Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

Press Release

Daiichi Sankyo Presents Updated Results for [Fam-] Trastuzumab Deruxtecan (DS-8201) in Patients with HER2 Mutated or HER2 Expressing Non-Small Cell Lung Cancer at IASLC 19th World Conference on Lung Cancer

- Updated subgroup analysis from ongoing phase 1 study of [fam-] trastuzumab deruxtecan (DS-8201) demonstrated a confirmed overall response rate of 72.7 percent and a disease control rate of 100 percent in 11 patients with heavily pretreated HER2 mutated non-small cell lung cancer (NSCLC)
- A 58.8 percent confirmed overall response rate and 88.2 percent disease control rate was demonstrated with [fam-] trastuzumab deruxtecan in 17 patients with HER2 mutated or HER2 expressing NSCLC
- A global phase 2 study is currently enrolling patients with HER2 mutated or HER2 overexpressing NSCLC as part of a broad development program evaluating [fam-] trastuzumab deruxtecan in various HER2 expressing cancers

Tokyo, Munich, and Basking Ridge, NJ – (September 24, 2018) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that updated phase 1 safety and efficacy data for [fam-] trastuzumab deruxtecan (DS-8201), an investigational HER2 targeting antibody drug conjugate (ADC), were presented for a subgroup of patients with heavily pretreated HER2 mutated or HER2 expressing non-small cell lung cancer (NSCLC) during an Oral Session at the IASLC 19th World Conference on Lung Cancer (#WCLC2018) hosted by the International Association for the Study of Lung Cancer in Toronto, Canada.

An updated subgroup analysis of 11 patients with HER2 mutated NSCLC receiving a recommended expansion dose of 6.4 mg/kg showed that [fam-] trastuzumab deruxtecan demonstrated a confirmed overall response rate of 72.7 percent (8 of 11 patients) and disease control rate of 100 percent (11 of 11 patients). Preliminary estimate of median duration of response has reached 11.5 months (95 percent CI: 0.03+, 11.5) and median progression-free survival has reached 14.1 months (95 percent CI: 4.0+, 14.1) for this subgroup of patients.

“These preliminary results seen with [fam-] trastuzumab deruxtecan are encouraging, particularly given the existing unmet medical need for patients with metastatic NSCLC with HER2 alterations that have progressed on several prior therapies,” said Junji Tsurutani, MD, PhD, Advanced Cancer Translational Research Institute, Showa University, Tokyo, Japan, a study investigator. “These results also demonstrate that continued evaluation of treatments that target the HER2 receptor is warranted in patients with NSCLC.”

The updated subgroup analysis of 17 patients with heavily pretreated HER2 mutated or HER2 expressing (defined as IHC ≥1+ or amplified) NSCLC showed that [fam-] trastuzumab deruxtecan demonstrated a

confirmed overall response rate of 58.8 percent (10 of 17 patients) and a disease control rate of 88.2 percent (15 of 17 patients). Preliminary estimate of median duration of response has reached 9.9 months (95 percent CI: 0.0+, 11.5) and median progression-free survival has reached 14.1 months (95 percent CI: 0.9, 14.1).

"Patient enrollment is currently underway into our phase 2 study of [fam-] trastuzumab deruxtecan in patients with advanced HER2 mutated or HER2 overexpressing NSCLC," said Gilles Gallant, BPharm, PhD, Vice President, DS-8201 Global Team Leader, Oncology Research and Development, Daiichi Sankyo. "Since there are no therapies specifically approved to treat patients with HER2 altered NSCLC, continued study of [fam-] trastuzumab deruxtecan is needed to better understand the potential role of a HER2 targeting antibody drug conjugate in treating these patients."

Updated preliminary safety data for this subgroup of patients with heavily pretreated HER2 mutated or HER2 expressing NSCLC receiving [fam-] trastuzumab deruxtecan were also reported. The most common adverse events (>30 percent, any grade) included nausea (50.0 percent), decreased appetite (50.0 percent), alopecia (50.0 percent), fatigue (44.4 percent) and vomiting (38.9 percent). Grade 3 adverse events occurring in >10 percent of patients included decreased neutrophil count (11.1 percent). As previously reported, one (1) grade 5 event of pneumonitis was observed in this cohort, which was adjudicated as unrelated to [fam-] trastuzumab deruxtecan by an independent adjudication committee. Any reported cases of interstitial lung disease (ILD)/pneumonitis in the [fam-] trastuzumab deruxtecan clinical development program are evaluated by an independent adjudication committee.

