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Press Release

New Biomarker Analyses from Patritumab Deruxtecan Phase 1 Study in Patients with EGFR-Mutated NSCLC Presented at WCLC 2020

Munich and Basking Ridge, NJ – (January 29, 2021) – Exploratory biomarker analyses from an ongoing phase 1 study of Daiichi Sankyo Company, Limited's (hereafter, Daiichi Sankyo) patritumab deruxtecan, a HER3 directed DXd antibody drug conjugate (ADC), in patients with previously treated EGFR-mutated metastatic/unresectable non-small cell lung cancer (NSCLC) were highlighted in a poster presentation today at the IASLC 2020 World Conference on Lung Cancer (WCLC), hosted by the International Association for the Study of Lung Cancer.

Lung cancer is the leading cause of cancer death among both men and women, and accounts for about one-fifth of all cancer deaths globally, with 80 to 85 percent classified as NSCLC.[1,2] For patients with metastatic disease, prognosis is particularly poor, as only 6 to 10 percent live beyond five years after diagnosis.[3]

Approximately 25 to 30 percent of lung cancers worldwide have an EGFR-activating mutation, and it is estimated that about 83 percent of all NSCLC tumors express the HER3 protein, which can be associated with an increased incidence of metastases, reduced survival and resistance to standard treatment.[4,5,6] There currently are no HER3 directed therapies approved for the treatment of NSCLC.

The exploratory analyses assessed genomic alterations in 56 evaluable patients with EGFR inhibitor resistant NSCLC receiving patritumab deruxtecan in the dose escalation (n=12) and cohort 1 of the dose expansion (n=45) part of the phase 1 study. HER3 expression was evaluated by H score, which is a method of assessing the percentage of tumor cells with cell membrane staining.

Nearly all evaluable tumors expressed high levels of HER3 at baseline, with a median membrane H score of 180 (range: 2-280). Preliminary assessments suggested that there was a trend toward higher HER3 membrane expression at baseline in patients who obtained a confirmed response to treatment with patritumab deruxtecan. Analysis is ongoing with specimens from additional patients in the study.

Diverse genomic alterations comprising known EGFR tyrosine kinase inhibitor (TKI) resistance mechanisms were present in pretreatment tumor tissues and circulating tumor DNA (ctDNA), including EGFR T790M

mutation (53 percent); MET amplification (8 percent); multiple oncogenic fusions involving FGFR3, NTRK1, BRAF, ALK, RET or ROS1 (8 percent); and HER2 mutation (4 percent). Clinical responses were observed in patients with diverse mechanisms of EGFR TKI resistance, including mechanisms not directly related to EGFR. Patients with evaluable ctDNA at pre- and post-treatment showed reduction of EGFR activation mutations, and primary analysis suggests that the majority of patients with confirmed clinical response were more likely to have ctDNA clearance of EGFR-activating mutations at week 3 or week 6. Absence of ctDNA clearance of EGFR-activating mutations was associated with a best overall response of progressive disease.

"These data provide important insights about how a HER3 directed therapy may interact in previously treated NSCLC tumors with diverse mechanisms of EGFR TKI resistance, including mechanisms not directly related to EGFR," said Pasi A. Jänne, MD, PhD, Director, Lowe Center for Thoracic Oncology at Dana-Farber Cancer Institute. "While an association between higher levels of HER3 expression and clinical activity was seen with patritumab deruxtecan, additional analyses from this study and additional studies are needed to better understand the role of HER3 expression alone in the optimal selection of patients."

"Translational research such as this is essential to advancing targeted therapy for patients with NSCLC with disease progression following standard treatments," said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. "In patients with NSCLC and other tumor types that overexpress HER3, we will continue our exploration of potential biomarkers for patient selection and tumor response in our ongoing clinical development of patritumab deruxtecan."

About the Phase 1 NSCLC Study

The global, multicenter, open label, two-part phase 1 study is evaluating patritumab deruxtecan in previously treated patients with metastatic or unresectable NSCLC.

The dose escalation part of the study evaluated patients with EGFR-mutated disease either with progression on osimertinib or T790M-negative after progression on erlotinib, gefitinib or afatinib. The primary objective of this part of the study was to assess the safety and tolerability of patritumab deruxtecan and determine the recommended dose for expansion (RDE).

