Press Release

Daiichi-Sankyo

Enhertu® and Datroway® Approved in Japan for Two New First-Line Indications for Patients with Metastatic Breast Cancer

- Enhertu approval based on DESTINY-Breast09 phase 3 trial where Enhertu in combination with pertuzumab reduced the risk of disease progression or death by 44% versus THP with a median progression-free survival exceeding three years in first-line HER2 positive metastatic breast cancer
- Datroway approval based on TROPION-Breast02 phase 3 trial where Datroway demonstrated a median overall survival of approximately two years versus chemotherapy in patients with first-line triple negative breast cancer who are not candidates for PD-1/PD-L1 inhibitor therapy
- These approvals underscore the strength of the DXd ADC portfolio of Daiichi Sankyo to change the standard of care across different subtypes of metastatic breast cancer in Japan

Tokyo – **(September 16, 2026)** – Enhertu® (trastuzumab deruxtecan) and Datroway® (datopotamab deruxtecan) have been approved in Japan for two new indications in the first-line setting of patients with metastatic breast cancer.

Enhertu in combination with pertuzumab was approved for the treatment of adult patients with HER2 positive unresectable or recurrent breast cancer. Datroway was approved for the treatment of adult patients with hormone receptor (HR) negative and HER2 negative unresectable or recurrent breast cancer, a subtype commonly referred to as triple negative breast cancer (TNBC).

Enhertu and Datroway are specifically engineered DXd antibody drug conjugates (ADC) discovered by Daiichi Sankyo (TSE: 4568) and being developed and commercialized by Daiichi Sankyo in Japan.

Breast cancer is the most common cancer among women in Japan.[1] Both HER2 positive and TNBC are aggressive breast cancer subtypes, with only about 30% and 15% of patients, respectively, living five years following diagnosis.[2,3] For patients with these aggressive subtypes, treatments that significantly delay disease progression in the first-line metastatic setting are needed to improve long-term outcomes.

“These two approvals represent significant advances for the treatment of metastatic breast cancer. Enhertu in combination with pertuzumab is the first new treatment regimen in more than a decade for patients with metastatic HER2 positive disease and Datroway is the only TROP2 directed medicine to demonstrate an overall survival benefit for patients with metastatic triple negative breast cancer in the first-line setting,” said Yuki Abe, PhD, Senior Executive Officer, Head of R&D Division in Japan and Head of Research, Daiichi Sankyo. “With these new approvals of Enhertu and Datroway, there are now two Daiichi Sankyo medicines available in Japan that can be used as first-line treatments across the most aggressive subtypes of metastatic breast cancer.”

Data Supporting Enhertu Approval

The approval of Enhertu by Japan’s Ministry of Health, Labour and Welfare (MHLW) is based on results from the DESTINY-Breast09 phase 3 trial. In the trial, Enhertu in combination with pertuzumab reduced the risk of disease progression or death by 44% versus taxane, trastuzumab and pertuzumab (THP) (hazard ratio [HR]=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). These data were presented at the 2025 American Society of Clinical Oncology Annual Meeting and subsequently published in *The New England Journal of Medicine*.

In DESTINY-Breast09, the safety profile of Enhertu was consistent with previous clinical trials with no new safety concerns identified. Adverse reactions occurred in 373 patients (97.9%) treated with Enhertu (5.4 mg/kg) in combination with pertuzumab including 39 Japanese patients. The most common adverse reactions were nausea (71.1%), diarrhea (55.9%), alopecia (46.2%), vomiting (42.0%) and anemia (34.9%). Interstitial lung disease (ILD) occurred in 33.3% of Japanese patients treated with Enhertu in combination with pertuzumab as determined by an independent ILD adjudication committee.

Data Supporting Datroway Approval

The approval of Datroway by Japan's MHLW is based on results from the TROPION-Breast02 phase 3 trial, which included patients with metastatic TNBC who experienced early relapse following prior treatment and were not candidates for PD-1/PD-L1 inhibitor therapy. In this trial, Datroway demonstrated a statistically significant and clinically meaningful 5.0 month improvement in median overall survival (OS) versus investigator's choice of chemotherapy (HR=0.79; 95% CI: 0.64-0.98; p=0.029). Median OS was 23.7 months for patients treated with Datroway versus 18.7 months for those treated with chemotherapy. Datroway reduced the risk of disease progression or death by 43% compared to chemotherapy (HR=0.57; 95% CI: 0.47-0.69; p<0.0001) as assessed by BICR. Median PFS was 10.8 months for patients treated with Datroway versus 5.6 months for those treated with chemotherapy. These data were presented at the 2025 European Society for Medical Oncology Congress and subsequently published in *Annals of Oncology*.

In TROPION-Breast02, the safety profile of Datroway was consistent with previous clinical trials with no new safety concerns identified. Adverse reactions occurred in 296 patients (92.8%) treated with Datroway (6 mg/kg) including 17 Japanese patients. The most common adverse reactions included stomatitis (57.1%), nausea (44.5%), alopecia (40.8%), dry eye (23.8%) and constipation (22.6%). ILD was not observed in the 17 Japanese patients treated with Datroway.

