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Daiichi-Sankyo

Press Release

ENHERTU® Type II Variation Application Validated in the EU as Post-Neoadjuvant Treatment for Patients with HER2 Positive Early Breast Cancer

- Based on DESTINY-Breast05 phase 3 trial results, which showed ENHERTU reduced the risk of invasive disease recurrence or death by 53% compared to T-DM1
- If approved, Daiichi Sankyo and AstraZeneca's ENHERTU has the potential to become a new standard of care in this early breast cancer setting

Tokyo and Munich – (February 19, 2026) – The European Medicines Agency (EMA) has validated the Type II Variation marketing authorization application for ENHERTU® (trastuzumab deruxtecan) as a monotherapy for adult patients with HER2 positive (immunohistochemistry [IHC] 3+ or *in-situ* hybridization [ISH]+) breast cancer who have residual invasive disease after neoadjuvant 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 validation confirms the completion of the application and commences the scientific review process by the EMA's Committee for Medicinal Products for Human Use (CHMP). The application is based on data 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*. In the trial, ENHERTU demonstrated a statistically significant and clinically meaningful improvement in invasive disease-free survival (IDFS) versus trastuzumab emtansine (T-DM1) in patients with HER2 positive breast cancer with residual invasive disease following neoadjuvant therapy.

"Patients who have residual invasive disease despite neoadjuvant therapy face a heightened risk of recurrence and are in need of better options following neoadjuvant treatment and surgery," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "This validation in the EU is an important step toward bringing ENHERTU to eligible patients earlier in the treatment journey to help reduce the risk of disease recurrence and progression to metastatic disease."

Additional regulatory submissions for ENHERTU also are underway in the EU, including in combination with pertuzumab for the first-line treatment of adult patients with unresectable or metastatic HER2 positive breast cancer based on data from DESTINY-Breast09 and for previously treated HER2 positive unresectable

or metastatic solid tumors based on data from DESTINY-PanTumor02, DESTINY-CRC02 and DESTINY-Lung01.

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 disease-free survival. 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 Post Neoadjuvant Treatment for HER2 Positive Early Breast Cancer

Breast cancer is the second most common cancer and one of the leading causes of cancer-related deaths worldwide.[1] More than two million breast cancer cases were diagnosed in 2022, with more than 665,000 deaths globally.[1] In Europe, approximately 557,000 cases of breast cancer are diagnosed annually, with more than 144,000 deaths.[1]

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

For patients with HER2 positive early breast cancer, achieving pathologic complete response (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 experience pCR, putting them at increased risk of disease recurrence.[5,6,7,8,9]

Despite receiving additional treatment for residual disease in the post-neoadjuvant setting, some patients still experience invasive disease or death and current treatment options have shown limited impact on central nervous system recurrence.[10] Once patients are diagnosed with metastatic disease, the five-year survival rate drops from nearly 90% to approximately 30%.[11]

Post-neoadjuvant therapy represents a key opportunity to minimize the risk of recurrence and prevent progression to metastatic disease for patients with residual disease. New treatment options are needed in the early breast cancer setting to help reduce the likelihood of disease progression and improve long-term outcomes for more patients.[12,13]

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 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 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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