Press Release

Daiichi-Sankyo

Enhertu® Recommended for Approval in the EU by CHMP as Adjuvant Treatment for Patients with Residual Disease After Neoadjuvant Treatment for HER2 Positive Early Breast Cancer

- Recommendation based on DESTINY-Breast05 phase 3 trial results that showed Enhertu reduced the risk of invasive disease recurrence or death by 53% versus T-DM1
- Daiichi Sankyo and AstraZeneca's Enhertu has the potential to become a new standard of care in this early breast cancer setting

Tokyo – (September 18, 2026) – Enhertu® (trastuzumab deruxtecan) has been recommended for approval in the European Union (EU) as a monotherapy for the adjuvant treatment of adult patients with resected HER2 positive breast cancer who have residual invasive disease after neoadjuvant taxane-based and HER2 targeted treatment.

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).

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on results from the DESTINY-Breast05 phase 3 trial presented at the 2025 European Society for Medical Oncology (#ESMO25) Congress and subsequently published in *The New England Journal of Medicine*. The recommendation will now be reviewed by the European Commission, which has the authority to grant marketing authorizations for medicines in the EU.

In DESTINY-Breast05, Enhertu significantly reduced the risk of invasive disease recurrence or death (invasive disease-free survival [IDFS]) by 53% (hazard ratio [HR]=0.47; 95% confidence interval [CI]: 0.34-0.66; p<0.0001) compared to trastuzumab emtansine (T-DM1) in patients with HER2 positive breast cancer with residual invasive disease following neoadjuvant therapy. Enhertu demonstrated a three-year IDFS rate of 92.4% (95% CI: 89.7-94.4) and 83.7% with T-DM1 (95% CI: 80.2-86.7). Data also showed that Enhertu significantly reduced the risk of disease recurrence or death (disease-free survival [DFS]) by 53% (HR=0.47; 95% CI: 0.34-0.66; p<0.0001) compared to T-DM1. Results showed a three-year DFS rate of 92.3% (95% CI: 89.5-94.3) in the Enhertu arm and 83.5% with T-DM1 (95% CI: 79.9-86.4).

"Patients with HER2 positive early breast cancer who have residual disease after neoadjuvant treatment experience a substantially higher risk of recurrence, making effective adjuvant treatment especially important," said John Tsai, MD, Global Head, R&D, Daiichi Sankyo. "This positive CHMP opinion underscores the potential role of Enhertu in the curative-intent setting where it is critical to maximize the potential for sustained long-term outcomes."

"This positive CHMP opinion marks a significant step towards bringing Enhertu into early-stage HER2 positive breast cancer in the EU," said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology Hematology R&D, AstraZeneca. "Enhertu cut the risk of disease recurrence by more than half compared to adjuvant standard of care for patients with residual disease, and if approved could redefine post-surgery care in the EU, keeping patients disease-free for longer and increasing the potential for cure."

The safety profile of Enhertu in DESTINY-Breast05 was consistent with the known profile with no new safety concerns identified. The most common treatment-related adverse events that occurred in patients treated with Enhertu were nausea (71.3%), constipation (32.0%), decreased neutrophil count (31.6%) and vomiting (31.0%). Interstitial lung disease (ILD) or pneumonitis occurred in 9.6% of patients treated with Enhertu as determined by an

independent adjudication committee. The majority of ILD or pneumonitis events were low grade (grade 1 [n=16; 2.0%] or grade 2 [n=52; 6.5%]). There were two grade 5 events (0.2%) of ILD or pneumonitis in the Enhertu arm.

Enhertu is approved in Brazil, Canada, India and the U.S. for the adjuvant treatment of adult patients with HER2 positive breast cancer and residual invasive disease following neoadjuvant treatment based on DESTINY-Breast05.