Both Enhertu and Datroway are approved in Japan with a Warning in their prescribing information for ILD. ILD occurred in 11.7% of patients treated with Enhertu and 3.1% of patients treated with Datroway across multiple clinical trials. As cases of ILD, including fatal cases, have occurred in Enhertu and Datroway treated patients, both medicines are to be used in close collaboration with a respiratory disease expert. Patients should be closely observed during therapy by monitoring for early signs or symptoms of ILD (such as dyspnea, cough or fever) and performing periodical percutaneous oxygen saturation (SpO2) tests, chest X-ray scans and chest CT scans. If abnormalities are observed, discontinue administration of Enhertu or Datroway and take appropriate measures, such as corticosteroid administration. Prior to initiation of Enhertu or Datroway therapy, a chest CT scan should be performed and medical history taken to confirm the absence of any comorbidity or history of ILD with the patient and carefully consider the eligibility of the patient for Enhertu or Datroway therapy.

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 the Enhertu monotherapy and Enhertu combination arms. Secondary endpoints include investigator-assessed PFS, OS, overall response rate (ORR), duration of response (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 TROPION-Breast02

TROPION-Breast02 is a global, multicenter, randomized, open-label phase 3 trial evaluating the efficacy and safety of Datroway versus investigator's choice of chemotherapy (paclitaxel, nab-paclitaxel, capecitabine, carboplatin or eribulin) in patients with previously untreated locally recurrent inoperable or metastatic TNBC for whom immunotherapy was not an option. This included patients whose tumors did not express PD-L1 as well as patients with PD-L1 expressing tumors who could not receive immunotherapy due to prior exposure in early-stage disease, comorbidities or immunotherapy not being accessible in their geography. Enrollment included patients with de novo or recurrent disease, regardless of disease-free interval, and those with poor prognostic factors such as stable brain metastases.

The dual primary endpoints of TROPION-Breast02 are OS and PFS as assessed by BICR. Secondary endpoints include PFS as assessed by investigator, ORR, DoR, disease control rate, pharmacokinetics and safety.

TROPION-Breast02 enrolled 644 patients at sites in Africa, Asia, Europe, North America and South America. For more information visit ClinicalTrials.gov.

About Metastatic Breast Cancer

Breast cancer is the most common cancer in women and the leading cause of cancer-related deaths among women worldwide.[4] Approximately 2.4 million breast cancer cases were diagnosed in 2024, with more than 690,000 deaths globally.[4] In Japan, breast cancer is the most common cancer in women, with approximately 94,000 cases diagnosed and 16,800 deaths in 2024.[1]

There are three main breast cancer subtypes: HR positive, HER2 positive and TNBC.[2,5,6] Approximately 15% to 20% of breast cancer cases are considered HER2 positive where the disease is driven by overexpression or amplification of HER2, and 15% are considered to be triple negative where the tumor tests negative for estrogen receptors, progesterone receptors or overexpression of HER2.[7,8] Both HER2 positive and TNBC are aggressive breast cancer subtypes, with only about 30% and 15% of patients, respectively, living five years following diagnosis.[2,3]

While HER2 targeted therapies have improved outcomes for patients with HER2 positive metastatic breast cancer, 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.[9,10,11,12]

For patients with metastatic TNBC with PD-L1 expressing tumors, the addition of immunotherapy to chemotherapy has improved outcomes in the first-line setting.[13,14] However, for approximately 70% of patients with metastatic TNBC who are not candidates for immunotherapy, chemotherapy was the standard first-line treatment.[15]

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 non-small cell lung cancer (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 Datroway

Datroway (datopotamab deruxtecan; datopotamab deruxtecan-dlnk in the U.S. only) is a TROP2 directed ADC. Designed using the proprietary DXd ADC Technology of Daiichi Sankyo, Datroway is one of seven DXd ADCs in the oncology pipeline of Daiichi Sankyo, and one of the most advanced programs in AstraZeneca's ADC scientific

platform. Datroway is comprised of a humanized anti-TROP2 IgG1 monoclonal antibody, developed in collaboration with Sapporo Medical University, attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

Datroway (6 mg/kg) is approved in more than 30 countries/regions worldwide for the treatment of adult patients with unresectable or metastatic TNBC who are not candidates for PD-1/PD-L1 inhibitor therapy based on the results from the TROPION-Breast02 trial.

Datroway (6 mg/kg) is approved in more than 45 countries/regions worldwide for the treatment of adult patients with unresectable or metastatic HR positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease based on the results from the TROPION-Breast01 trial.

Datroway (6 mg/kg) is approved in Brazil, Russia, Singapore and the U.S. for the treatment of adult patients with locally advanced or metastatic EGFR-mutated non-small cell lung cancer (NSCLC) who have received prior EGFR-directed therapy and platinum-based chemotherapy, based on the results from TROPION-Lung05 and TROPION-Lung01 trials. Continued approval for this indication in the U.S. may be contingent upon verification and description of clinical benefit in a confirmatory trial.

About the Enhertu and Datroway Clinical Development Programs

A comprehensive global clinical development program is underway with more than 30 trials evaluating the efficacy and safety of Enhertu across multiple cancers, including breast, NSCLC, gastric, colorectal, biliary tract, ovarian, endometrial cancers. The program includes nine phase 3 trials in breast cancer, two phase 3 trials in NSCLC, two phase 3 trials in gastric cancer, two phase 3 trials in endometrial cancer, one phase 3 trial in ovarian cancer and one phase 3 trial in BTC evaluating Enhertu as a monotherapy and in combination or sequentially with other cancer treatments in various settings.

A comprehensive global clinical development program is underway with more than 20 trials evaluating the efficacy and safety of Datroway across multiple cancers, including NSCLC, TNBC and urothelial cancer. The program includes eight phase 3 trials in lung cancer, five phase 3 trials in breast cancer, and one phase 3 trial and one phase 2/3 trial in urothelial cancer evaluating Datroway as a monotherapy and in combination with other cancer treatments in various settings.

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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