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Press Release

Daiichi Sankyo Presents Preliminary Phase 1 Data for TROP2 Targeting ADC DS-1062 in Patients with Non-Small Cell Lung Cancer at 2019 ASCO Annual Meeting

- First-in-human results presented for DS-1062, an investigational TROP2 targeting ADC, in patients with advanced NSCLC where no standard treatment is available
- Preliminary data show DS-1062 is well-tolerated with partial responses seen with increasing dose levels
- No TROP2 targeting therapy is approved for NSCLC or any cancer
- Findings represent proof-of-concept for Daiichi Sankyo's third ADC in clinical development utilizing its proprietary DXd ADC technology in different targets and tumor types

Tokyo, Basking Ridge, NJ, and Munich – (June 2, 2019) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that preliminary results from the dose escalation part of a phase 1 study with DS-1062, an investigational TROP2 targeting antibody drug conjugate (ADC), in 39 patients with advanced non-small cell lung cancer (NSCLC) were presented today during a Poster Session at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL (Abstract #9051).

Preliminary efficacy data for 35 evaluable patients who received DS-1062 at the dose levels between 0.27 mg/kg and 8.0 mg/kg every 21 days showed three confirmed and four not yet confirmed partial responses at the time of data cut-off on April 12, 2019.

An additional three partial responses have been reported with the 8.0 mg/kg dose of DS-1062 since data cut-off, bringing the total partial responses to 10. The median number of prior therapies for the partial responders is 3.5 and includes patients with prior EGFR or ALK inhibitors and checkpoint inhibitors.
A maximum tolerated dose of DS-1062 has not yet been reached and the dose escalation portion of the study is ongoing. Sixteen patients remain on-treatment at the time of data cut-off.

"Despite recent advances in the treatment of NSCLC, we need new precision treatment options for patients with advanced disease who currently have no available standard treatment options," said Jacob Sands, MD, Physician, Dana-Farber Cancer Institute, Instructor, Harvard Medical School, and lead investigator for the study. "These early results are encouraging as we have seen increased activity with higher doses of DS-1062 including several partial responses. Additional study is warranted to further determine the potential for targeting TROP2 with DS-1062 in these patients with advanced NSCLC."

Preliminary data for 39 patients evaluable for safety as of April 12, 2019 showed that DS-1062 was well-tolerated at a median treatment exposure time of 8.86 weeks (range 3.0-31.1). Common treatment emergent adverse events (occurring in ≥ 30 percent of patients) included fatigue (33.3 percent) and nausea (30.8 percent). Sixteen patients (41.0 percent) experienced at least one treatment emergent adverse event ≥ grade 3. One dose-limiting toxicity of maculopapular rash, grade 3 was observed in a patient in the 6.0 mg/kg cohort. Ten patients (25.6 percent) experienced serious adverse events not related to study drug, and one patient (2.5 percent) in the 4.0 mg/kg cohort experienced a treatment-related serious adverse event of pyrexia.

“We are encouraged by these preliminary results with DS-1062, which was designed using our proprietary DXd ADC technology to target and deliver treatment directly to tumors that express TROP2, a promising therapeutic target for many types of cancer, including NSCLC,” said Eric Slosberg, PhD, Head, Global Translational Development, Oncology Research and Development, Daiichi Sankyo. “Currently, there are no TROP2 targeting therapies approved for any cancer, and we will continue to study DS-1062 as part of our commitment to developing new targeted therapy options for patients with non-small cell lung and other cancers.”

DS-1062 is designed using Daiichi Sankyo’s proprietary DXd ADC technology, which consists of a humanized monoclonal antibody attached to a novel topoisomerase I inhibitor payload by a tetrapeptide-based linker. DS-1062 was designed to target and deliver chemotherapy inside cancer cells that express TROP2 as a cell surface antigen. The DXd ADC technology provides flexibility to adapt the drug-to-antibody ratio (DAR) or the number of DXd molecules conjugated per antibody. DS-1062 has a DAR of four, which is based on initial research into the construct necessary for intended efficacy and safety in TROP2 expressing tumors.

About the Phase 1 Study

The phase 1, first-in-human open-label study is investigating the safety and tolerability of DS-1062 in patients with unresectable advanced NSCLC who are refractory to or have relapsed following standard treatment or for whom no standard treatment is available. The first part of the study (dose escalation) is assessing the safety and tolerability of increasing doses of DS-1062 to determine the maximum tolerated dose and recommended dose for expansion. The second part of the study (dose expansion) will evaluate the safety and tolerability of DS-1062 at the recommended dose for expansion. Study endpoints include safety, pharmacokinetics, objective response rate, duration of response, disease control rate, time to response, progression-free survival, overall survival, biomarker analysis and immunogenicity. The study is currently enrolling patients with unresectable advanced NSCLC in the United States and Japan.

Based on the results of the study, additional cohorts may be initiated for other solid tumors where high expression of TROP2 is frequently observed. For more information about the study, visit ClinicalTrials.gov.

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.[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.[3] 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.[4]

TROP2 (trophoblast cell-surface antigen 2) is a transmembrane glycoprotein that is highly expressed on several types of solid tumors, including NSCLC.[5,6] Researchers have recognized TROP2 as a promising molecular target for therapeutic development in various types of malignancies, including NSCLC.[6,7] Overexpression of TROP2 has been associated with increased tumor aggressiveness and decreased survival in several cancers.[8] High TROP2 expression was identified in 64 percent of non-small cell adenocarcinomas and 75 percent of non-small cell squamous cell carcinomas in one study.[5] Currently, no TROP2 targeting therapy is approved for NSCLC or any cancer.

About DS-1062

Part of the investigational ADC Franchise of the Daiichi Sankyo Cancer Enterprise, DS-1062 is an investigational TROP2 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, DS-1062 is comprised of a humanized anti-TROP2 monoclonal 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.

DS-1062 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 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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