

Press Release

Datopotamab Deruxtecan New Drug Application Submitted in Japan for Patients with Previously Treated Advanced HR Positive, HER2 Negative Breast Cancer

- Submission based on results from the TROPION-Breast01 phase 3 trial

Tokyo – (March 14, 2024) – Daiichi Sankyo (TSE: 4568) has submitted a New Drug Application (NDA) to Japan’s Ministry of Health, Labour and Welfare (MHLW) for datopotamab deruxtecan (Dato-DXd) 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.

The NDA is based on results from the pivotal [TROPION-Breast01](#) phase 3 trial presented at a Presidential Symposium at the European Society for Medical Oncology (#ESMO23) 2023 Congress. In the trial, datopotamab deruxtecan demonstrated a statistically significant and clinically meaningful improvement for the dual primary endpoint of progression-free survival (PFS) compared to investigator’s choice of chemotherapy in patients with unresectable or metastatic HR positive, HER2 negative breast cancer previously treated with endocrine-based therapy and at least one systemic therapy. For the dual primary endpoint of overall survival (OS), interim results numerically favored datopotamab deruxtecan over chemotherapy but were not statistically significant at the time of data cut-off. The trial is ongoing and OS will be assessed at future analyses. The safety profile of datopotamab deruxtecan was consistent with that observed in other ongoing trials with no new safety concerns identified.

“Today’s submission for datopotamab deruxtecan in Japan is a significant step forward in our goal to create new standards of care globally with our pipeline of DXd antibody drug conjugates,” said Wataru Takasaki, PhD, Executive Officer, Head of R&D Division in Japan, Daiichi Sankyo. “We will work closely with the Japan Health Authority to bring this TROP2 directed antibody drug conjugate to patients with previously treated HR positive, HER2 negative metastatic breast cancer.”

About TROPION-Breast01

[TROPION-Breast01](#) is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan versus investigator's choice of single-agent chemotherapy (eribulin, capecitabine, vinorelbine or gemcitabine) in 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 additional systemic therapy for unresectable or metastatic disease.

The dual primary endpoints of TROPION-Breast01 are PFS as assessed by blinded independent central review and OS. Key secondary endpoints include objective response rate, duration of response, investigator-assessed PFS, disease control rate, time to first subsequent therapy and safety. TROPION-Breast01 enrolled more than 700 patients in Africa, Asia, Europe, North America and South America. For more information visit [ClinicalTrials.gov](#).

About Hormone Receptor Positive, HER2 Negative Breast Cancer

More than 90,000 breast cancer cases were diagnosed in Japan in 2022.¹ HR positive, HER2 negative breast cancer is the most common subtype, accounting for more than 65% of diagnosed cases.² Breast cancer is considered HR positive, HER2 negative when tumors test positive for estrogen and/or progesterone hormone receptors and negative for HER2 (measured as HER2 score of IHC 0, IHC 1+ or IHC 2+/ISH-).^{2,3} Standard initial treatment for this subtype of breast cancer includes endocrine therapy but most patients with advanced disease will develop resistance, underscoring the need for additional options.^{4,5}

TROP2 is a protein broadly expressed in HR positive, HER2 negative breast cancer and high TROP2 expression is associated with increased tumor progression and poor survival.^{6,7} There is currently no TROP2 directed ADC approved for the treatment of cancer in Japan.

About Datopotamab Deruxtecan (Dato-DXd)

Datopotamab deruxtecan (Dato-DXd) is an investigational TROP2 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, datopotamab deruxtecan 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. Datopotamab deruxtecan 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.

A comprehensive development program called TROPION is underway globally with more than 14 trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple cancers, including NSCLC, triple negative breast cancer and HR positive, HER2 negative breast cancer. Beyond the TROPION program, datopotamab deruxtecan also is being evaluated in novel combinations in several ongoing trials.

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 datopotamab deruxtecan (Dato-DXd) 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 datopotamab deruxtecan.

About the DXd ADC Portfolio of Daiichi Sankyo

The DXd ADC portfolio of Daiichi Sankyo currently consists of six ADCs in clinical development across multiple types of cancer. ENHERTU, a HER2 directed ADC, and datopotamab deruxtecan, a TROP2 directed ADC, 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, N.J. USA. DS-3939, a TA-MUC1 directed ADC, is being developed by Daiichi Sankyo.

Designed using Daiichi Sankyo's proprietary DXd ADC Technology to target and deliver a cytotoxic payload inside cancer cells that express a specific cell surface antigen, 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.

Datopotamab deruxtecan, ifinatamab deruxtecan, patritumab deruxtecan, raludotatug deruxtecan and DS-3939 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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