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Press Release

HERTHENA-Lung01 Phase 2 Study of Daiichi Sankyo's Patritumab Deruxtecan Initiated in Patients with EGFR-Mutated NSCLC

Tokyo, Basking Ridge, N.J. and Munich – **(February 3, 2021)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that the first patient has been dosed in HERTHENA-Lung01, a phase 2 study evaluating patritumab deruxtecan, a HER3 directed DXd antibody drug conjugate (ADC), in patients with epidermal growth factor receptor (EGFR)-mutated metastatic or locally advanced non-small cell lung cancer (NSCLC) previously treated with a tyrosine kinase inhibitor (TKI) and platinum-based chemotherapy.

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 of care treatment.[4,5,6] There currently are no HER3 directed medicines approved for the treatment of NSCLC.

"Our focus is to rapidly and strategically advance the clinical development program of patritumab deruxtecan in cancers where HER3 is frequently overexpressed and is associated with poor prognosis," said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. "This study will further inform whether targeting HER3 with an antibody drug conjugate may become a potential treatment strategy to overcome diverse mechanisms of EGFR TKI and chemotherapy resistance seen in patients with metastatic EGFR-mutated non-small cell lung cancer."

Exploratory biomarker analyses from the ongoing phase 1 study of patritumab deruxtecan in patients with previously treated metastatic or locally advanced EGFR-mutated NSCLC were recently presented at the IASLC 2020 World Conference on Lung Cancer (WCLC), hosted by the International Association for the Study of Lung Cancer. Encore clinical results from this phase 1 study also were presented at WCLC.

About HERTHENA-Lung01

HERTHENA-Lung01 is a global, multicenter, open-label, phase 2 study evaluating the safety and efficacy of patritumab deruxtecan in patients with locally advanced or metastatic NSCLC with an EGFR-activating mutation (exon 19 deletion or L858R) who have progressed after receiving at least one EGFR TKI and at least one platinum-based chemotherapy regimen.

The study will randomize patients into one of two patritumab deruxtecan treatment arms in a 1:1 ratio. Patients in the first arm of the study will receive a 5.6 mg/kg fixed dose regimen of patritumab deruxtecan intravenously every three weeks. Patients in the second arm will receive an up-titration dose regimen of patritumab deruxtecan in three week cycles, with a 3.2 mg/kg dose given in the first cycle, a 4.8 mg/kg dose in the second, and 6.4 mg/kg in the third and subsequent cycles.

The primary endpoint of HERTHENA-Lung01 is objective response rate (ORR), as assessed by blinded independent central review (BICR). Secondary endpoints include duration of response, progression-free survival, disease control rate, and time to response – all assessed by both BICR and investigator assessment – as well as investigator-assessed ORR, overall survival, safety and tolerability. The level of HER3 protein expression in tumor tissue and its relationship with efficacy will be analyzed. Pharmacokinetics and immunogenicity also will be assessed.

HERTHENA-Lung01 is expected to enroll up to approximately 420 patients in the U.S., Europe and Asia, including Japan. For more information about the study, 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 all NSCLC 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 HERTHENA-Lung01, a phase 2 study in patients with EGFR-mutated metastatic or locally advanced NSCLC previously treated with a TKI and platinum-based chemotherapy; 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 NSCLC; 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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