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Daiichi-Sankyo

Press Release

DATROWAY® Launched in Japan as the First TROP2 Directed Therapy for Patients with Previously Treated Unresectable or Recurrent HR Positive, HER2 Negative Breast Cancer

- Second DXd antibody drug conjugate to be launched in Japan based on Daiichi Sankyo's DXd Technology

Tokyo – (March 19, 2025) – Daiichi Sankyo's (TSE:4568) DATROWAY® (datopotamab deruxtecan) has been launched in Japan for the treatment of adult patients with hormone receptor (HR) positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) unresectable or recurrent breast cancer after prior chemotherapy.

DATROWAY is the first ever TROP2 directed medicine to be launched in Japan for HR positive, HER2 negative breast cancer and is the second DXd antibody drug conjugate (ADC) available based on Daiichi Sankyo's DXd ADC Technology.

Marketing approval of DATROWAY was granted by the Japan Ministry of Health, Labour and Welfare (MHLW) in December 2024 based on the results from the TROPION-Breast01 phase 3 trial where DATROWAY significantly reduced the risk of disease progression or death by 37% compared to investigator's choice of chemotherapy (hazard ratio [HR]=0.63, 95% confidence interval [CI]: 0.52-0.76; p<0.0001) in patients with HR positive, HER2 negative metastatic breast cancer as assessed by blinded independent central review (BICR). Median progression-free survival (PFS) was 6.9 months in patients treated with DATROWAY compared to 4.9 months in those treated with chemotherapy.

"HR positive, HER2 negative unresectable or recurrent breast cancer has historically been treated with conventional chemotherapy after progression with hormone therapy, which is associated with poor response rates and a low five-year survival rate," said Kei Kiuchi, Vice President, Oncology Marketing Department, Japan Business Unit, Daiichi Sankyo. "Patients now will have access to DATROWAY, the first TROP2 directed medicine available in Japan for this specific type of metastatic breast cancer."

In TROPION-Breast01, adverse reactions occurred in 93.6% (337/360 patients) of the 360 patients (including 31 Japanese patients) in the DATROWAY (6 mg/kg) arm. The most common adverse reactions included nausea (51.1%), stomatitis (50.0%), alopecia (36.4%), fatigue (23.6%) and dry eye (21.7%). In Japanese patients, interstitial lung disease (ILD) occurred in 6.5% of patients treated with DATROWAY.

DATROWAY is approved in Japan with a Warning for ILD. As cases of ILD, including fatal cases, have occurred in DATROWAY-treated patients, DATROWAY is 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 (SpO_2) tests, chest X-ray scans and chest CT scans. If abnormalities are observed, discontinue administration of DATROWAY and take appropriate measures, such as corticosteroid administration. Prior to initiation of 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 DATROWAY therapy.

Additional regulatory submissions for DATROWAY in breast cancer are under review in the EU, China and other regions.

About TROPION-Breast01

TROPION-Breast01 is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of intravenous DATROWAY (6 mg/kg) once per 21-day cycle versus investigator's choice of single-agent chemotherapy (eribulin, capecitabine, vinorelbine or gemcitabine) in adult patients with unresectable or metastatic HR positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who progressed on and are not suitable for endocrine therapy per investigator assessment and have received at least one additional systemic therapy for unresectable or metastatic disease.

Following disease progression or discontinuation of DATROWAY or chemotherapy, patients had the option to receive subsequent treatment at the discretion of their physician. Crossover between trial arms was not permitted.

The dual primary endpoints of TROPION-Breast01 are PFS as assessed by BICR and overall survival (OS). Key secondary endpoints include overall response rate, duration of response, investigator-assessed PFS, disease control rate, time to first subsequent therapy and safety. The PFS data and additional results for key secondary endpoints of TROPION-Breast01 were published in the *Journal of Clinical Oncology*. The OS data were presented at a Virtual Plenary session hosted by the European Society for Medical Oncology in February 2025.

TROPION-Breast01 enrolled 732 patients in Africa, Asia, Europe, North America and South America. For more information visit ClinicalTrials.gov.

About Hormone Receptor Positive, HER2 Negative 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 Japan, breast cancer is the most common cancer in women, with approximately 92,000 cases diagnosed in 2022.[2] While survival rates are high for those diagnosed with early breast cancer, only about 30% of patients diagnosed with or who progress to metastatic disease are expected to live five years following diagnosis.[3]

Approximately 70% of diagnosed cases are considered what has been historically called HR positive, HER2 negative breast cancer (measured as HER2 score of IHC 0, IHC 1+ or IHC 2+/ISH-).[3] Endocrine therapy is widely given consecutively in the early lines of treatment for HR positive metastatic breast cancer.[4] However, after initial treatment, further efficacy from endocrine therapy is often limited.[4] The current standard of care following endocrine therapy is chemotherapy, which is associated with poor response rates and outcomes.[4,5,6,7]

About DATROWAY

DATROWAY (datopotamab deruxtecan; datopotamab deruxtecan-dlnk in the U.S. only) is a TROP2 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, DATROWAY is one of six 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 is approved in Japan and the U.S. for the treatment of adult patients with unresectable or metastatic HR positive, HER2 negative 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.

About the DATROWAY Clinical Development Program

A comprehensive global clinical development program is underway with more than 20 trials evaluating the efficacy and safety of DATROWAY across multiple cancers, including non-small cell lung cancer, triple negative breast cancer and HR positive, HER2 negative breast cancer. The program includes eight phase 3 trials in lung cancer and five phase 3 trials in breast cancer evaluating DATROWAY as a monotherapy and in combination with other anticancer 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 seven ADCs in clinical development crafted from two distinct ADC technology platforms discovered in-house by Daiichi Sankyo.

The ADC platform furthest in clinical development is Daiichi Sankyo's DXd ADC Technology where each ADC consists of a monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers. The DXd ADC portfolio currently consists of ENHERTU, a HER2 directed ADC, and DATROWAY, a TROP2 directed ADC, which are being jointly developed and commercialized globally with AstraZeneca. Patritumab deruxtecan (HER3-DXd), a HER3 directed ADC, ifinatamab deruxtecan (I-DXd), a B7-H3 directed ADC, and raludotatug deruxtecan (R-DXd), a CDH6 directed ADC, are being jointly developed and commercialized globally with Merck & Co., Inc, Rahway, NJ, USA. DS-3939, a TA-MUC1 directed ADC, is being developed by Daiichi Sankyo.

The second Daiichi Sankyo ADC platform consists of a monoclonal antibody attached to a modified pyrrolobenzodiazepine (PBD) payload. DS-9606, a CLDN6 directed PBD ADC, is the first of several planned ADCs in clinical development utilizing this platform.

Ifinatamab deruxtecan, patritumab deruxtecan, raludotatug deruxtecan, DS-3939 and DS-9606 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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