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Daiichi-Sankyo

Press Release

ENHERTU® Approved in China for Patients with Previously Treated HER2 Positive Advanced or Metastatic Gastric Cancer

- Approval based on DESTINY-Gastric06 results which showed ENHERTU demonstrated a clinically meaningful efficacy in this setting
- Third approval in China for Daiichi Sankyo and AstraZeneca's ENHERTU in less than two years

Tokyo – (August 13, 2024) – Daiichi Sankyo (TSE: 4568) and AstraZeneca's (LSE/STO/Nasdaq: AZN) ENHERTU® (trastuzumab deruxtecan) has received conditional approval in China as a monotherapy for the treatment of adult patients with locally advanced or metastatic HER2 positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received two or more prior treatment regimens. This indication was granted conditional approval based on results from the DESTINY-Gastric06 phase 2 trial. Full approval for this indication will depend on whether a randomized controlled confirmatory clinical trial can demonstrate clinical benefit in this population.

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

Approximately one in five gastric cancers globally are HER2 positive.[1,2] More than one third of the global cases of gastric cancer occur in China, with about 65% of patients presenting with advanced disease at the time of diagnosis.[3,4,5] Approximately 359,000 new cases of gastric cancer and 260,000 deaths were reported in China in 2022.[3]

The conditional approval by China's National Medical Products Administration (NMPA) is based on results from the DESTINY-Gastric06 phase 2 trial, where ENHERTU demonstrated clinically meaningful responses in patients in China with HER2 positive locally advanced or metastatic gastric or GEJ adenocarcinoma previously treated with two or more prior regimens including a fluoropyrimidine agent and a platinum agent.

In DESTINY-Gastric06, treatment with ENHERTU (6.4 mg/kg) resulted in a confirmed objective response rate (ORR) of 28.8% (95% confidence interval [CI]: 18.8-40.6) as assessed by independent central review, with one complete response and 20 partial responses observed. Median progression-free survival (PFS) with ENHERTU was 5.7 months (95% CI: 4.0-6.8).

The approval also was supported by results from the DESTINY-Gastric01 phase 2 trial, which included patients from Japan and South Korea. In the trial, patients with HER2 positive metastatic gastric cancer treated with ENHERTU showed a statistically significant improvement in confirmed ORR (40.5% with ENHERTU versus 11.3% with chemotherapy; $p<0.0001$) and median overall survival (OS) (12.5 months with ENHERTU versus 8.4 months with chemotherapy; hazard ratio [HR] 0.59; 95% confidence interval [CI] 0.39-0.88; $p=0.0097$) versus chemotherapy.

"HER2 positive metastatic gastric cancer can be particularly aggressive and difficult-to-treat. Patients often face poor outcomes following disease progression on first-line treatment and subsequent chemotherapy," said Lin Shen, MD, Director of the Department of Gastrointestinal Oncology, Peking University Cancer Hospital, China. "With the approval of ENHERTU, patients in China with HER2 positive metastatic gastric cancer will now have an important anti-HER2 treatment option that has demonstrated clinically meaningful efficacy following progression on previous therapies."

"This milestone marks the third approval in China for ENHERTU in less than two years, following approvals for HER2 positive metastatic breast cancer and HER2 low metastatic breast cancer," said Kiminori Nagao, Head of the Asia, South & Central America Business Unit, Daiichi Sankyo. "Our DESTINY clinical trial program continues to reinforce ENHERTU as a practice-changing treatment option for patients with HER2 expressing cancers and this latest approval in China further illustrates the global impact of this innovative antibody drug conjugate."

"China accounts for more than a third of patients with gastric cancer globally and most patients are diagnosed with advanced disease," said Dave Fredrickson, Executive Vice President, Oncology Business Unit, AstraZeneca. "This approval of ENHERTU brings a much-needed, new targeted treatment option to patients with HER2 positive metastatic gastric cancer in China and underscores our commitment to bringing this innovative medicine to more patients across the globe living with HER2 expressing cancers."

The safety profile of ENHERTU in DESTINY-Gastric06 was consistent with previous clinical trials of ENHERTU in gastric cancer with no new safety concerns identified. Grade 3 or grade 4 treatment-related adverse events (AEs) from a pooled safety analysis of patients treated with ENHERTU (6.4 mg/kg) across multiple tumor types in clinical studies included neutropenia (27.9%), anemia (23.1%), leukopenia (12.9%), thrombocytopenia (9.0%), fatigue (8.2%), decreased appetite (8.1%), lymphopenia (7.4%), nausea (5.8%), transaminases increased (4.7%), hypokalemia (4.2%), pneumonia (2.9%), febrile neutropenia (2.9%), vomiting (2.4%), diarrhea (2.1%), decreased weight (2.1%), blood alkaline phosphatase increased (1.8%), interstitial lung disease (ILD) (1.6%), dyspnea (1.3%), and ejection fraction decreased (1.1%). Grade 5 adverse reactions occurred in 2.6% of patients, including ILD (1.9%). Discontinuation of treatment due to an

AE occurred in 17.0% of patients. The most frequent adverse event associated with permanent discontinuation was ILD (12.4%).

About DESTINY-Gastric06

DESTINY-Gastric06 is an open-label, single-arm phase 2 trial in China evaluating the safety and efficacy of ENHERTU (6.4 mg/kg) in patients with HER2 positive locally advanced or metastatic gastric or GEJ adenocarcinoma previously treated with two or more prior regimens including a fluoropyrimidine agent and a platinum agent.

