Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

Press Release

ENHERTU® Approved in China as the First and Only HER2 Directed ADC 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 a statistically significant and clinically meaningful improvement in overall survival compared to ramucirumab plus paclitaxel
- Sixth approval for Daiichi Sankyo and AstraZeneca's ENHERTU in China across three tumor types in less than three years

Tokyo – (January 22, 2026) – ENHERTU® (trastuzumab deruxtecan) has been approved in China 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 one prior trastuzumab based regimen. ENHERTU previously received conditional approval for third-line or later treatment based on later-line phase 2 data.

ENHERTU is a specifically engineered HER2 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo (TSE: 4568) and being jointly developed and commercialized by Daiichi Sankyo and AstraZeneca (LSE/STO/Nasdaq: AZN).

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.[1,2,3] Approximately 359,000 cases of gastric cancer and 260,000 deaths were reported in China in 2022.[1] About one in five gastric cancers are considered HER2 positive.[4,5] 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.[6]

The approval of ENHERTU by China's National Medical Products Administration (NMPA) is based on results from the DESTINY-Gastric04 phase 3 trial 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*. The China Center for Drug Evaluation (CDE) granted Breakthrough Therapy Designation for ENHERTU for the second-line gastric cancer indication in 2020 due to efficacy data from early trials and the unmet clinical need. ENHERTU also was granted Priority Review by the CDE in this setting, enabling approval in China in approximately six months.

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 GEJ adenocarcinoma (hazard ratio [HR]: 0.70; confidence interval [CI]: 0.55-0.90; 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).

In the secondary endpoint analysis of progression-free survival (PFS), ENHERTU demonstrated a 26% reduction in the risk of disease progression or death versus ramucirumab plus paclitaxel (HR: 0.74; 95% CI: 0.59-0.92; p=0.0074) as assessed by investigator. Median PFS was 6.7 months (95% CI: 5.6-7.1) with ENHERTU versus 5.6 months (95% CI: 4.9-5.8) with ramucirumab plus paclitaxel. A confirmed objective response rate (ORR) of 44.3% (95% CI: 37.8-50.9) was seen in patients treated with ENHERTU with seven complete responses (CR) and 97 partial responses (PR) versus a confirmed ORR of 29.1% (95% CI: 23.4-35.3) with three CRs and 66 PRs in the ramucirumab plus paclitaxel arm (p=0.0006). Median duration of response (DOR) was 7.4 months (95% CI: 5.7-10.1) in the ENHERTU arm and 5.3 months (95% CI: 4.1-5.7) in the ramucirumab plus paclitaxel arm.

“Most patients with gastric cancer are diagnosed with advanced disease, which has a low survival rate and is particularly challenging to treat,” said Lin Shen, MD, Director of the Department of Gastrointestinal Oncology, Peking University Cancer Hospital and lead investigator of the DESTINY-Gastric04 trial in China. “This approval is an important milestone for the clinical community in China, addressing a critical gap in second-line targeted therapy for HER2 positive gastric cancer. This development is driving a paradigm shift from chemotherapy towards precision therapy in the second-line setting for patients with HER2 positive gastric cancer. At the same time, it provides clinicians with a powerful new option capable of significantly extending patient survival. We will be able to bring this innovative treatment to earlier lines of therapy, benefit a broader patient population, improve long-term outcomes and achieve longer survival.”

“This sixth approval for ENHERTU in China in less than three years fully demonstrates the potential of this innovative medicine to make significant contributions in clinical practice,” said Michio Hayashi, China President, Daiichi Sankyo. “DESTINY-Gastric04 is the first randomized phase 3 trial ever to show a survival benefit in the second-line HER2 positive metastatic gastric cancer setting and also confirmed the results of the DESTINY-Gastric01 and DESTINY-Gastric06 trials.”

“ENHERTU is already established in China in the third-line or later treatment setting for patients with HER2 positive metastatic gastric cancer and this approval brings this important medicine to an earlier line of therapy,” said Dave Fredrickson, Executive Vice President, Oncology Hematology Business Unit, AstraZeneca. “This latest approval in China underscores our commitment to bringing ENHERTU to patients in earlier treatment settings to improve outcomes and expand the number of people who may benefit.”

