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Daiichi-Sankyo

Press Release

ENHERTU® Now Available in Japan as First Antibody Drug Conjugate for the Second-Line Treatment of Patients with HER2 Positive Metastatic Gastric Cancer

- Based on DESTINY-Gastric04 phase 3 trial results that showed ENHERTU demonstrated statistically significant and clinically meaningful improvement in overall survival compared to ramucirumab plus paclitaxel

Tokyo – (March 23, 2026) – The Japan Pharmaceuticals and Medical Devices Agency (PMDA) has accepted the update of the ENHERTU® (trastuzumab deruxtecan) prescribing information following review of data from the DESTINY-Gastric04 phase 3 trial, which now expands the use of ENHERTU in Japan to include the second-line treatment of patients with HER2 positive (immunohistochemistry [IHC] 3+ or IHC 2+/*in-situ* hybridization [ISH]+) unresectable advanced or recurrent gastric cancer. ENHERTU previously was approved as a third-line treatment based on the results from the DESTINY-Gastric01 phase 2 trial.

ENHERTU is a specifically engineered HER2 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo (TSE: 4568) and being developed and commercialized by Daiichi Sankyo in Japan.

Gastric cancer is the third most common cancer in Japan.[1] More than 125,000 cases of gastric cancer were diagnosed in Japan in 2022, with more than 43,000 deaths.[1] Approximately one in five gastric cancers are considered HER2 positive.[2,3] Prior to the results of DESTINY-Gastric04, no other HER2 directed medicine has demonstrated a survival benefit in the second-line metastatic setting in a randomized clinical trial.[4]

In DESTINY-Gastric04, ENHERTU demonstrated a 30% reduction in risk of death compared to ramucirumab plus paclitaxel in patients with second-line HER2 positive unresectable and/or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma (hazard ratio [HR]: 0.70; 95% confidence interval [CI]: 0.550-0.896; p=0.0044). Median overall survival (OS) was 14.7 months with ENHERTU (n=246; 95% CI: 12.1-16.6) compared to 11.4 months with ramucirumab plus paclitaxel (n=248; 95% CI: 9.9-15.5). DESTINY-Gastric04 was presented as a late-breaking oral presentation at the 2025 American Society of Clinical Oncology (#ASCO25) Annual Meeting and simultaneously published in *The New England Journal of Medicine*.

“Gastric cancer can be particularly challenging to treat and is associated with a poor prognosis, especially in the metastatic setting where outcomes are notably worse for patients with disease progression after first-line treatment,” said Yuki Abe, PhD, Head of R&D Division in Japan and Head of Research, Daiichi Sankyo. “The impressive survival results seen in DESTINY-Gastric04 support the expanded use of ENHERTU in Japan, making it available as a new second-line option for patients with HER2 positive metastatic gastric cancer.”

In DESTINY-Gastric04, the safety profile of ENHERTU was consistent with previous clinical trials with no new safety concerns identified. Adverse reactions occurred in 227 patients (93.0%) treated with ENHERTU (6.4 mg/kg), including 26 Japanese patients. The most common adverse reactions were fatigue (48.0%), decreased neutrophil count (48.0%), nausea (44.3%), anemia (31.1%), decreased appetite (29.1%), decreased leukocyte count (26.6%), decreased platelet count (26.6%), diarrhea (25.8%), alopecia (24.2%), increased transaminase (21.7%) and vomiting (20.1%).

ENHERTU is approved in Japan with a Warning in its prescribing information for interstitial lung disease (ILD). ILD occurred in 262 patients (11.6%) treated with ENHERTU across multiple clinical trials. As cases of ILD, including fatal cases, have occurred in ENHERTU-treated patients, ENHERTU is to be used in close collaboration with a respiratory disease expert. Patients should be closely observed during therapy by monitoring for early signs or symptoms of ILD (such as dyspnea, cough or fever) and performing regular peripheral artery oxygen saturation (SpO2) tests, chest X-ray scans and chest CT scans. If abnormalities are observed, discontinue administration of ENHERTU and take appropriate measures, such as corticosteroid administration. Prior to initiation of ENHERTU therapy, a chest CT scan should be performed and medical history taken to confirm the absence of any comorbidity or history of ILD with the patient and carefully consider the eligibility of the patient for ENHERTU therapy.

