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Daiichi-Sankyo

Press Release

Daiichi Sankyo Announces Clinical Research Collaboration with Merck KGaA, Darmstadt, Germany and Pfizer to Evaluate [Fam-] Trastuzumab Deruxtecan (DS-8201) with Avelumab and a DNA Damage Response Inhibitor in Patients with HER2 Expressing and Mutated Solid Tumors

Tokyo, Munich, and Basking Ridge, NJ – (October 25, 2018) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that it has entered into a clinical trial collaboration agreement with Merck KGaA, Darmstadt, Germany and Pfizer, Inc. to evaluate the combination of [fam-] trastuzumab deruxtecan (DS-8201), an investigational HER2 targeting antibody drug conjugate (ADC), in combination with the checkpoint inhibitor avelumab and/or an investigational Merck KGaA, Darmstadt, Germany DNA damage response (DDR) inhibitor, in patients with HER2 expressing or mutated solid tumors.

A separate research collaboration to conduct preclinical studies evaluating [fam-] trastuzumab deruxtecan in combination with avelumab, the DDR inhibitor and other investigational compounds in Merck KGaA, Darmstadt, Germany's and Pfizer's pipelines is also underway.

"The collaboration is another milestone in our development strategy to maximize the potential of [fam-] trastuzumab deruxtecan for various HER2 expressing and mutated cancers in combination with immunotherapy and other agents with novel mechanisms of action," said Tom Held, Vice President, Head, Antibody Drug Conjugate Task Force, Oncology Research and Development, Daiichi Sankyo. "We look forward to working with Merck KGaA, Darmstadt, Germany and Pfizer to determine an appropriate combination strategy to help further improve outcomes for patients. In particular, we are enthusiastic about better understanding the potential of combining [fam-] trastuzumab deruxtecan with DNA damage response agents."

About the Study

Under the terms of the agreement, Daiichi Sankyo will conduct a three-part phase 1b multicenter, open-label study to determine the safety and efficacy of [fam-] trastuzumab deruxtecan in combination with avelumab and/or a DDR inhibitor.

The first part of the study (Part A) will include a dose-escalation and dose-expansion phase to evaluate the maximum tolerated dose, safety and efficacy of [fam-] trastuzumab deruxtecan in combination with

avelumab. Patients with HER2 expressing cancer refractory to standard treatment will be enrolled into the dose-escalation phase of Part A of the study. Four cohorts of patients will be enrolled into the dose-expansion phase.

The second part of the study (Part B) will include a dose-escalation and dose-expansion phase to evaluate the maximum tolerated dose, safety and efficacy of [fam-] trastuzumab deruxtecan in combination with the DDR inhibitor in patients with HER2 expressing or mutated advanced/metastatic solid tumors.

The third part of the study (Part C) will evaluate the triple combination of [fam-] trastuzumab deruxtecan, avelumab and the DDR inhibitor in patients with HER2 expressing cancer once the recommended expansion doses are known from Parts A and B.

The primary endpoints of each part of the study are maximum tolerated dose, recommended expansion dose and objective response rate. Secondary endpoints include duration of response, disease control rate, progression-free survival, overall survival, time to response and key safety endpoints. The study is expected to enroll approximately 200 patients in the U.S., Europe and Asia.

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 phase 3 development versus ado-trastuzumab emtansine (T-DM1) (DESTINY-Breast03) and versus investigator's choice post T-DM1 (DESTINY-Breast02) for HER2 positive metastatic breast cancer; pivotal phase 2 clinical development for HER2 positive metastatic breast cancer resistant or refractory to T-DM1 (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 Avelumab

Avelumab is a human anti-programmed death ligand-1 (PD-L1) antibody. Avelumab has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.[1-3] Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.[3-5] In November 2014, Merck KGaA, Darmstadt, Germany and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

Avelumab is currently being evaluated in the JAVELIN clinical development program, which involves at least 30 clinical programs, including eight Phase III trials, and more than 9,000 patients across more than 15 different tumor types. For a comprehensive list of all avelumab trials, please visit clinicaltrials.gov.

Indications in the US**

The US Food and Drug Administration (FDA) granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Important Safety Information from the US FDA-Approved Label

The warnings and precautions for avelumab (BAVENCIO®) include immune-mediated adverse reactions (such as pneumonitis, hepatitis, colitis, endocrinopathies, nephritis and renal dysfunction and other adverse reactions), infusion-related reactions and embryo-fetal toxicity.

Common adverse reactions (reported in at least 20% of patients) in patients treated with BAVENCIO for mMCC and patients with locally advanced or metastatic UC include fatigue, musculoskeletal pain, diarrhea, nausea, infusion-related reaction, peripheral edema, decreased appetite/hypophagia, urinary tract infection and rash.

For full prescribing information and medication guide for BAVENCIO, please see www.BAVENCIO.com.

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.

Alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, U.S.

Immuno-oncology is a top priority for Merck KGaA, Darmstadt, Germany, and Pfizer Inc. The global strategic alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US, enables the companies to benefit from each other's strengths and capabilities and further explore the therapeutic potential of avelumab, an anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance will jointly develop and commercialize avelumab and advance Pfizer's PD-1 antibody. The alliance is focused on developing high-priority international clinical programs to investigate avelumab as a monotherapy, as well as in combination regimens, and is striving to find new ways to treat cancer.

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