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Press Release

Datopotamab Deruxtecan Continues to Show Promising Durable Response and Disease Control in Patients with Metastatic Triple Negative Breast Cancer

- Updated data from the TNBC cohort of the TROPION-PanTumor01 phase 1 trial of Daiichi Sankyo and AstraZeneca's datopotamab deruxtecan featured as oral presentation at SABCS

Tokyo, Munich and Basking Ridge, NJ – (December 7, 2021) – New data from the TROPION-PanTumor01 phase 1 trial of datopotamab deruxtecan (Dato-DXd), a TROP2 directed DXd antibody drug conjugate (ADC) being developed by Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca (LSE/STO/Nasdaq: AZN), continue to show encouraging durable tumor response and disease control in patients with metastatic triple negative breast cancer (TNBC) with disease progression following standard treatment. These data were featured during an oral presentation (GS1-05) at the 2021 San Antonio Breast Cancer Symposium (#SABCS21).

TNBC accounts for approximately 10 to 15% of breast cancer cases and is associated with higher disease recurrence and worse prognosis compared to other breast cancer subtypes.[1,2,3] It is estimated that only 12.2% of patients with metastatic TNBC survive five years and median overall survival is generally less than two years.[2,3]

An objective response rate (ORR) of 34% was observed in 15 of 44 patients treated with datopotamab deruxtecan (6 mg/kg [n=42] and 8 mg/kg [n=2]) as assessed by blinded independent central review. Fourteen confirmed complete/partial responses (CR/PRs) with one additional CR/PR awaiting confirmation and stable disease in 17 additional patients were reported after a median follow-up of 7.6 months (range, 4 – 13 months). Median duration of response (DOR) was not reached (range, 2.7 – 7.4+ months) with the majority ongoing at the data cut-off of July 30, 2021. A disease control rate (DCR) of 77% was observed.

In a subgroup of 27 patients with measurable disease and previously untreated with a topoisomerase I inhibitor-based ADC, an ORR of 52% was reported with datopotamab deruxtecan. Thirteen confirmed CR/PRs with one additional CR/PR awaiting confirmation and stable disease were reported in nine additional patients after a median follow-up of 8.8 months (range, 4 – 13 months). A DCR of 81% was observed in this subgroup of patients.

“Despite recent advances in the treatment of triple negative breast cancer, a significant need remains to improve patient outcomes, underscoring the importance of developing new and effective therapies,” said Ian E. Krop, MD, PhD, Associate Chief, Division of Breast Oncology, Susan F. Smith Center for Women’s Cancers, Dana Farber Cancer Institute. “These preliminary results with datopotamab deruxtecan in pre-treated patients with metastatic triple negative breast cancer are very encouraging and further evaluation of this TROP2 directed ADC is warranted.”

The overall safety profile of datopotamab deruxtecan in TNBC in TROPION-PanTumor01 was consistent with what has been previously reported with no new safety signals. Treatment emergent adverse events (TEAEs) occurring in ≥15% of patients included nausea, stomatitis, vomiting, fatigue, alopecia, mucosal inflammation, constipation, headache, decreased lymphocyte count, decreased neutrophil count, pyrexia, anemia, pruritis, hypokalemia, diarrhea and cough. Grade 3 or greater treatment-related TEAEs occurred in 23% of patients. No cases of interstitial lung disease (ILD) were observed.

“These updated results continue to show the promise of datopotamab deruxtecan as a durable treatment strategy for patients with previously treated triple negative breast cancer, a historically difficult-to-treat form of breast cancer,” said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. “We are committed to further developing datopotamab deruxtecan and establishing where this specifically engineered TROP2 may be most effective in treating triple negative breast cancer.”

“Patients with metastatic triple negative breast cancer face rapid disease progression with currently available treatment options and unmet need remains high for these patients,” said Cristian Massacesi, MD, Chief Medical Officer and Oncology Chief Development Officer, AstraZeneca. “Based on these encouraging results of datopotamab deruxtecan in the triple negative breast cancer cohort of TROPION-PanTumor01, plans are underway to initiate a registrational phase 3 study.”

