Press Release

Daiichi-Sankyo

Enhertu® Plus Pertuzumab Recommended for Approval in the EU by CHMP as First-Line Treatment for Patients with HER2 Positive Metastatic Breast Cancer

- Recommendation based on DESTINY-Breast09 phase 3 trial results that showed Enhertu plus pertuzumab reduced the risk of disease progression or death by 44% versus THP with a median progression-free survival exceeding three years
- If approved, Daiichi Sankyo and AstraZeneca's Enhertu plus pertuzumab would become first new treatment in the EU in more than a decade for first-line HER2 positive metastatic breast cancer

Tokyo – (July 24, 2026) – Enhertu® (trastuzumab deruxtecan) in combination with pertuzumab has been recommended for approval in the European Union (EU) for the first-line treatment of adult patients with unresectable or metastatic HER2 positive (immunohistochemistry [IHC] 3+ or *in-situ* hybridization [ISH]+) 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).

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on results from the DESTINY-Breast09 phase 3 trial presented at the 2025 American Society of Clinical Oncology Annual Meeting 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-Breast09, Enhertu in combination with pertuzumab reduced the risk of disease progression or death by 44% versus a taxane, trastuzumab and pertuzumab (THP) (hazard ratio: 0.56; 95% confidence interval [CI]: 0.44-0.71; p<0.00001) in patients (n=383) with HER2 positive metastatic breast cancer who had not received prior chemotherapy or HER2 targeted therapy or had received neoadjuvant or adjuvant HER2 targeted therapy more than six months before the diagnosis of advanced or metastatic disease. Median progression-free survival (PFS) was 40.7 months (95% CI: 36.5-not estimable [NE]) with Enhertu in combination with pertuzumab compared to 26.9 months (95% CI: 21.8-NE) with THP as assessed by blinded independent central review (BICR). The PFS benefit was consistent across subgroups, including the prespecified stratification factors of hormone receptor (HR) status, *de novo* or recurrent disease and *PIK3CA* mutation status.

Confirmed objective response rate (ORR) was 85.1% (95% CI: 81.2-88.5) for Enhertu in combination with pertuzumab compared to 78.6% (95% CI: 74.1-82.5) with THP. There were 58 (15.1%) complete responses (CR) and 268 (70.0%) partial responses (PR) with Enhertu plus pertuzumab compared to 33 (8.5%) CRs and 271 (70.0%) PRs with THP. Median duration of response (DOR) for Enhertu plus pertuzumab exceeded three years (39.2 months) versus 26.4 months for THP.

"Enhertu in combination with pertuzumab improved progression-free survival by more than one year compared with the current first-line standard of care, representing a meaningful advantage early in the treatment of patients with metastatic HER2 positive disease," said John Tsai, MD, Global Head, R&D, Daiichi Sankyo. "Today's positive CHMP opinion brings us closer to making Enhertu available in the EU as a first-line treatment option for eligible patients with HER2 positive metastatic breast cancer, marking an important milestone in moving this medicine earlier in the treatment pathway."

"HER2 positive metastatic breast cancer is an aggressive subtype, so starting patients on an effective HER2 targeted treatment early and continuing it for as long as they benefit can have a meaningful impact on long-term outcomes," said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology Hematology R&D, AstraZeneca. "DESTINY-Breast09 sets a new benchmark with a median progression-free survival of more than three years, underscoring the potential of Enhertu plus pertuzumab to redefine first-line treatment for patients with HER2 positive metastatic breast cancer."

The safety profile of Enhertu in combination with pertuzumab in DESTINY-Breast09 was consistent with the known profiles of each individual treatment with no new safety concerns identified. The most common grade 3 or higher treatment-related adverse events that occurred in patients treated with Enhertu in combination with pertuzumab (n=381) were neutropenia (23.9%), hypokalemia (10.2%), and anemia (8.4%). Interstitial lung disease (ILD) or pneumonitis occurred in 12.1% of patients treated with Enhertu in combination with pertuzumab as determined by an independent adjudication committee. The majority of ILD or pneumonitis events were low grade (grade 1 [n=17; 4.5% or grade 2 [n=27; 7.1%]). There were two grade 5 events (0.5%) of ILD or pneumonitis in the Enhertu plus pertuzumab arm.

Enhertu (5.4 mg/kg) in combination with pertuzumab is approved in India, Israel, Saudi Arabia, Singapore, South Korea, Switzerland, the United Arab Emirates and 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 a locally or regionally approved test, based on the results from the DESTINY-Breast09 trial.

Enhertu is also under review in the EU for patients with HER2 positive breast cancer who have residual invasive disease after neoadjuvant HER2 targeted treatment based on data from the DESTINY-Breast05 trial.

About DESTINY-Breast09

DESTINY-Breast09 is a global, multicenter, randomized, open-label, phase 3 trial evaluating the efficacy and safety of Enhertu (5.4 mg/kg) either alone or in combination with pertuzumab versus standard of care THP as first-line treatment in patients with HER2 positive metastatic breast cancer.

Patients were randomized 1:1:1 to receive either Enhertu monotherapy with a pertuzumab matching placebo; Enhertu in combination with pertuzumab; or THP. Randomization was stratified by prior treatment (*de novo* metastatic disease versus progression from early-stage disease), HR status and *PIK3CA* mutation status.

The primary endpoint of DESTINY-Breast09 is PFS as assessed by BICR in both the Enhertu monotherapy and Enhertu combination arms. Secondary endpoints include investigator-assessed PFS, overall survival, ORR, DOR, pharmacokinetics and safety. The investigational arm assessing Enhertu monotherapy versus THP remains blinded to patients and investigators and will continue to the final PFS analysis.

DESTINY-Breast09 enrolled 1,157 patients across multiple sites in Africa, Asia, Europe, North America and South America. For more information about the trial, visit ClinicalTrials.gov.

About HER2 Positive Metastatic 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 are diagnosed annually, with more than 140,000 deaths.[2] While survival rates are high for those diagnosed with early breast cancer, only about 30% of patients diagnosed with or whose disease has progressed to metastatic disease are expected to live five years following diagnosis.[3]

HER2 is a tyrosine kinase receptor growth-promoting protein expressed on the surface of many types of tumors including breast cancer.[4] HER2 protein overexpression may occur as a result of *HER2* gene amplification.[4] Approximately one in five cases of breast cancer is considered HER2 positive.[5]

HER2 positive metastatic breast cancer is an aggressive disease driven by overexpression or amplification of HER2 that affects 15% to 20% of patients with metastatic breast cancer.[5] While HER2 targeted therapies have improved outcomes, prognosis remains poor with most patients experiencing disease progression within two years of first-line treatment with THP, which has been the standard of care for more than a decade.[6,7,8] Further, approximately one in three patients do not receive any treatment following first-line therapy due to disease progression or death.[9,10]

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, Singapore 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 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 India, Israel, Saudi Arabia, Singapore, South Korea, Switzerland, the United Arab Emirates and 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 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 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 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 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 (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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