Press Release

Daiichi-Sankyo

Enhertu® Approved in the EU as First Tumor Agnostic HER2 Directed Therapy and Antibody Drug Conjugate for Patients with Previously Treated HER2 Positive Metastatic Solid Tumors

- Approval based on three phase 2 trials of Daiichi Sankyo and AstraZeneca's Enhertu that demonstrated clinically meaningful responses across a broad range of tumors
- Enhertu now approved for six indications in the EU

Tokyo – (June 29, 2026) – Enhertu® (trastuzumab deruxtecan) has been approved in the European Union (EU) as a monotherapy for the treatment of adult patients with unresectable or metastatic HER2 positive (immunohistochemistry [IHC] 3+) solid tumors who have received prior treatment and who have no satisfactory treatment options.

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 approval by the European Commission follows the positive opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency and is based on results from subgroups of patients with HER2 positive (IHC 3+) tumors across three phase 2 trials, including DESTINY-PanTumor02, DESTINY-Lung01 and DESTINY-CRC02.

In DESTINY-PanTumor02, Enhertu demonstrated a confirmed objective response rate (ORR) of 52.3% (95% confidence interval [CI]: 42.6-61.8) and median duration of response (DOR) of 21.1 months (95% CI: 10.6-25.0) in a subgroup of previously treated patients (n=111) with centrally or locally assessed HER2 positive solid tumors, including biliary tract, bladder, cervical, endometrial, ovarian, pancreatic or other tumors. In DESTINY-Lung01, Enhertu demonstrated a confirmed ORR of 52.9% (95% CI: 27.8-77.0) and median DOR of 6.9 months (95% CI: 4.0-9.8) in a subgroup of previously treated patients (n=17) with centrally confirmed HER2 positive non-small cell lung cancer (NSCLC). In DESTINY-CRC02, Enhertu demonstrated a confirmed ORR of 46.9% (95% CI: 34.3-59.8) and median DOR of 5.5 months (95% CI: 4.2-8.1) in a subgroup of previously treated patients (n=64) with centrally confirmed HER2 positive colorectal cancer.

"HER2 overexpression occurs across multiple tumor types and is associated with aggressive disease and a poor prognosis. Until now, HER2 directed therapies were only available for specific tumor types," said Benedikt Westphalen, MD, Head of the Precision Oncology Program, Comprehensive Cancer Center of the University of Munich, Germany. "The approval of trastuzumab deruxtecan as a tumor agnostic therapy opens a new treatment option for patients with HER2 positive cancers regardless of where the tumor originated."

In DESTINY-PanTumor02, DESTINY-Lung01 and DESTINY-CRC02, the safety profile of Enhertu was consistent with previous clinical trials with no new safety concerns identified. Grade 3 or grade 4 adverse reactions from a pooled safety analysis of patients treated with Enhertu (5.4 mg/kg) across multiple tumor types in clinical studies included neutropenia (18.5%), anemia (9.9%), fatigue (8.2%), leukopenia (5.8%), thrombocytopenia (5.2%), nausea (4.8%), lymphopenia (4.2%), hypokalemia (3.6%), increased transaminases (3.6%), diarrhea (2.5%), vomiting (2.4%), decreased appetite (1.6%), pneumonia (1.4%) and decreased ejection fraction (1.0%). Grade 5 adverse reactions occurred in 1.1% of patients, including interstitial lung disease/pneumonitis (1.0%).

"This approval of Enhertu marks a significant milestone in the EU for patients with HER2 positive metastatic solid tumors and establishes the first tumor agnostic indication for a HER2 directed therapy and antibody drug conjugate in the region," said Ken Keller, Global Head of Oncology Business, and President and CEO, Daiichi Sankyo, Inc.

"Enhertu is now approved for six indications in the EU, which demonstrates our commitment to advancing innovative medicines in areas of high unmet need to patients with cancer."

"Precision medicine is reshaping cancer care by helping inform treatment decisions based on the molecular and biological characteristics of a patient's disease," said Dave Fredrickson, Executive Vice President, Oncology Hematology Business Unit, AstraZeneca. "Enhertu is already approved in breast, gastric and lung cancers, and with this approval, clinicians may now consider Enhertu for patients with HER2 positive status across multiple additional tumor types. This highlights the importance of biomarker testing to identify eligible patients and ensure that those with HER2 positive disease are considered for targeted treatment."

Enhertu (5.4 mg/kg) is approved in more than 40 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/or have no satisfactory alternative treatment options based on efficacy results from the DESTINY-PanTumor02, DESTINY-Lung01, DESTINY-CRC02 and/or HERALD trials.