About DESTINY-Breast05

DESTINY-Breast05 is a global, multicenter, randomized, open-label, phase 3 trial evaluating the efficacy and safety of Enhertu (5.4 mg/kg) versus T-DM1 in patients with HER2 positive early breast cancer with residual invasive disease in breast or axillary lymph nodes following neoadjuvant therapy and a high risk of recurrence. High risk of recurrence was defined as presentation with inoperable cancer (prior to neoadjuvant therapy) or pathologically positive axillary lymph nodes following neoadjuvant therapy.

The primary endpoint of DESTINY-Breast05 is investigator-assessed IDFS, which is defined as the time from randomization until first invasive local, axillary or distant recurrence or death from any cause. The key secondary endpoint is investigator-assessed DFS. Other secondary endpoints include overall survival, distant recurrence-free interval, brain metastases-free interval and safety.

DESTINY-Breast05 enrolled 1,635 patients in Asia, Europe, North America, Oceania and South America. For more information about the trial, visit ClinicalTrials.gov.

About HER2 Positive Early Breast Cancer

Breast cancer is the most common cancer in women worldwide and the leading cause of cancer-related deaths among women.[1] Approximately 2.4 million breast cancer cases were diagnosed in 2024, with more than 690,000 deaths globally.[1] In Europe, approximately 540,000 cases of breast cancer were diagnosed in 2024, with more than 140,000 deaths.[2]

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.[4]

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.[5] The current standard of care in the HER2 positive adjuvant (after surgery) setting for patients with residual invasive disease in the EU is T-DM1.[6]

Despite receiving additional treatment with current standard of care for residual disease, some patients still experience invasive disease or death.[7] Once patients are diagnosed with metastatic disease, the five-year survival rate drops from nearly 100% to approximately 34%.[8]

Adjuvant therapy represents a key opportunity to minimize the risk of recurrence and prevent progression to metastatic disease for patients with residual disease.[9,10,11] New treatment options are needed in the early breast cancer setting to improve long-term outcomes for more patients.

About Enhertu

Enhertu (trastuzumab deruxtecan; fam-trastuzumab deruxtecan-nxki in the U.S. only) is a HER2 directed ADC. Designed using the proprietary DXd ADC Technology of Daiichi Sankyo, 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 Brazil, China, India, Singapore, Taiwan and the U.S. as a neoadjuvant treatment for adult patients with HER2 positive (IHC 3+ or ISH+) stage 2 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) is approved in Brazil, Canada, India and the U.S. for the adjuvant treatment of adult patients with HER2 positive breast cancer who have residual invasive disease following neoadjuvant trastuzumab (with or without pertuzumab) and taxane-based treatment based on the DESTINY-Breast05 trial.

Enhertu (5.4 mg/kg) in combination with pertuzumab is approved in more than 40 countries/regions worldwide as a first-line treatment for adult patients with unresectable or metastatic HER2 positive (IHC 3+ or ISH+) breast cancer, as determined by a locally or regionally approved test, based on the results from the DESTINY-Breast09 trial.

Enhertu (5.4 mg/kg) is approved in more than 100 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 75 countries/regions worldwide for the treatment of adult patients with unresectable or metastatic hormone receptor 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 100 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 80 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 90 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 45 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 nine 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.

Additional ADCs being developed by Daiichi Sankyo include DS3610, which consists of an antibody attached to a novel payload that acts as an agonist of STING, and DS1025, which consists of a CD25 directed antibody attached to an immuno-oncology optimized cytotoxic payload.

Ifinatamab deruxtecan, raludotatug deruxtecan, patritumab deruxtecan, DS-3939, DS3610, DS3790 and DS1025 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 (TSE: 4568) is a global healthcare company committed to becoming a trusted healthcare innovator, transforming the lives of people through its strength in science and technology. The company discovers and develops new standards of care to address diverse medical needs to fulfill its purpose of contributing to the enrichment of quality of life around the world. With a strategic focus on oncology, Daiichi Sankyo is advancing an industry-leading antibody drug conjugate portfolio along with identifying new breakthrough generating technologies to deliver practice-changing medicines to patients, healthcare professionals and society. For more information, please visit www.daiichisankyo.com.

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