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Daiichi-Sankyo

Press Release

DATROWAY® Approved in the EU for Patients with Previously Treated Metastatic HR Positive, HER2 Negative Breast Cancer

- First approval in the EU for Daiichi Sankyo and AstraZeneca's DATROWAY based on TROPION-Breast01 trial showing 37% reduction in the risk of disease progression or death versus chemotherapy
- Second DXd antibody drug conjugate approved in EU based on Daiichi Sankyo's DXd technology

Tokyo and Munich – (April 8, 2025) – DATROWAY® (datopotamab deruxtecan) has been approved in the European Union (EU) for the treatment of adult patients with unresectable or metastatic hormone receptor (HR) positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received endocrine therapy and at least one line of chemotherapy in the advanced setting.

DATROWAY is a specifically engineered TROP2 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/Nasdaq: AZN).

The approval by the European Commission follows the positive opinion of the Committee for Medical Products for Human Use of the European Medicines Agency and is based on results from the TROPION-Breast01 phase 3 trial.

In TROPION-Breast01, 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 versus 4.9 months with chemotherapy. A confirmed objective response rate (ORR) of 36% was observed in the DATROWAY arm compared to an ORR of 23% observed in the chemotherapy arm. The median duration of response (DoR) was 6.7 months (95% CI: 5.6-9.8) in the DATROWAY arm compared to 5.7 months (95% CI: 4.9-6.8) in the chemotherapy arm. The final overall survival (OS) results of the trial did not achieve statistical significance (median OS of 18.6 months in the DATROWAY arm versus 18.3 months in the chemotherapy arm [HR 1.01; 95% CI: 0.83-1.22]) and may have been affected by subsequent ADC treatment.

"With the majority of breast cancer cases historically considered HR positive, HER2 negative, additional treatment options are needed to improve outcomes for patients with metastatic disease that continues to progress following endocrine-based therapy and initial chemotherapy," said Barbara Pistilli, MD, Head of the Breast Cancer Unit in the Medical Oncology Department of Gustave Roussy Cancer Center, Villejuif, France. "The approval of DATROWAY in the EU will provide these patients with a new treatment option that can help slow the progression of this disease."

"Treating metastatic HR positive, HER2 negative breast cancer presents challenges, particularly treatment resistance and disease progression that occur following endocrine-based therapy and initial chemotherapy," said Ken Keller, Global Head of Oncology Business, and President and CEO, Daiichi Sankyo, Inc. "DATROWAY represents the second antibody drug conjugate approved for breast cancer based on Daiichi Sankyo's DXd technology and the third medicine to be approved in the EU from our oncology pipeline, underscoring our commitment to creating new medicines for patients with cancer."

"Though the HR positive breast cancer treatment landscape has evolved in the last several years, disease progression on front-line therapies remains a common and complex challenge for patients with metastatic disease," said Dave Fredrickson, Executive Vice President, Oncology Hematology Business Unit, AstraZeneca. "With today's approval of DATROWAY, patients in the EU with HR positive, HER2 negative breast cancer now have a new and needed alternative to conventional chemotherapy."

Grade 3 or higher adverse events from a pooled safety analysis of two clinical studies, including 443 patients who received DATROWAY (6 mg/kg) for a median duration of 6.2 months (range: 0.7-28.5), were stomatitis (7.9%), fatigue (4.3%), anemia (3.2%), AST increased (2.7%), vomiting (1.6%), ALT increased (1.6%), nausea (1.4%), urinary tract infection (1.4%), COVID-19 (1.1%), decreased appetite (1.1%), neutropenia (1.1%) and pneumonia (1.1%). Grade 5 adverse events occurred in 0.7% of patients due to interstitial lung disease/pneumonitis, dyspnea and sepsis.

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 have progressed on and are not suitable for endocrine therapy per investigator assessment and have received at least one prior line of chemotherapy for unresectable or metastatic disease.

Following disease progression or discontinuation of DATROWAY or chemotherapy, patients had the option to receive a 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 OS. Key secondary endpoints include ORR, DoR, 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* and OS results 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 Europe, approximately 557,000 cases of breast cancer are diagnosed annually.[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 metastatic HR positive breast cancer.[4] However, after initial treatment, further efficacy from endocrine therapy is often limited.[4]

About DATROWAY

DATROWAY (datopotamab deruxtecan) 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 more than 30 countries 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 of 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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