Press Release

Daiichi-Sankyo

Enhertu® Supplemental New Drug Application Submitted in Japan for Patients with HER2 Expressing Advanced or Recurrent Uterine Carcinosarcoma

- Submission based on STATICE phase 2 trial results where Enhertu demonstrated durable responses in this patient population
- Enhertu is the first HER2 directed medicine to demonstrate clinical activity in HER2 expressing advanced or recurrent uterine carcinosarcoma in Japan

Tokyo – (November 12, 2026) – Daiichi Sankyo (TSE: 4568) has submitted a supplemental New Drug Application (sNDA) to Japan's Ministry of Health, Labour and Welfare (MHLW) for Enhertu® (trastuzumab deruxtecan) for the treatment of patients with HER2 expressing (immunohistochemistry [IHC] 3+, IHC 2+ or IHC 1+) advanced or recurrent uterine carcinosarcoma.

Enhertu is a specifically engineered HER2 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo and being developed and commercialized by Daiichi Sankyo in Japan.

The sNDA is based on data from the STATICE phase 2 trial, an investigator-initiated trial conducted in Japan, which was published in the *Journal of Clinical Oncology*. In the trial, Enhertu (5.4 mg/kg) demonstrated durable responses across levels of HER2 expression in patients with advanced or recurrent uterine carcinosarcoma previously treated with chemotherapy (including adjuvant chemotherapy). STATICE is the first prospective trial to show clinical activity with a HER2 directed medicine in this rare form of cancer.

"Patients with HER2 expressing advanced uterine carcinosarcoma in Japan face a poor prognosis, with treatment relying on chemotherapy rather than options directed at a specific molecular target," said Yuki Abe, PhD, Senior Executive Officer, Head of R&D Division in Japan and Head of Research, Daiichi Sankyo. "The durable activity demonstrated in the STATICE trial underscores the benefit of targeting HER2 with Enhertu in this difficult-to-treat cancer. If approved, Enhertu could provide an important targeted treatment option for patients with uterine carcinosarcoma in Japan."

Enhertu currently is approved in more than 50 countries/regions worldwide to treat patients with HER2 positive (IHC 3+) solid tumors who have received prior treatment and/or who have no satisfactory treatment options. In Japan, Enhertu can be considered as a treatment option for patients with HER2 positive (*HER2* [*ERBB2*] gene amplification or IHC 3+) uterine carcinosarcoma when standard treatment is not appropriate.

Enhertu also is under review in Japan as an adjuvant treatment for patients with HER2 positive (IHC 3+ or in-situ hybridization (ISH)+) breast cancer with residual invasive disease after neoadjuvant therapy based on data from DESTINY-Breast05.

About STATICE

STATICE is a multicenter, open-label, single-arm investigator-initiated phase 2 trial evaluating the efficacy and safety of Enhertu (6.4 or 5.4 mg/kg) in patients in Japan with HER2 expressing (HER2 IHC 3+, IHC 2+ or IHC 1+) advanced or recurrent uterine carcinosarcoma who have received prior chemotherapy (including adjuvant chemotherapy). At trial initiation, Enhertu 6.4 mg/kg was administered; however, based on an assessment of risk/benefit, the dosing was modified mid-trial to 5.4 mg/kg and was determined to be the preferred dose for this patient population.

The primary endpoint of STATICE is objective response rate (ORR) as assessed by central review in patients with HER2 expressing tumors with IHC ≥ 2+. Secondary endpoints include investigator-assessed ORR in patients with HER2 expressing tumors with IHC ≥ 2+, ORR by central review and investigator assessment in patients with HER2 IHC 1+ tumors, progression-free survival (PFS), overall survival (OS) and safety. Results from STATICE were published in the *Journal of Clinical Oncology*.

STATICE enrolled 34 patients across seven sites in Japan. For more information about the trial, visit Japan's University Hospital Medical Information Network.

About Uterine Carcinosarcoma

Uterine carcinosarcoma is a rare, highly aggressive form of endometrial cancer that accounts for fewer than 5% of endometrial cancer cases in Japan.[1,2,3] Despite its rarity, uterine carcinosarcoma is estimated to account for approximately 15% of endometrial cancer-related deaths.[3] Prognosis remains poor, with lower overall survival for uterine carcinosarcoma compared to other types of endometrial cancer and particularly poor outcomes reported following later lines of treatment in recurrent or metastatic uterine carcinosarcoma.[1,4,5]

HER2 is a tyrosine kinase receptor protein involved in cell growth and differentiation and expressed on the surface of multiple tumor types.[6] HER2 expression (IHC 3+, IHC 2+, or IHC 1+) was observed in 72.3% of patients with uterine carcinosarcoma, supporting HER2 as a potential therapeutic target.[7] Pre-clinical trials evaluating HER2 targeted therapies showed promising antitumor effects, supporting the potential of HER2 as a therapeutic target in uterine carcinosarcoma.[8,9,10]

In Japan, paclitaxel plus carboplatin chemotherapy is commonly used as systemic treatment for unresectable, advanced uterine carcinosarcoma, including recurrent disease.[11,12,13] However, median disease-free survival with this regimen is less than two years and disease recurrence occurs in 57% of patients with uterine carcinosarcoma.[12]

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 more than five countries/regions worldwide 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.

Enhertu (5.4 mg/kg) is approved in more than 35 countries/regions worldwide 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 (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 50 countries/regions worldwide for the treatment of adult patients with unresectable or metastatic HER2 positive (IHC 3+) solid tumors who have received prior treatment and/or have no satisfactory alternative treatment options based on efficacy results from the DESTINY-PanTumor02, DESTINY-Lung01, DESTINY-CRC02, DESTINY-PanTumor03 and/or HERALD 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.

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 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 being a trusted healthcare innovator, contributing to the enrichment of quality of life around the world through its strengths in science and technology. At Daiichi Sankyo, we believe progress depends on asking more of science, challenging assumptions and pursuing better answers. Progress like this is built by people who never stop learning, questioning and pushing what's possible. Together, we work to bring new breakthrough medicines within reach for patients and help shape what comes next in oncology and beyond. For more information, please visit www.daiichisankyo.com and connect with us on LinkedIn.

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