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Press Release

Daiichi Sankyo Presents Preliminary Phase 1 Data for HER3 Targeting ADC U3-1402 in Patients with EGFR Mutated Non-Small Cell Lung Cancer at 2019 ASCO Annual Meeting

- First phase 1 results presented for U3-1402, a potential first-in-class HER3 targeting antibody drug conjugate (ADC), in patients with metastatic EGFR mutated, TKI resistant NSCLC
- Preliminary data show manageable safety, and reduction in tumor size was observed in all 16 evaluable patients across all doses of U3-1402, with a median best percentage change of -29 percent (range -3 to -80 percent) at a median follow-up time of 4.2 months
- HER3 is frequently expressed in NSCLC but no HER3 targeting therapies are currently approved
- Findings add to previous results seen with U3-1402 in metastatic HER3 positive breast cancer, supporting the broad applicability of Daiichi Sankyo's proprietary DXd ADC technology to different targets and tumor types

Tokyo, Munich, and Basking Ridge, NJ – (May 31, 2019) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that preliminary results from the dose escalation part of the phase 1 study with U3-1402, an investigational and potential first-in-class HER3 targeting antibody drug conjugate (ADC), in 23 patients with metastatic EGFR mutated, TKI resistant non-small cell lung cancer (NSCLC), will be presented today during an Oral Symposium at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL. (Abstract #9010)

Preliminary efficacy data for 16 evaluable patients at the time of data cut-off who received U3-1402 at dose levels from 3.2 mg/kg to 6.4 mg/kg showed that a reduction in tumor size was observed in all 16 evaluable patients across all doses, with a median best percentage change of -29 percent (range -3 to -80 percent). All 16 patients had received prior treatment with an EGFR tyrosine kinase inhibitor (TKI), including 15 with osimertinib. Seven patients also had prior chemotherapy. A total of 16 patients remained on treatment at the time of data cut-off on February 25, 2019.

"These initial clinical data demonstrate activity with U3-1402, including early tumor shrinkage in patients who had developed resistance to approved EGFR TKIs," said Pasi A. Jänne, MD, PhD, Director, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute, and a trial investigator. "There is a need for new treatment approaches for EGFR mutated non-small cell lung cancer that develops resistance to TKIs, especially osimertinib, and preliminary results from this study indicate that targeting HER3 with U3-1402 is a strategy that may be effective across multiple different resistance mechanisms."

HER3 expression has been reported in up to 75 percent of non-small cell lung cancers.[1] In study patients, all tumors available for assessment in retrospective immunohistochemistry (IHC) analysis (n=19) showed some level of HER3 expression.

Preliminary safety data in 23 evaluable patients showed a manageable safety profile for U3-1402 with median treatment exposure of 105 days. A maximum tolerated dose has not yet been reached. The most common treatment-emergent adverse events of any grade (in ≥30 percent of patients) included nausea (60.9 percent), fatigue (39.1 percent), vomiting (34.7 percent), decreased appetite (30.4 percent) and platelet count decrease (30.4 percent). One treatment-emergent adverse event grade ≥3 occured in >10 percent of patients (platelet count decrease, 26.1 percent). The following dose-limiting toxicities were observed in four patients: grade 4 platelet count decrease (4 patients) and grade 3 febrile neutropenia (1 patient). Six patients (26.1 percent) experienced treatment-emergent serious adverse events regardless of causality, with three patients (13.0 percent) experiencing treatment-emergent serious adverse events that were related to study treatment. One patient experienced a treatment-emergent adverse event leading to treatment discontinuation (4.3 percent).

“U3-1402 was designed using Daiichi Sankyo’s proprietary DXd ADC technology to target and deliver chemotherapy inside cancer cells that express HER3 as a cell surface antigen,” said Dalila Sellami, MD, Vice President, U3-1402 Global Team Leader, Global Oncology Research and Development, Daiichi Sankyo. “These findings provide evidence of promising activity of U3-1402 in non-small cell lung cancer and add to our previous preliminary research demonstrating its potential use in HER3 positive metastatic breast cancer.”

