients with HER2 positive metastatic breast cancer will often experience disease progression.[6,7]

About ENHERTU

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

ENHERTU (5.4 mg/kg) is approved in more than 40 countries for the treatment of adult patients with unresectable or metastatic HER2 positive breast cancer who have received a (or one or more) prior anti-HER2-based regimen, either in the metastatic setting or in the neoadjuvant or adjuvant setting, and have developed disease recurrence during or within six months of completing therapy based on the results from the DESTINY-Breast03 trial.

ENHERTU (5.4 mg/kg) is approved in more than 30 countries for the treatment of adult patients with unresectable or metastatic HER2 low (immunohistochemistry (IHC) 1+ or IHC 2+/*in-situ* hybridization (ISH)-) breast cancer who have received a prior systemic therapy in the metastatic setting or developed disease recurrence during or within six months of completing adjuvant chemotherapy based on the results from the DESTINY-Breast04 trial.

ENHERTU (5.4 mg/kg) is approved under accelerated approval in the U.S. for the treatment of adult patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating *HER2 (ERBB2*) mutations, as detected by a FDA-approved test, and who have received a prior systemic therapy based on the results from the DESTINY-Lung02 trial. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

ENHERTU (6.4 mg/kg) is approved in more than 30 countries for the treatment of adult patients with locally advanced or metastatic HER2 positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen based on the results from the DESTINY-Gastric01 and/or DESTINY-Gastric02 trial.

About the ENHERTU Clinical Development Program

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

About the Daiichi Sankyo and AstraZeneca Collaboration

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize ENHERTU 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 ENHERTU and datopotamab deruxtecan.

About the DXd ADC Portfolio of Daiichi Sankyo

The DXd ADC portfolio of Daiichi Sankyo currently consists of five ADCs in clinical development across multiple types of cancer. The company's clinical trial stage DXd ADCs include ENHERTU, a HER2 directed ADC and datopotamab deruxtecan (Dato-DXd), a TROP2 directed ADC, which are being jointly developed and commercialized globally with AstraZeneca; and, patritumab deruxtecan (HER3-DXd), a HER3 directed ADC. Two additional ADCs including ifinatamab deruxtecan (I-DXd; DS-7300), a B7-H3 directed ADC, and DS-6000, a CDH6 directed ADC, are being developed through a strategic early-stage research collaboration with Sarah Cannon Research Institute.

Designed using Daiichi Sankyo's proprietary DXd ADC technology to target and deliver a cytotoxic payload inside cancer cells that express a specific cell surface antigen, each ADC consists of a monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

Datopotamab deruxtecan, ifinatamab deruxtecan, patritumab deruxtecan and DS-6000 are investigational medicines that have not been approved for any indication in any country. Safety and efficacy have not been established.

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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