Press Release

Daiichi-Sankyo

Enhertu® Recommended for Approval in the EU by CHMP for Patients with Previously Treated HER2 Positive Metastatic Solid Tumors

- Recommendation based on three phase 2 trials in which Daiichi Sankyo and AstraZeneca's Enhertu showed clinically meaningful responses across a broad range of tumors
- If approved, Enhertu would become the first HER2 directed therapy and antibody drug conjugate to receive a tumor agnostic indication in the EU

Tokyo – (May 22, 2026) – Enhertu® (trastuzumab deruxtecan) has been recommended for approval 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 Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on results from patients with HER2 positive (IHC 3+) tumors in three phase 2 trials including DESTINY-PanTumor02, DESTINY-Lung01 and DESTINY-CRC02 where Enhertu demonstrated clinically meaningful responses across a broad range of tumors. 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-PanTumor02, Enhertu demonstrated a confirmed objective response rate (ORR) of 51.4% (95% confidence interval [CI]: 41.7-61.0) and median duration of response (DOR) of 14.2 months (range: 10.3-23.6) in previously treated patients (n=111) with centrally or locally assessed HER2 positive solid tumors including either 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 (range: 4.0-11.7) in 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 (range: 1.3-9.7) in previously treated patients (n=64) with centrally confirmed HER2 positive colorectal cancer.

"This positive CHMP opinion acknowledges the clinical value of Enhertu as the potential first HER2 directed medicine and antibody drug conjugate available for patients with HER2 positive metastatic solid tumors in the EU," said John Tsai, MD, Global Head, R&D, Daiichi Sankyo. "Enhertu offers meaningful responses for patients with advanced cancers that overexpress HER2, who have limited treatment options. We look forward to continuing to work with the EMA to bring Enhertu to these patients."

"HER2 directed therapies have already transformed care for certain HER2 expressing cancers, including breast and gastric cancers. However, many other cancers overexpress HER2 and targeted treatment options remain unavailable for most of these tumor types," said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology Hematology R&D, AstraZeneca. "This positive CHMP opinion underscores the importance of precision oncology and marks an important step toward bringing a new targeted option to more patients in the EU living with HER2 positive solid tumors."

The safety profile of Enhertu (5.4 mg/kg) across the trials was consistent with previous clinical trials with no new safety concerns identified. In DESTINY-PanTumor02, the most common grade 3 or higher drug-related adverse events that occurred in all patients treated with Enhertu (n=267) were neutropenia (10.9%) and anemia (10.9%). Interstitial lung disease (ILD) or pneumonitis occurred in 10.5% of patients. The majority of ILD or pneumonitis events were low grade (grade 1 or 2), with one grade 3 event (0.4%), no grade 4 events (0.0%) and three grade 5 events (1.1%) observed, as determined by an independent adjudication committee. In DESTINY-Lung01, the most common grade 3 or higher treatment-emergent adverse events (TEAEs) occurring in all patients treated with Enhertu (cohort 1a; n=41) were disease progression (10%), fatigue (7%), pneumonia (5%) and dyspnea (4%). ILD or pneumonitis occurred in 5% of patients. The majority of ILD or pneumonitis events were low grade (grade 1 or 2), with no grade 3 or grade 4 events (0.0%), and one grade 5 event (2%) observed, as determined by an independent adjudication committee. One additional patient experienced grade 4 pneumonitis after the data cutoff, which was subsequently adjudicated as a drug-related grade 5 event. In DESTINY-CRC02, the most common grade 3 or worse TEAEs occurring in all patients treated with Enhertu (n=83) were decreased neutrophil count (16%), anemia (7%), nausea (7%) and decreased white blood cell count (6%). ILD or pneumonitis occurred in 8% of patients. All ILD or pneumonitis events were low grade (grade 1 or 2) with no grade 3, grade 4 or grade 5 events (0.0%) observed, as determined by an independent adjudication committee.

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 directed therapies have been used to treat HER2 overexpression in breast, gastric and salivary gland cancers in the EU.[1,3,4,5] Although HER2 is overexpressed in additional solid tumor types including biliary tract, lung, bladder, cervical, colorectal, endometrial, ovarian and pancreatic cancers, HER2 testing is not routinely performed in these additional tumor types and there are currently no HER2 directed treatments approved in the EU to treat a broad range of solid tumors.[2,6,7]

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 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 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 an FDA-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 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 (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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