

Press Release

TROPION-Breast01 Phase 3 Trial of Datopotamab Deruxtecan Initiated in Patients with Hormone Receptor Positive, HER2 Negative Metastatic Breast Cancer

Tokyo, Munich and Basking Ridge, NJ – (November 18, 2021) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that the first patient was dosed in the global **TROPION-Breast01** phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan (Dato-DXd), a TROP2 directed DXd antibody drug conjugate (ADC) being jointly developed by Daiichi Sankyo and AstraZeneca (LSE/STO/Nasdaq: AZN), in patients with hormone receptor (HR) positive, human epidermal growth factor 2 receptor (HER2) negative inoperable or metastatic breast cancer previously treated with chemotherapy.

Breast cancer is the most common cancer worldwide with more than two million cases diagnosed in 2020, resulting in nearly 685,000 deaths globally.¹ Approximately 70% of all breast cancers are considered HR positive, HER2 negative.² For patients with HR positive, HER2 negative metastatic breast cancer that progresses on or is not suitable for hormone therapy-based regimens, current standard of care is single-agent chemotherapy, which demonstrates diminishing efficacy with each subsequent line of treatment.³

“There are no TROP2 directed therapies currently approved for HR positive, HER2 negative breast cancer and we are encouraged by the emerging clinical profile of datopotamab deruxtecan in patients with breast cancer,” said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. “TROPION-Breast01 is the first pivotal trial of datopotamab deruxtecan in breast cancer and the third pivotal study in our clinical development program, underscoring our efforts to accelerate development of this TROP2 directed ADC in breast and lung cancer.”

“Most patients with HR positive, HER2 negative metastatic breast cancer will inevitably progress on available treatments, including hormonal therapy and standard of care chemotherapy. In this setting, the unmet need is high, and new therapeutic approaches are necessary to delay disease progression and extend survival,” said Cristian Massacesi, MD, Chief Medical Officer and Oncology Chief Development Officer, AstraZeneca. “The TROPION-Breast01 trial will evaluate whether datopotamab deruxtecan may be a more effective treatment than chemotherapy for patients with previously treated HR positive, HER2 negative advanced breast cancer previously treated with one to two lines of chemotherapy.”

About TROPION-Breast01

TROPION-Breast01 is a global, randomized, open-label, phase 3 trial evaluating the efficacy and safety of datopotamab deruxtecan (6 mg/kg) compared with investigator's choice of chemotherapy (eribulin, capecitabine, vinorelbine or gemcitabine) in patients with inoperable or metastatic HR positive, HER2 negative breast cancer (per ASCO/CAP guidelines, on local laboratory results) who have progressed on or were not suitable for endocrine therapy and previously treated with one or two prior lines of systemic chemotherapy in the inoperable or metastatic setting.

The dual primary endpoints of TROPION-Breast01 are progression-free survival (PFS) assessed by blinded independent central review and overall survival. Secondary endpoints include PFS assessed by investigator, objective response rate, duration of response, disease control rate, and patient reported outcomes, as well as safety and pharmacokinetics.

TROPION-Breast01 will enroll approximately 700 patients at sites in Africa, Asia, Europe, North America and South America. For more information visit [ClinicalTrials.gov](https://clinicaltrials.gov).

About HR Positive, HER2 Negative Breast Cancer

Breast cancer is the most common cancer and is one of the leading causes of cancer-related deaths worldwide. More than two million cases of breast cancer were diagnosed in 2020, resulting in nearly 685,000 deaths globally.¹ Approximately 5% to 10% of women diagnosed with breast cancer have metastatic disease at diagnosis, and up to 30% of women with early-stage breast cancer will develop metastatic disease.⁴

Approximately 70% of all breast cancers are considered HR positive, HER2 negative, meaning tumors test positive for estrogen and/or progesterone hormone receptors and negative for HER2.² Current standard of care treatment for patients with HR positive, HER2 negative metastatic breast cancer that progresses on hormone therapy-based regimens is sequential single-agent chemotherapy. However, response rates are low with PFS ranging from 4 to 6.3 months with second-line chemotherapy, and 2.4 to 5.5 months with third-line chemotherapy.^{5,6,7,8} Data in subsequent lines of treatment show decreasing median PFS and OS with each further line of chemotherapy. There remains a need to improve outcomes including survival for patients living with advanced HR positive, HER2 negative breast cancer.⁹

About TROP2

TROP2 (trophoblast cell-surface antigen 2) is a transmembrane glycoprotein overexpressed in several types of solid tumors, including breast cancer.¹⁰ TROP2 expression has been detected in a wide range of breast cancer subtypes, including the HR positive, HER2 negative subtype.^{11,12} High TROP2 expression is an

unfavorable prognostic factor for overall survival in all types of breast cancer.¹³ There are currently no TROP2 directed therapies approved for treatment of HR positive, HER2 negative breast cancer.

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 three lead 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 IgG1³ monoclonal antibody, developed in collaboration with Sapporo Medical University, attached to a topoisomerase I inhibitor payload, an exatecan derivative, via a tetrapeptide-based cleavable linker.¹⁴

A comprehensive development program called TROPION is underway globally with trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple solid tumors, including non-small cell lung cancer (NSCLC), triple negative breast cancer (TNBC), HR positive/HER2 negative breast cancer, small cell lung cancer (SCLC), urothelial, gastric and esophageal cancer. Trials in combination with other anticancer treatments, such as immunotherapy, are also underway.

About the Daiichi Sankyo and AstraZeneca Collaboration

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize datopotamab deruxtecan in [July 2020](#), except in Japan where Daiichi Sankyo maintains exclusive rights. Daiichi Sankyo is responsible for the manufacturing and supply of datopotamab deruxtecan.

About Daiichi Sankyo in Oncology

The oncology portfolio of Daiichi Sankyo is powered by our team of world-class scientists that push beyond traditional thinking to create transformative medicines for people with cancer. Anchored by our DXd antibody drug conjugate (ADC) technology, our research engines include biologics, medicinal chemistry, modality and other research laboratories in Japan, and [Plexxikon Inc.](#), our small molecule structure-guided R&D center in the U.S. We also work alongside leading academic and business collaborators to further advance the understanding of cancer as Daiichi Sankyo builds towards our ambitious goal of becoming a global leader in oncology by 2025.

About Daiichi Sankyo

Daiichi Sankyo is dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose "to contribute to the enrichment of quality of life around the world." In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases

with high unmet medical needs. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 16,000 employees around the world draw upon a rich legacy of innovation to realize our 2030 Vision to become an “Innovative Global Healthcare Company Contributing to the Sustainable Development of Society.” For more information, please visit: www.daiichisankyo.com.

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