

Press Release

Datopotamab Deruxtecan Biologics License Application Accepted in the U.S. for Patients with Previously Treated Metastatic HR Positive, HER2 Negative Breast Cancer

- Application based on results from the TROPION-Breast01 phase 3 trial
- Additional BLA under review in the U.S. for Daiichi Sankyo and AstraZeneca's datopotamab deruxtecan for patients with advanced nonsquamous non-small cell lung cancer

Tokyo and Basking Ridge, NJ – (April 2, 2024) – Daiichi Sankyo (TSE: 4568) and AstraZeneca's (LSE/STO/Nasdaq: AZN) Biologics License Application (BLA) for datopotamab deruxtecan (Dato-DXd) has been accepted in the U.S. 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 prior systemic therapy for unresectable or metastatic disease.

Datopotamab deruxtecan is a specifically engineered TROP2 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo and being jointly developed by Daiichi Sankyo and AstraZeneca.

The Prescription Drug User Fee Act (PDUFA) date, the U.S. Food and Drug Administration (FDA) action date for its regulatory decision, is January 29, 2025.

The BLA is based on results from the pivotal [TROPION-Breast01](#) phase 3 trial, which were [presented](#) at a Presidential Symposium at the European Society for Medical Oncology (#ESMO23) 2023 Congress and in an oral presentation at the 2023 San Antonio Breast Cancer Symposium (#SABCS23). 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 mature 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. The most common grade 3 or higher treatment-related adverse events in the datopotamab deruxtecan and chemotherapy arms, respectively, were neutropenia (1% vs. 31%), stomatitis (6% vs. 3%), fatigue (2% vs. 2%) and anemia (1% vs. 2%).

“The FDA’s acceptance of the BLA brings us closer to providing patients with previously treated HR positive, HER2 negative breast cancer an alternative option to conventional chemotherapy earlier in the metastatic setting,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “Following our recently accepted application for advanced nonsquamous non-small cell lung cancer in the U.S., along with additional regulatory reviews underway in China, the EU, Japan and other regions, we are working swiftly to bring datopotamab deruxtecan as a potential new treatment option to patients around the world.”

“Despite marked progress in the treatment of HR positive, HER2 negative breast cancer, most patients with advanced disease develop endocrine resistance and face the prospect of one or several lines of chemotherapy,” said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology R&D, AstraZeneca. “If approved, datopotamab deruxtecan has the potential to provide these patients an efficacious and better tolerated alternative to conventional chemotherapy.”

An additional BLA for datopotamab deruxtecan based on results from the pivotal [TROPION-Lung01](#) phase 3 trial is under review in the U.S. for the treatment of adult patients with locally advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) who have received prior systemic therapy. Additional regulatory submissions for datopotamab deruxtecan in lung and breast cancer are underway globally.

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 275,000 breast cancer cases were diagnosed in the U.S. 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 is 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 is associated with increased tumor progression and poor survival.^{6,7}

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 global clinical development program is underway with more than 20 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.

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 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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