About DESTINY-Gastric04

DESTINY-Gastric04 is a global, randomized, open-label, phase 3 trial evaluating the efficacy and safety of ENHERTU (6.4 mg/kg) versus ramucirumab and paclitaxel in patients with HER2 positive (IHC 3+ or IHC 2+/ISH+) unresectable and/or metastatic gastric or GEJ adenocarcinoma with disease progression on or after a trastuzumab-containing regimen.

The primary endpoint is OS. Secondary endpoints include investigator-assessed progression-free survival, objective response rate, duration of response, disease control rate and safety.

At disclosure of the topline results, an Independent Data Monitoring Committee recommended unblinding DESTINY-Gastric04 based on the superior efficacy of ENHERTU seen at a planned interim analysis.

DESTINY-Gastric04 enrolled 494 patients in Asia, Europe and South America. 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%.[5,6] Approximately one million cases of gastric cancer were diagnosed in 2022.[5] Gastric cancer is the third most common cancer in Japan.[1] More than 125,000 cases of gastric cancer were diagnosed in Japan in 2022, with more than 43,000 deaths.[1]

HER2 is a tyrosine kinase receptor growth-promoting protein expressed on the surface of many types of tumors, including gastric cancer.[3,7] Approximately one in five gastric cancers are considered HER2 positive.[2,3]

Prior to the results of the DESTINY-Gastric04 trial of ENHERTU, no other HER2 directed medicine has demonstrated a survival benefit in the second-line metastatic setting in a randomized clinical trial.[4]

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) in combination with pertuzumab is approved in the U.S. as a first-line treatment for adult patients with unresectable or metastatic HER2 positive (IHC 3+ or ISH+) breast cancer, as determined by an FDA-approved test, based on the results from the DESTINY-Breast09 trial.

ENHERTU (5.4 mg/kg) is approved in more than 90 countries/regions worldwide for the treatment of adult patients with unresectable or metastatic HER2 positive (IHC 3+ or 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 90 countries/regions 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 60 countries/regions worldwide for the treatment of adult patients with unresectable or metastatic hormone receptor (HR) positive, HER2 low (IHC 1+ or IHC 2+/ ISH-) or HER2 ultralow (IHC 0 with membrane staining) breast cancer, as determined by a locally or regionally approved test, that have progressed on one or more endocrine therapies in the metastatic setting based on the results from the DESTINY-Breast06 trial.

ENHERTU (5.4 mg/kg) is approved in more than 70 countries/regions 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 and/or DESTINY-Lung05 trials. Continued approval in China and 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 80 countries/regions worldwide for the treatment of adult patients with locally advanced or metastatic HER2 positive (IHC 3+ or IHC 2+/ISH+) gastric or GEJ adenocarcinoma who have received a prior trastuzumab-based regimen based on the results from the DESTINY-Gastric01, DESTINY-Gastric02 and/or DESTINY-Gastric04 trials.

ENHERTU (5.4 mg/kg) is approved in more than 15 countries/regions worldwide 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, DESTINY-CRC02 and/or HERALD trials. Continued approval in the U.S. for this indication 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 as a monotherapy or in combination or sequentially with other cancer medicines across multiple HER2 targetable cancers.

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 DATROWAY® 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 DATROWAY.

About the ADC Portfolio of Daiichi Sankyo

The Daiichi Sankyo ADC portfolio consists of eight ADCs in clinical development crafted from ADC technology discovered in-house by Daiichi Sankyo.

The DXd ADC Technology platform of Daiichi Sankyo consists of seven ADCs in clinical development where each ADC is comprised of a monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers. The DXd ADCs include ENHERTU and DATROWAY, which are being jointly developed and commercialized globally with AstraZeneca, and ifinatamab deruxtecan (I-DXd), raludotatug deruxtecan (R-DXd) and patritumab deruxtecan (HER3-DXd), which are being jointly developed and commercialized globally with Merck & Co., Inc, Rahway, NJ, USA. DS-3939 and DS3790 are being developed by Daiichi Sankyo.

An additional ADC being developed by Daiichi Sankyo is DS3610, which consists of an antibody attached to a novel payload that acts as an agonist of STING.

Ifinatamab deruxtecan, raludotatug deruxtecan, patritumab deruxtecan, DS-3939, DS3610 and DS3790 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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