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Daiichi-Sankyo

Press Release

Two Datopotamab Deruxtecan Applications Validated in the EU for Patients with Advanced Nonsquamous Non-Small Cell Lung Cancer or HR Positive, HER2 Negative Breast Cancer

- Parallel applications based on TROPION-Lung01 and TROPION-Breast01 phase 3 trial results demonstrating Daiichi Sankyo and AstraZeneca's datopotamab deruxtecan significantly improved progression-free survival versus chemotherapy in two types of cancer

Tokyo and Munich – (March 4, 2024) – The European Medicines Agency (EMA) has validated two marketing authorization applications (MAAs) for Daiichi Sankyo (TSE: 4568) and AstraZeneca's (LSE/STO/Nasdaq: AZN) datopotamab deruxtecan (Dato-DXd) in two types of cancer. One MAA is for the treatment of adult patients with locally advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) who require systemic therapy following prior treatment. The other MAA is 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 progressed on and are not suitable for endocrine therapy and received at least one additional systemic therapy.

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 validations confirm the completion of the applications and commence the scientific review process by the EMA's Committee for Medicinal Products for Human Use. The applications are based on data from the pivotal TROPION-Lung01 and TROPION-Breast01 phase 3 trials presented during two Presidential Symposia at the European Society for Medical Oncology (#ESMO23) 2023 Congress.

"The EMA validation is an important first step toward bringing this TROP2 directed antibody drug conjugate to eligible patients in Europe with nonsquamous lung cancer and HR positive, HER2 negative breast cancer," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "This news builds on our recent regulatory progress in the U.S., where our lung cancer application has been accepted and our breast cancer application is underway, underscoring our commitment to changing the standard of care by developing new medicines to help as many patients worldwide as possible."

"Our ambition is for datopotamab deruxtecan to improve upon and replace conventional chemotherapy in the treatment of multiple cancer types," said Susan Galbraith, MBBChir, PhD, Executive Vice President,

Oncology R&D, AstraZeneca. “Today’s dual validation of our applications in lung and breast cancers brings this potential medicine a meaningful step closer to redefining treatment expectations for patients with two of the most common cancers in Europe.”

Additional regulatory submissions for datopotamab deruxtecan in lung cancer and breast cancer are underway in the U.S. and globally.

About TROPION-Lung01

TROPION-Lung01 is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan versus docetaxel in patients with locally advanced or metastatic NSCLC with and without actionable genomic alterations who require systemic therapy following prior treatment. Patients with actionable genomic alterations were previously treated with platinum-based chemotherapy and an approved targeted therapy. Patients without known actionable genomic alterations were previously treated, either in combination or sequentially, with platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor.

The dual primary endpoints of TROPION-Lung01 are progression-free survival (PFS) as assessed by blinded independent central review (BICR) and overall survival (OS). Key secondary endpoints include investigator-assessed PFS, objective response rate (ORR), duration of response (DoR), time to response, disease control rate (DCR) as assessed by both BICR and investigator, and safety. TROPION-Lung01 enrolled approximately 600 patients in Asia, Europe, North America and South America. For more information visit ClinicalTrials.gov.

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 BICR and OS. Key secondary endpoints include ORR, DoR, investigator-assessed PFS, DCR, 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 Advanced Non-Small Cell Lung Cancer

Nearly 500,000 lung cancer cases were diagnosed in Europe in 2022.[6] NSCLC is the most common type of lung cancer, accounting for about 80% of cases.[1] Approximately 70% and 30% of NSCLC tumors are of nonsquamous or squamous histology, respectively.[2] While immunotherapy and targeted therapies have improved outcomes in the first-line setting, most patients eventually experience disease progression and receive chemotherapy.[3,4,5] For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC, despite limited effectiveness and known side effects.[3,4,5]

About Hormone Receptor Positive, HER2 Negative Breast Cancer

More than 500,000 breast cancer cases were diagnosed in Europe in 2022.[6] HR positive, HER2 negative breast cancer is the most common subtype, accounting for more than 65% of diagnosed cases.[7] 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-).[7,8] 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.[9,10]

About TROP2

TROP2 is a protein broadly expressed in several solid tumors, including the majority of NSCLC and HR positive, HER2 negative breast cancer cases.[11,12] High TROP2 expression is associated with increased tumor progression and poor survival.[12,13] There is currently no TROP2 directed ADC approved for the treatment of lung cancer.[14,15]

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 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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