The dose expansion part of the study is evaluating patritumab deruxtecan at the RDE (5.6 mg/kg every three weeks) in three cohorts. Cohort 1 includes patients with metastatic or unresectable EGFR-mutated NSCLC who experienced disease progression after taking one or more EGFR TKIs and one or more platinum based chemotherapy regimens. Cohort 2 includes patients with squamous or non-squamous NSCLC without EGFR-activating mutations, following platinum-based chemotherapy and following an anti-PD-1 or anti-PD-

L1 antibody regimen. Cohort 3 includes patients with NSCLC with EGFR-activating mutations including any histology other than combined small cell and non-small cell lung cancer; patients in Cohort 3 will be randomized 1:1 to receive the RDE regimen (Cohort 3a) or an escalating up-titration regimen of patritumab deruxtecan (Cohort 3b).

Preliminary data from the dose escalation part of the study were presented previously at the 2019 World Conference on Lung Cancer, and early data from the dose escalation part (5.6 mg/kg dose) and Cohort 1 of the dose expansion were presented at the 2020 European Society of Medical Oncology (ESMO) Virtual Congress.

The primary objective of the dose expansion part of the study is to assess efficacy of patritumab deruxtecan as measured by confirmed objective response rate (ORR) assessed by blinded independent central review. Secondary study endpoints include investigator-assessed ORR; safety, tolerability and preliminary efficacy; and characterization of the pharmacokinetics of patritumab deruxtecan. The study is currently enrolling patients at multiple sites in the U.S., Europe, Japan and other countries in Asia. For more information, visit ClinicalTrials.gov.

About Non-Small Cell Lung Cancer

Lung cancer is the most common cancer and the leading cause of cancer mortality worldwide; there were an estimated 2.2 million new cases of lung cancer and 1.8 million deaths in 2020.[1] Most lung cancers are diagnosed at an advanced or metastatic stage.[2] Non-small cell lung cancer (NSCLC) accounts for 80 to 85 percent of all lung cancers.[7]

The introduction of targeted therapies and checkpoint inhibitors in the past decade has improved the treatment landscape for patients with advanced or metastatic NSCLC; however, the prognosis is particularly poor among patients who have progressed after treatment with standard therapies. For those who are not eligible for current treatments, or whose cancer continues to progress, new therapeutic approaches are needed.[8]

The mutationally-activated EGFR tyrosine kinase is a well-established oncogenic driver and molecular target for management of advanced stage NSCLC.[9] For patients with advanced EGFR-mutated NSCLC, targeted therapy with EGFR TKIs offer higher response rates and progression-free survival compared to chemotherapy.[8] However, most patients eventually develop resistance to these therapies, and standard treatment options are limited.[10] Clinical resistance to EGFR TKIs has been linked to multiple molecular mechanisms, and in many cases, the underlying mechanism of resistance remains unknown.[11,12,13]

About HER3

HER3 is a member of the EGFR family of receptor tyrosine kinases, which are associated with aberrant cell proliferation and survival.[14] Approximately 25 to 30 percent of lung cancers worldwide have an EGFR-activating mutation, and it is estimated that about 83 percent of tumors express the HER3 protein, which can be associated with an increased incidence of metastases, reduced survival and resistance to standard of care treatment.[4,5,6] Currently, no HER3 directed medicines are approved for the treatment of cancer.

About Patritumab Deruxtecan

Patritumab deruxtecan (HER3-DXd; U3-1402) is one of three lead DXd antibody drug conjugates (ADC) in the oncology pipeline of Daiichi Sankyo. Designed using Daiichi Sankyo's proprietary DXd ADC technology, patritumab deruxtecan is comprised of a human anti-HER3 antibody attached to a topoisomerase I inhibitor payload, an exatecan derivative, via a stable tetrapeptide-based cleavable linker.

Patritumab deruxtecan is currently being evaluated in a comprehensive development program across multiple cancers as both a monotherapy and in combination with other anticancer treatments. The development program includes a phase 2 study in patients with advanced/metastatic colorectal cancer with progression following at least two prior lines of systemic therapy; a phase 1/2 study in HER3 expressing metastatic breast cancer; a phase 1 study in combination with osimertinib in locally advanced/metastatic EGFR-mutated NSCLS; and, a phase 1 study in previously treated patients with metastatic or unresectable NSCLC.

Patritumab deruxtecan is an investigational agent that has not been approved for any indication in any country. Safety and efficacy have not been established.

About Daiichi Sankyo Cancer Enterprise

The mission of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. Anchored by our DXd antibody drug conjugate (ADC) technology, our powerful 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 Berkeley, CA. For more information, please visit: www.DSCancerEnterprise.com.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical therapies to improve standards of care and address diversified, unmet medical needs of people globally by leveraging our world-class science and technology. With more than 100 years of scientific expertise and a presence in more

than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for cardiovascular diseases, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo is primarily focused on providing novel therapies in oncology, as well as other research areas centered around rare diseases and immune disorders. For more information, please visit: www.daiichisankyo.com.

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