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Daiichi-Sankyo

Press Release

ENHERTU® Followed by THP Approved in China as the First and Only HER2 Directed ADC for the Neoadjuvant Treatment of HER2 Positive Breast Cancer

- First approval of Daiichi Sankyo and AstraZeneca's ENHERTU globally in curative-intent early breast cancer setting
- Based on results from DESTINY-Breast11 which showed ENHERTU followed by THP achieved a superior pathologic complete response rate versus standard treatment
- Seventh approval for ENHERTU in China in three years and third approval in three months

Tokyo – (March 27, 2026) – ENHERTU® (trastuzumab deruxtecan) followed by paclitaxel, trastuzumab and pertuzumab (THP) has been approved in China for the neoadjuvant treatment (before surgery) of adult patients with HER2 positive (immunohistochemistry [IHC] 3+ or *in-situ* hybridization [ISH]+) stage 2 (high risk) or stage 3 breast cancer. This indication was granted conditional approval based on the DESTINY-Breast11 phase 3 trial, which showed an improvement in pathologic complete response (pCR) rate. Full approval will depend on whether ongoing adjuvant studies confirm long-term clinical benefit in patients with early or locally advanced breast cancer.

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/NYSE: AZN).

Breast cancer is the second most common cancer in women in China, with approximately 357,000 cases of breast cancer diagnosed and nearly 75,000 deaths in 2022.[1] Approximately one in five cases of breast cancer is considered HER2 positive, a breast cancer subtype which is often associated with aggressive disease and poor prognosis.[2,3] For patients with HER2 positive early breast cancer, reaching a pCR with neoadjuvant treatment is the earliest indicator of improved long-term survival.[4] However, approximately half of patients who receive neoadjuvant treatment do not reach pCR, putting them at increased risk of disease recurrence.[5,6,7,8,9]

The conditional approval of ENHERTU by China's National Medical Products Administration (NMPA) is based on results from the DESTINY-Breast11 phase 3 trial presented at the 2025 European Society for Medical Oncology (ESMO) Congress and simultaneously published in the *Annals of Oncology*.

In DESTINY-Breast11, ENHERTU followed by THP demonstrated a statistically significant and clinically meaningful improvement in pCR rate compared to dose-dense doxorubicin and cyclophosphamide followed by THP (ddAC-THP) in patients with high-risk HER2 positive early-stage breast cancer. The pCR rate with ENHERTU followed by THP was 67.29% compared to 56.25% with ddAC-THP, representing an improvement of 11.17% (95% confidence interval [CI]: 3.95-18.28; p=0.003). Similar improvement in pCR rate was observed across most prespecified subgroups, including hormone receptor positive and negative patients. At the time of the analysis, the secondary endpoint of event-free survival (EFS) was not mature (4.5% maturity at data cut-off). However, an early analysis showed a trend favoring ENHERTU followed by THP versus ddAC-THP (hazard ratio [HR]=0.56; 95% CI: 0.26-1.17). Efficacy results were consistent in the China subgroup.

“In patients with high-risk HER2 positive early-stage breast cancer, effective neoadjuvant treatment is critical to lower the risk of disease recurrence and maximize the chance of cure while potentially enabling less intensive surgery,” said Professor Jiong Wu, Secretary of the Party Committee of Fudan University Shanghai Cancer Center and China leading primary investigator of the DESTINY-Breast11 trial. “Findings from DESTINY-Breast11 showed that approximately 67% of patients had a pathologic complete response with ENHERTU followed by THP, suggesting a potential new standard of care in this setting.”

“As the first approval of ENHERTU globally for the neoadjuvant treatment of HER2 positive early-stage breast cancer and the first HER2 directed antibody drug conjugate approved in China in this setting, ENHERTU followed by THP offers patients in China a new treatment option with the opportunity to reach a pathologic complete response and the potential for improved long-term outcomes,” said Michio Hayashi, China President, Daiichi Sankyo. “This third approval of ENHERTU in the last three months and seventh approval in three years reinforces the rapid progress we are making in bringing ENHERTU to more patients in China, where there is a high incidence of breast cancer and a continued need for new treatment approaches.”

“ENHERTU followed by THP is the first treatment regimen in more than a decade to demonstrate a clinically meaningful improvement in pathologic complete response and safety in the neoadjuvant setting for patients with HER2 positive early-stage breast cancer, underscoring the significance of this new approval,” said Dave Fredrickson, Executive Vice President, Oncology Hematology Business Unit, AstraZeneca. “ENHERTU is already an important option in the metastatic setting, and this decision will bring it into early-stage disease where cure is possible."