The safety profile of ENHERTU in DESTINY-Gastric04 was consistent with previous clinical trials with no new safety concerns identified. The most common grade 3 or grade 4 adverse reactions from a pooled safety population receiving at least one dose of ENHERTU 6.4 mg/kg (n=1,133) across multiple tumor types in clinical studies were nausea (64.3%), fatigue (57.3%), anemia (47.9%), decreased appetite (46.8%), neutropenia (45.9%), vomiting (34.7%), diarrhea (33.0%), thrombocytopenia (32.9%), leukopenia (31.2%), alopecia (29.0%), constipation (28.2%) and increased transaminases (26.4%). Grade 5 adverse reactions occurred in 2.2% of patients, including interstitial lung disease (ILD; 1.6%). Discontinuation of treatment due to an adverse reaction occurred in 13.2% of patients. The most frequent adverse reaction associated with permanent discontinuation was ILD (9.8%).

ENHERTU also is being evaluated as a potential first-line treatment for HER2 positive metastatic gastric cancer through two ongoing phase 3 trials – DESTINY-Gastric05 and ARTEMIDE-Gastric01.

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 PFS, ORR, DOR, disease control rate and safety.

In March 2025, 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% for advanced or metastatic disease.[2,7] Approximately one million cases of gastric cancer were diagnosed in 2022.[2]

Incidence rates for gastric cancer are markedly higher in eastern Asia, particularly in China where more than one third of all global cases occur.[1,2] Gastric cancer is the fifth most common cancer in China with about 359,000 new cases diagnosed in 2022.[1] Additionally, it is the third leading cause of cancer-related death in

China, with approximately 260,000 deaths reported in 2022.[1] Approximately 65% of patients in China present with advanced disease at the time of diagnosis.[3]

HER2 is a tyrosine kinase receptor growth-promoting protein expressed on the surface of many types of tumors, including gastric cancer.[8] Approximately one in five gastric cancers are considered HER2 positive.[4,5] 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.[9] For patients with metastatic gastric cancer that progresses following initial treatment with a trastuzumab-based regimen, subsequent anti-HER2 treatment options are limited.[9]

Prior to the results of the DESTINY-Gastric04 trial of ENHERTU, no other HER2 directed medicine had demonstrated a survival benefit in the second-line metastatic setting in a randomized clinical trial.[6]

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 (immunohistochemistry [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 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 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-Gastric04 trials.

ENHERTU (5.4 mg/kg) is approved in more than 10 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 and DESTINY-CRC02 trials. Continued approval 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 six 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 is being developed by Daiichi Sankyo.

Additional ADCs being developed by Daiichi Sankyo include DS-9606, which consists of a monoclonal antibody attached to a modified pyrrolobenzodiazepine (PBD) payload and DS3610, which consists of an antibody attached to a novel immunomodulatory payload that acts as an agonist of STING.

Ifinatamab deruxtecan, raludotatug deruxtecan, patritumab deruxtecan, DS-3939, DS-9606 and DS-3610 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.

Media Contacts:

Global:
Jennifer Brennan
Daiichi Sankyo
jennifer.brennan@daiichisankyo.com
+1 908 900 3183 (mobile)

China:
Lingling Zhang
Daiichi Sankyo
zhang.lingling.dg@daiichisankyo.com.cn
+86 21 6039 7200 (office)

Japan:
Daiichi Sankyo Co., Ltd.
DS-PR_jp@daiichisankyo.com

Investor Relations Contact:
DaiichiSankyoIR_jp@daiichisankyo.com

References

[1] Globocan 2022. *China.* Accessed January 2026.
[2] Globocan 2022. *Stomach Cancer*. Accessed January 2026.
[3] Zeng H, et al. *Lancet Public Health.* 2021 Dec;6(12):e877-e887.
[4] Abrahao-Machado LF, et al. *World J Gastroenterol*. 2016;22(19):4619-4625.
[5] Iqbal N, et al. *Mol Biol Int.* 2014:852748.
[6] Mitani S, et al. *Cancers (Basel).* 2020;12(2):400.
[7] Casamayor M, et al. *Ecancermedicalscience*. 2018;12:883.
[8] Cheng X. *Genes (Basel).* 2024;15(7):903.
[9] Wang F, et al. *Cancer Commun (Lond).* 2024 Jan;44(1):127-172.