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Daiichi-Sankyo

Press Release

Datopotamab Deruxtecan Recommended for Approval in the EU by CHMP for Patients with Previously Treated Metastatic HR Positive, HER2 Negative Breast Cancer

- Recommendation based on TROPION-Breast01 results showing Daiichi Sankyo and AstraZeneca's datopotamab deruxtecan reduced risk of disease progression or death by 37% versus chemotherapy
- Datopotamab deruxtecan approved in the U.S. and Japan for same patient population

Tokyo and Munich – (January 31, 2025) – Datopotamab deruxtecan (Dato-DXd) has been recommended for approval 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.

Datopotamab deruxtecan is a specifically engineered TROP2 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo (TSE:45680) and being jointly developed and commercialized by Daiichi Sankyo and AstraZeneca (LSE/STO/Nasdaq: AZN).

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on results from the TROPION-Breast01 phase 3 trial published in the *Journal of Clinical Oncology*. The recommendation will now be reviewed by the European Commission, which has the authority to grant marketing authorizations for medicines in the EU.

In TROPION-Breast01, datopotamab deruxtecan 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 datopotamab deruxtecan versus 4.9 months with chemotherapy. A confirmed objective response rate (ORR) of 36% was observed in the datopotamab deruxtecan arm compared to an ORR of 23% observed in the chemotherapy arm. Two (0.5%) complete responses (CR) and 131 (36%) partial responses (PR) were observed in the datopotamab deruxtecan arm compared to zero CR and 84 PR (23%) in the chemotherapy arm. The median duration of response (DoR) was 6.7 months (95% CI: 5.6-9.8) in the datopotamab deruxtecan arm compared to 5.7 (95% CI: 4.9-6.8) in the chemotherapy arm.

Datopotamab deruxtecan demonstrated a favorable safety profile over chemotherapy with no new safety concerns identified. Grade 3 or higher treatment-related adverse events (TRAEs) occurred in 21% and 45% of patients in the datopotamab deruxtecan and chemotherapy arms, respectively. The most common grade 3 or higher TRAEs were neutropenia (1% vs. 31%), stomatitis (6% vs. 3%), fatigue (2% vs. 2%) and anemia (1% vs. 2%). In the datopotamab deruxtecan arm, the all-grade interstitial lung disease (ILD) rate was low (3%) and the majority of events were low grade. There was one grade 5 ILD event adjudicated as drug related by an independent committee. The primary cause of death in this case was attributed to disease progression by the treating investigator.

“Disease progression after endocrine and initial chemotherapy is common in patients with metastatic HR positive, HER2 negative breast cancer,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “This positive recommendation by the CHMP for datopotamab deruxtecan, which follows recent approvals in the U.S. and Japan, underscores the potential of this TROP2 directed antibody drug conjugate to offer a new treatment option to patients in the EU with this type of breast cancer.”

“Only one in three patients live more than five years after a metastatic HR positive, HER2 negative breast cancer diagnosis, underscoring the urgent need for additional effective therapies,” said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology Hematology R&D, AstraZeneca. “Today’s recommendation for datopotamab deruxtecan brings us closer to offering these patients in the EU a new and needed alternative to conventional chemotherapy.”

Datopotamab deruxtecan is approved in Japan and the U.S. for the treatment of 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. Additional regulatory submissions for datopotamab deruxtecan in breast cancer are under review in 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 datopotamab deruxtecan (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 datopotamab deruxtecan 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 objective 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*.

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 500,000 breast cancer cases were diagnosed in Europe 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 therapies are 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.**Error! Bookmark not defined.** The current standard of care following endocrine therapy is chemotherapy, which is associated with poor response rates and outcomes.[4,5,6,7]

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.

Datopotamab deruxtecan is approved in Japan and the U.S. under the brand name DATROWAY for the treatment of adult patients with HR positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) unresectable or recurrent breast cancer after prior chemotherapy based on the results of the TROPION-Breast01 trial.

About the Datopotamab Deruxtecan Clinical Development Program

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 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 datopotamab deruxtecan 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 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 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 datopotamab deruxtecan, 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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