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 the DESTINY-Breast09 trial and for patients with HER2 positive breast cancer with residual invasive disease after neoadjuvant HER2 targeted treatment based on data from the DESTINY-Breast05 trial.

Financial Considerations

Following this approval in the EU, an amount of $25 million is due from AstraZeneca to Daiichi Sankyo as a milestone payment for the HER2 positive metastatic solid tumor indication. Sales of Enhertu in most EU territories are recognized by Daiichi Sankyo. For further details on the financial arrangements, please consult the collaboration agreement from March 2019.

About DESTINY-PanTumor02

DESTINY-PanTumor02 is a global, multicenter, multi-cohort, open-label, phase 2 trial evaluating the efficacy and safety of Enhertu (5.4 mg/kg) for the treatment of previously treated HER2 expressing tumors, including biliary tract, bladder, cervical, endometrial, ovarian, pancreatic cancer or other tumors.

The primary endpoint of DESTINY-PanTumor02 is confirmed ORR as assessed by investigator. Secondary endpoints include DOR, disease control rate (DCR), progression-free survival (PFS), overall survival (OS), safety, tolerability and pharmacokinetics. Results from DESTINY-PanTumor02 were published in the *Journal of Clinical Oncology*.

DESTINY-PanTumor02 enrolled 267 patients, including 111 HER2 positive (IHC 3+) adult patients at multiple sites in Asia, Europe, North America, South America and Oceania. For more information about the trial, visit ClinicalTrials.gov.

About DESTINY-Lung01

DESTINY-Lung01 is a global, open-label, two-cohort, phase 2 trial evaluating the efficacy and safety of Enhertu (5.4 mg/kg or 6.4 mg/kg) in patients with *HER2* mutant (Cohort 2, n=91) or HER2 overexpressing (defined as IHC 3+ or IHC 2+) (Cohort 1 and 1a, n=90) unresectable or metastatic NSCLC who had progressed after one or more systemic therapies.

The primary endpoint of DESTINY-Lung01 is confirmed ORR by independent central review. Key secondary endpoints include DOR, DCR, PFS, OS and safety. Results from the *HER2* mutant cohort were published in

The New England Journal of Medicine and results from the HER2 overexpressing cohort were published in *The Lancet Oncology*.

DESTINY-Lung01 enrolled 181 patients, including 17 HER2 positive (IHC 3+) adult patients at multiple sites in Asia, Europe and North America. For more information about the trial, visit ClinicalTrials.gov.

About DESTINY-CRC02

DESTINY-CRC02 is a global, randomized, two arm, parallel, multicenter, phase 2 trial evaluating the efficacy and safety of two doses (5.4 mg/kg or 6.4 mg/kg) of Enhertu in patients with locally advanced, unresectable or metastatic HER2 positive colorectal cancer of BRAF wild-type, RAS wild-type or RAS mutant tumor types previously treated with standard therapy. The trial was conducted in two stages. In the first stage, patients (n=80) were randomized 1:1 to receive either 5.4 mg/kg or 6.4 mg/kg of Enhertu. In the second stage, additional patients (n=42) were enrolled in the 5.4 mg/kg arm.

The primary endpoint in DESTINY-CRC02 is confirmed ORR as assessed by blinded independent central review. Secondary endpoints include DOR, DCR, investigator-assessed confirmed ORR, clinical benefit ratio, PFS, OS and safety. Results from DESTINY-CRC02 were published in *The Lancet Oncology*.

DESTINY-CRC02 enrolled 122 patients, including 64 HER2 positive (IHC 3+) adult patients at multiple sites in Asia, Europe, North America and Oceania. For more information about the trial, visit ClinicalTrials.gov.

About HER2 Expression in Solid Tumors

HER2 is a tyrosine kinase receptor growth-promoting protein expressed on the surface of various tissue cells throughout the body and is involved in normal cell growth.[1] HER2 protein overexpression may occur as a result of *HER2* gene amplification and is often associated with aggressive disease and poor prognosis in some cancers.[2] HER2 overexpression occurs in a range of solid tumors with the prevalence varying by tumor type.[3]

HER2 directed therapies have been used to treat HER2 overexpression in breast, gastric and biliary tract cancers in the EU.[1,4,5,6] Although HER2 is overexpressed in additional solid tumor types including biliary tract, lung, bladder, cervical, colorectal, endometrial, ovarian, salivary gland and pancreatic cancers, HER2 testing is not routinely performed in these additional tumor types and prior to this approval there were no HER2 directed treatments approved in the EU to treat a broad range of solid tumors.[2,7,8]

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) 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) followed by THP is approved in China 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) in combination with pertuzumab is approved in Brazil, India, Israel, Saudi Arabia, 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 95 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 95 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 70 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 75 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 40 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/or 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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