The safety profile of ENHERTU followed by THP in DESTINY-Breast11 was consistent with the known profiles of each individual therapy with no new safety concerns identified. The most common grade 3 or 4 adverse reactions in patients that received at least one dose of ENHERTU 5.4 mg/kg followed by THP in

DESTINY-Breast11 (N=320) were neutropenia (13.8%), diarrhea (5.9%), increased transaminases (5.0%), leukopenia (4.4%), nausea (1.9%), peripheral neuropathy (1.9%) and anemia (1.6%). Grade 5 adverse reactions occurred in 0.3% of patients, including interstitial lung disease (ILD; 0.3%). The most frequent adverse reactions associated with permanent discontinuation were peripheral neuropathy (2.2%), ILD (1.9%) and increased transaminases (1.3%).

An application for ENHERTU followed by a taxane, trastuzumab and pertuzumab (THP) also is under review in the U.S. for the neoadjuvant treatment of patients with HER2 positive early-stage breast cancer based on the results from the DESTINY-Breast11 trial**.**

About DESTINY-Breast11

DESTINY-Breast11 is a global, multicenter, randomized, open-label, phase 3 trial evaluating the efficacy and safety of neoadjuvant ENHERTU (5.4 mg/kg) monotherapy or ENHERTU followed by THP compared to ddAC-THP in patients with high-risk HER2 positive early-stage breast cancer.

Patients were randomized 1:1:1 to receive either eight cycles of ENHERTU monotherapy; four cycles of ENHERTU followed by four cycles of THP; or four cycles of ddAC followed by four cycles of THP.

The primary endpoint of DESTINY-Breast11 is rate of pCR (absence of invasive disease in the breast and lymph nodes). Secondary endpoints include EFS, invasive disease-free survival, overall survival and safety.

DESTINY-Breast11 enrolled 927 patients across multiple sites in Asia, Europe, North America and South America. For more information about the trial, visit ClinicalTrials.gov.

About Neoadjuvant HER2 Positive Early Breast Cancer

Breast cancer is the second most common cancer and one of the leading causes of cancer-related deaths worldwide.[10] More than two million breast cancer cases were diagnosed in 2022, with more than 665,000 deaths globally.[10] In China, breast cancer is the second most common cancer in women.[1] Approximately 357,000 cases of breast cancer were diagnosed in China in 2022, with nearly 75,000 deaths.[1]

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

Approximately one in three patients with HER2 positive early-stage breast cancer is considered high-risk, meaning they are more likely to experience disease recurrence and have a poor prognosis.[11] For patients with

HER2 positive early breast cancer, reaching pCR with neoadjuvant treatment is the earliest indicator of improved long-term survival.[4] However, approximately half of patients who receive neoadjuvant treatment do not reach pCR, putting them at increased risk of disease recurrence.[5,6,7,8,9]

The current standard of care in the HER2 positive neoadjuvant setting in China consists of a combination regimen of carboplatin, trastuzumab, pertuzumab and a taxane.[12]

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) followed by THP is approved in China as a neoadjuvant treatment for adult patients with HER2 positive (IHC 3+ or ISH+) stage 2 (high risk) or stage 3 breast cancer based on the results from the DESTINY-Breast11 trial. Continued approval in China for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

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 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 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.

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] World Health Organization. Global Cancer Observatory: China. Accessed March 2026.
[2] Tarantino P, et al. *Ann Oncol.* 2023;34(8):645-659.
[3] Cheng X. *Genes*. (Basel). 2024;15(7):903.
[4] Spring LM, et al. *Clin Cancer Res*. 2020;26(12):2838-2848.
[5] Schneeweiss A, et al. *Ann Oncol*. 2013;24(9):2278-2284.
[6] Swain SM, et al. *Ann Oncol*. 2018;29(3):646-653.
[7] Huober J, et al. *J Clin Oncol.* 2022;40(25):2946-2956.
[8] Masuda N, et al. *Breast Cancer Res Treat*. 2020;180(1):135-146.
[9] Gao HF, et al. Presented at ASCO Annual Meeting 2025, May 29 – June 2. Chicago, IL. Abstract #LBA500.
[10] World Health Organization. Breast Fact Sheet. Accessed March 2026.
[11] Mahtani R, et al. *Cancers* (Basel). 2025;17(11):1848.
[12] Li J, et al. *Transl Breast Cancer Res*. 2024;5(18):1-20.