About the Study

The global, phase 1, open label, two-part study is enrolling patients with metastatic or unresectable EGFR mutated NSCLC that has progressed while taking an EGFR TKI. This includes patients who either experienced disease progression on erlotinib, gefitinib, dacomitinib or afatinib and tested negative for the T790M mutation or who experienced disease progression on osimertinib regardless of T790M status. The primary objectives of the study are to assess the safety and tolerability of U3-1402 and determine the recommended dose for expansion. The secondary objectives are to characterize the pharmacokinetics of U3-1402 and to evaluate preliminary efficacy by measuring antitumor activity of U3-1402. The study is expected to enroll more than 60 patients at approximately 17 sites globally. For more information about the study, visit ClinicalTrials.gov.

About U3-1402

Part of the investigational ADC Franchise of the Daiichi Sankyo Cancer Enterprise, U3-1402 is an investigational and potential first-in-class HER3 targeting ADC. ADCs are targeted cancer medicines that deliver cytotoxic chemotherapy ("payload") to cancer cells via a linker attached to a monoclonal

antibody that binds to a specific target expressed on cancer cells. Designed using Daiichi Sankyo's proprietary DXd ADC technology, U3-1402 is comprised of a human anti-HER3 antibody attached to a novel topoisomerase I inhibitor payload by a tetrapeptide-based linker. It is designed to target and deliver chemotherapy inside cancer cells and reduce systemic exposure to the cytotoxic payload (or chemotherapy) compared to the way chemotherapy is commonly delivered.

U3-1402 is an investigational agent that has not been approved for any indication in any country. Safety and efficacy have not been established.

Unmet Need in Non-Small Cell Lung Cancer (NSCLC)

Lung cancer is the most common cancer and the leading cause of cancer mortality worldwide; there were an estimated 2.1 million new cases of lung cancer in 2018 and 1.8 million deaths.[2] Most lung cancers are diagnosed at an advanced or metastatic stage.[3] Non-small cell lung cancer (NSCLC) accounts for 80 to 85 percent of all lung cancers.[4] 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, for those who are not eligible for current treatments, or whose cancer continues to progress, new therapeutic approaches are needed.[5]

For patients with advanced EGFR mutated NSCLC, EGFR TKIs offer higher response rates and progression free survival compared to chemotherapy; however, most patients eventually develop resistance to the drugs, usually within a year, at which point treatment options become more limited.[6]

HER3 is a member of the human epidermal growth factor receptor family of tyrosine kinase receptors, which are associated with aberrant cell growth.[7] HER3 is overexpressed in several types of cancers and has been linked to tumor progression and worse overall survival.[8] HER3 expression is associated with increased metastases and reduced survival in patients with non-small cell lung cancer, where frequency has been reported as high as 75 percent.[1] In recent years, researchers have recognized potential for HER3 as a therapeutic target.[7] Currently, no HER3 targeting agents are approved for NSCLC or any cancer.

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 three pillars including our investigational Antibody Drug Conjugate Franchise, Acute Myeloid Leukemia Franchise and Breakthrough Science, we aim to deliver seven distinct new molecular entities over eight years during 2018 to 2025. Our powerful research engines include two laboratories for biologic/immuno-oncology and small molecules in Japan, and Plexxikon

Inc., our small molecule structure-guided R&D center in Berkeley, CA. Compounds in pivotal stage development include: [fam-] trastuzumab deruxtecan, an antibody drug conjugate (ADC) for HER2 expressing breast, gastric and other cancers; quizartinib, an oral selective FLT3 inhibitor, for newly-diagnosed and relapsed/refractory *FLT3*-ITD acute myeloid leukemia (AML); and pexidartinib, an oral CSF1R inhibitor, for tenosynovial giant cell tumor (TGCT). For more information, please visit: www.DSCancerEnterprise.com.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 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 hypertension and thrombotic disorders, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo research and development is primarily focused on bringing forth novel therapies in oncology, including immuno-oncology, with additional focus on new horizon areas, such as pain management, neurodegenerative diseases, heart and kidney diseases, and other rare diseases. For more information, please visit: www.daiichisankyo.com.

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