The primary endpoint of DESTINY-Gastric06 is confirmed ORR by independent central review. Secondary endpoints include investigator assessed ORR, PFS, duration of response (DoR), disease control rate, OS and safety.

DESTINY-Gastric06 enrolled 95 patients at multiple sites in China. For more information about the trial, visit clinicaltrials.gov.

About DESTINY-Gastric01

DESTINY-Gastric01 is an open label, randomized, controlled phase 2 trial evaluating the efficacy and safety of ENHERTU (6.4 mg/kg) versus investigator's choice of chemotherapy in a primary cohort of patients from Japan and South Korea with HER2 positive, locally advanced or metastatic gastric or GEJ adenocarcinoma who have progressed on at least two or more prior regimens including trastuzumab plus a fluoropyrimidine- and platinum-based chemotherapy combination. Patients were randomized 2:1 to receive ENHERTU or physician's choice of chemotherapy (paclitaxel or irinotecan monotherapy).

The primary endpoint is ORR assessed by independent central review. Key secondary endpoints include OS, PFS and DoR.

DESTINY-Gastric01 enrolled 188 patients at multiple sites in Japan and South Korea. For more information about the trial, visit clinicaltrials.gov.

About HER2 Positive Gastric Cancer

Gastric (stomach) cancer is the fifth most common cancer worldwide and the fifth leading cause of cancer-related death, with a five-year global survival rate of 5% to 10% for advanced or metastatic disease.[4,6] Approximately one million patients were diagnosed with gastric cancer in 2022, with more than 660,000 deaths reported globally.[4]

Incidence rates for gastric cancer are markedly higher in eastern Asia, particularly in China where more than one third of all global cases occur.[3,4] Gastric cancer is the fifth most common cancer in China with about 359,000 new cases diagnosed in 2022.[3] Additionally, it is the third leading cause of cancer-related death in China, with approximately 260,000 deaths reported in 2022.[3] Approximately 65% of patients in China present with advanced disease at the time of diagnosis.[5]

Approximately one in five gastric cancers globally are HER2 positive.[1,2] HER2 is a tyrosine kinase receptor growth promoting protein expressed on the surface of many types of tumors, including gastric cancer.[2] Recommended first-line treatment in China for HER2 positive advanced or metastatic gastric cancer is combination chemotherapy and trastuzumab, an anti-HER2 medicine, with or without pembrolizumab.[7] For patients with metastatic gastric cancer that progresses following initial treatment with a trastuzumab-based regimen, subsequent anti-HER2 treatment options are limited.[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 number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

ENHERTU (5.4 mg/kg) is approved in more than 65 countries worldwide for the treatment of adult patients with unresectable or metastatic HER2 positive (IHC 3+ or in-situ hybridization (ISH)+) breast cancer who have received a 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 65 countries worldwide for the treatment of adult patients with unresectable or metastatic HER2 low (IHC 1+ or IHC 2+/ (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 in more than 35 countries worldwide for the treatment of adult patients with unresectable or metastatic NSCLC whose tumors have activating HER2 (ERBB2) mutations, as detected by a locally or regionally approved test, and who have received a prior systemic therapy based on the results from the DESTINY-Lung02 trial. Continued approval in the U.S. 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 45 countries worldwide for the treatment of adult patients with locally advanced or metastatic HER2 positive (IHC 3+ or IHC 2+/ISH+) gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen based on the results from the DESTINY-Gastric01, DESTINY-Gastric02 and/or DESTINY-Gastric06 trials. Full approval in China for this indication will depend on whether a randomized controlled confirmatory clinical trial can demonstrate clinical benefit in this population.

ENHERTU (5.4 mg/kg) is approved in the U.S. for the treatment of adult patients with unresectable or metastatic HER2 positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options based on efficacy results from the DESTINY-PanTumor02, DESTINY-Lung01 and DESTINY-CRC02 trials. Continued approval for this indication in the U.S. may be contingent upon verification and description of clinical benefit in a confirmatory trial.

About the ENHERTU Clinical Development Program

A comprehensive global clinical development program is underway evaluating the efficacy and safety of ENHERTU monotherapy across multiple HER2 targetable 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 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 six ADCs in clinical development across multiple types of cancer. ENHERTU, a HER2 directed ADC, and datopotamab deruxtecan (Dato-DXd), a TROP2 directed ADC, are being jointly developed and commercialized globally with AstraZeneca. Patritumab deruxtecan (HER3-DXd), a HER3 directed ADC, ifinatamab deruxtecan (I-DXd), a B7-H3 directed ADC, and raludotatug deruxtecan (R-DXd), a CDH6 directed ADC, are being jointly developed and commercialized globally with Merck & Co., Inc., Rahway, N.J. USA. DS-3939, a TA-MUC1 directed ADC, is being developed by Daiichi Sankyo.

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, raludotatug deruxtecan and DS-3939 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 an innovative global healthcare company contributing to the sustainable development of society that discovers, develops and delivers new standards of care to enrich the quality of life around the world. With more than 120 years of experience, Daiichi Sankyo leverages its world-class science and technology to create new modalities and innovative medicines for people with cancer, cardiovascular and other diseases with high unmet medical need. For more information, please visit www.daiichisankyo.com.

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