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

Lung cancer is the most common cancer in the world and the leading cause of cancer deaths.[1] There were approximately 1.8 million new cases of lung cancer reported globally and approximately 1.6 million deaths in 2012.[1] Non-small cell lung cancer (NSCLC) accounts for approximately 80 to 85 percent of all cases.[2] The five-year survival rate for metastatic NSCLC is only one percent.[3]

The introduction of targeted therapies and checkpoint inhibitors in recent years has improved the treatment landscape for metastatic NSCLC patients, who previously had limited options beyond systemic chemotherapy.[4,5] However, for those who are not eligible for available treatments, or whose cancer continues to progress, new approaches are needed to help manage the disease.[6]

HER2 overexpression has been reported in rates ranging from 4 to 35 percent of NSCLC, depending on the published series and methods, and is associated with poor disease prognosis and shortened overall survival.[4,6] HER2 mutations have more recently been identified as distinct molecular targets for NSCLC and have been reported in up to 5 percent of NSCLC.[7,8] Currently, no therapy is specifically approved for HER2 mutated or HER2 overexpressing non-small cell lung cancer.

About the [Fam-] Trastuzumab Deruxtecan Phase 1 Study

An open-label, two-part phase 1 study is currently evaluating [fam-] trastuzumab deruxtecan in patients with advanced/unresectable or metastatic solid tumors that are refractory or intolerant to standard treatment, or for whom no standard treatment is available. The primary objective of the dose escalation phase of this study was to assess the safety and tolerability of and determine the maximum tolerated dose. Data from this part of the study were published in the *Lancet Oncology*.[9]

In the dose expansion part of the phase 1 study, [fam-] trastuzumab deruxtecan is given in one of two doses (5.4 mg/kg and 6.4 mg/kg) to patients with HER2 positive advanced or metastatic breast cancer and gastric cancer, HER2 low expressing breast cancer and other HER2 expressing solid tumors including NSCLC. Overall, 292 patients have been enrolled into this phase 1 study of [fam-] trastuzumab deruxtecan. For more information about the study, visit ClinicalTrials.gov.

About [Fam-] Trastuzumab Deruxtecan

[Fam-] trastuzumab deruxtecan (DS-8201; [fam-] trastuzumab deruxtecan in U.S. only; trastuzumab deruxtecan in other regions of world) is the lead product in the investigational ADC Franchise of the Daiichi Sankyo Cancer Enterprise. 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 ADC technology, [fam-] trastuzumab deruxtecan is comprised of a humanized HER2 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.

A broad and comprehensive development program with [fam-] trastuzumab deruxtecan is underway in North America, Europe and Asia. [Fam-] trastuzumab deruxtecan is in pivotal phase 2 clinical development for HER2 positive metastatic breast cancer resistant or refractory to ado-trastuzumab emtansine (DESTINY-Breast01); pivotal phase 2 development for HER2 positive advanced gastric cancer resistant or refractory to trastuzumab (DESTINY-Gastric01); phase 2 development for HER2 expressing advanced colorectal cancer; phase 2 development for metastatic non-squamous HER2 overexpressing or HER2 mutated NSCLC; and, phase 1 development in combination with nivolumab for HER2 expressing metastatic breast and bladder cancer.

[Fam-] trastuzumab deruxtecan has been granted Breakthrough Therapy designation for the treatment of patients with HER2 positive, locally advanced or metastatic breast cancer who have been treated with trastuzumab and pertuzumab and have disease progression after ado-trastuzumab emtansine (T-DM1), and Fast Track designation for the treatment of HER2 positive unresectable and/or metastatic breast cancer in patients who have progressed after prior treatment with HER2 targeted therapies including T-DM1 by the U.S. Food and Drug Administration (FDA). [Fam-] trastuzumab deruxtecan has received

SAKIGAKE Designation for the treatment of HER2 positive advanced gastric or gastroesophageal junction cancer by the Japan Ministry of Health, Labour and Welfare (MHLW).

[Fam-] trastuzumab 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 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. Daiichi Sankyo, Inc., headquartered in Basking Ridge, New Jersey, is a member of the Daiichi Sankyo Group. For more information on Daiichi Sankyo, Inc., please visit: www.dsi.com.

Contact
Jennifer Brennan
Daiichi Sankyo, Inc.
jbrennan2@dsi.com
+1 908 992 6631 (office)
+1 201 709 9309 (mobile)

References:

1. Ferlay J, et al. GLOBOCAN 2012. International Agency for Research on Cancer. 2014.
2. American Cancer Society. About Non-Small Cell Lung Cancer. Types of Non-Small Cell Lung Cancer. 2018.
3. American Cancer Society. Non-Small Cell Lung Cancer Survival Rates, by Stage. 2018.
4. Ricciardi, et al. Journal of Thoracic Oncology. 2014;9(12):1750-62.
5. The National Comprehensive Care Network (NCCN). NCCN Clinical Practice Guidelines in Non-Small Cell Lung Cancer Version 3. 2018.
6. Nakamura H et al. Cancer. 2005 May 1;103(9):1865-73.
7. Landi and Cappuzzo. Expert Review of Anticancer Therapy. 2013;13(10):1219-28.
8. Pillai RN et al. Cancer. 2017 Nov 1;123(21):4099-4105.
9. Doi T, et al. Lancet Oncology. November 2017; 18: 1512-22.