Patients were treated with a median of three prior therapies in the metastatic setting (range, 1-10), including taxanes (91%), platinum-based chemotherapy (52%), immunotherapy (43%), topoisomerase I inhibitor-based ADCs (30%; sacituzumab govitecan, n=10; trastuzumab deruxtecan, n=2; patritumab deruxtecan, n=1) and PARP inhibitors (16%). As of data cut-off on July 30, 2021, 30% of patients remained on treatment with datopotamab deruxtecan.

Summary of TROPION-PanTumor01 TNBC Results

Efficacy Measure	All TNBC Patients (n=44)[i]	Patients without Prior Topoisomerase I-Based ADC and with Measurable Disease (n=27)[ii]
ORR, %	34% (n=15)	52% (n=14)
(CR/PR) (confirmed)	n=14	n=13
(CR/PR) (pending confirmation)	n=1[iii]	n=1[iii]
SD, %	39% (n=17)	33% (n=9)
PD, %	18% (n=8)	15% (n=4)
DCR, %	77% (n=34)	81% (n=22)

CR; complete response; DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease

[i] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments were not yet available for 2 patients at the data cut-off. Three patients were not confirmed to have a target lesion per BICR and therefore had a best overall response of non-CR/non-PD.
[ii] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments were not yet available for 1 patient at the data cut-off.
[iii] Includes patients with an unconfirmed response but are ongoing treatment.

About TROPION-PanTumor01

TROPION-PanTumor01 is a first-in-human, open-label, two-part, multicenter phase 1 trial evaluating the safety, tolerability and preliminary efficacy of datopotamab deruxtecan in patients with advanced solid tumors refractory to or relapsed from standard treatment or for whom no standard treatment is available, including non-small cell lung cancer (NSCLC), TNBC, hormone receptor (HR) positive/HER2 negative breast cancer, small cell lung cancer, urothelial, gastric and esophageal cancer.

The dose escalation part of the study, which was limited to patients with NSCLC, assessed the safety and tolerability of increasing doses of datopotamab deruxtecan to determine the maximum tolerated dose and/or recommended dose for expansion. The dose expansion part of the study further assessed the safety and tolerability of datopotamab deruxtecan in patients with additional solid tumors. Based on the preliminary efficacy and safety profile, the 6 mg/kg dose has been chosen for further development.[4,5]

Safety endpoints include dose limiting toxicities and serious adverse events. Efficacy endpoints include ORR, DCR, DOR, time to response, progression-free survival and overall survival. Pharmacokinetic, biomarker and immunogenicity endpoints also are being evaluated.

About Triple Negative Breast Cancer

Approximately 10 to 15% of breast cancers are considered triple negative, a breast cancer subtype that is defined by tumors that test negative for estrogen and progesterone hormone receptors (HRs) as well as human epidermal growth factor 2 receptor (HER2).[1,2,6] An estimated 260,000 new cases of TNBC were

reported globally in 2018 with it being more common in younger women and those who are Black.[1,2,7] Compared to patients with other breast cancer subtypes, prognosis for patients with metastatic TNBC is generally worse and the disease is more likely to recur following treatment with initial chemotherapy.[1,3] Five-year survival of metastatic TNBC is estimated at 12.2% and median overall survival is generally less than two years.[2,9]

About TROP2

TROP2 (trophoblast cell-surface antigen 2) is a transmembrane glycoprotein overexpressed in several types of solid tumors, including breast cancer.[8] TROP2 overexpression has been detected in multiple breast cancer subtypes, including approximately 80% of patients with TNBC.[9,10,11] High TROP2 expression is an unfavorable prognostic factor for overall survival in all types of breast cancer.[12]

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 IgG1^{3} 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.[13]

A comprehensive development program called TROPION is underway globally with trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple solid tumors, including NSCLC, TNBC, HR positive/HER2 negative breast cancer, small cell lung cancer, 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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