

Press Release

Phase 2 DESTINY-Gastric01 Trial of DS-8201 Versus Chemotherapy Met Primary Endpoint

- Trial met primary endpoint of objective response rate and key secondary endpoint of overall survival in patients with previously treated HER2 positive metastatic gastric cancer

Tokyo, Munich and Basking Ridge, NJ – (January 27, 2020) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca today announced positive topline results from the pivotal phase 2 DESTINY-Gastric01 trial of DS-8201, a HER2 directed antibody drug conjugate (ADC), in patients with HER2 positive unresectable or metastatic gastric or gastroesophageal junction cancer that had progressed following two or more treatment regimens including trastuzumab and chemotherapy.

The trial met its primary endpoint, achieving a statistically significant and clinically meaningful improvement in objective response rate (ORR), as assessed by an independent review committee, in patients treated with DS-8201 versus investigator's choice of chemotherapy (irinotecan or paclitaxel monotherapy). DS-8201 also showed a statistically significant and clinically meaningful improvement in overall survival (OS), a key secondary endpoint. The safety profile observed for DS-8201 in DESTINY-Gastric01 was consistent with previous clinical trials.

These results confirm activity seen in the non-randomized phase 1 study of DS-8201 in patients with HER2 positive advanced gastric cancer published in *The Lancet Oncology*.¹ Data from DESTINY-Gastric01 will be presented at an upcoming medical meeting.

Daiichi Sankyo will initiate discussions with the Japan Ministry of Health, Labour and Welfare (MHLW) to determine next steps for a regulatory submission based on the results of DESTINY-Gastric01. Both companies also plan to discuss the data with other health authorities. DS-8201 is being jointly developed and commercialized worldwide with AstraZeneca except in Japan where Daiichi Sankyo maintains exclusive rights.

The overall safety and tolerability profile of DS-8201 in DESTINY-Gastric01 was consistent with that seen in the published phase 1 trial in which the most common adverse events (≥ 30 percent, any grade) were hematologic and gastrointestinal including neutrophil count decrease, anemia, nausea and decreased appetite. There were cases of drug-related interstitial lung disease (ILD) and pneumonitis, the majority of which were grade 1 and 2 with two grade 3 and one grade 4. No ILD-related deaths (grade 5) occurred in gastric patients in the phase 1 trial or in the DESTINY-Gastric01 trial.

“We are excited to report positive topline results from this trial,” said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. “Our development plan remains on track for gastric cancer, including an initial regulatory application in Japan where gastric cancer is highly prevalent and where SAKIGAKE designation has been granted for this indication. We are strongly committed to bringing this therapy as rapidly as possible to patients in need.”

“Gastric cancer is usually diagnosed in the advanced stage and patients face markedly high mortality rates, making the need for new therapies especially urgent,” said José Baselga, MD, PhD, Executive Vice President, Oncology R&D, AstraZeneca. “Given the previous results seen in our HER2 positive development program and now in HER2 positive gastric cancer, we believe this antibody drug conjugate has the potential to redefine the treatment of patients with HER2 expressing cancers.”

About DESTINY-Gastric01

DESTINY-Gastric01 is a pivotal phase 2, open-label, multi-center trial assessing the safety and efficacy of DS-8201 in 189 patients from Japan and South Korea with HER2 expressing advanced gastric cancer or gastroesophageal junction adenocarcinoma (defined as IHC3+ or IHC2+/ISH+) who have progressed on two or more prior treatment regimens including fluoropyrimidine (5-FU), platinum chemotherapy and trastuzumab. Patients were randomized 2:1 to receive DS-8201 or physician’s choice of chemotherapy (paclitaxel or irinotecan monotherapy). Patients were treated with DS-8201 6.4 mg/kg once every three weeks or chemotherapy given on the same schedule. The primary endpoint of the study is objective response rate. Secondary endpoints include overall survival, progression-free survival, duration of response, disease control rate and time to treatment failure as well as pharmacokinetic and safety endpoints.

About HER2

HER2 is a tyrosine kinase receptor growth-promoting protein expressed on the surface of many types of tumors including gastric, breast and lung cancers. HER2 overexpression is often associated with aggressive disease and poorer prognosis.² When a patient is diagnosed with gastric cancer, guidelines recommend evaluating HER2 expression levels by an immunohistochemistry (IHC) test.³ A finding of IHC 3+ is considered positive. A result of IHC 2+ is considered equivocal, in which case an additional testing method of in situ hybridization (ISH) is recommended to confirm HER2 status.

About Gastric Cancer

Gastric (stomach) cancer is the fifth most common cancer worldwide and the third leading cause of cancer mortality; there were approximately one million new cases reported in 2018 and 783,000 deaths.⁴ Incidence rates for gastric cancer are markedly higher in eastern Asia, where approximately half of all cases occur.⁸ South Korea and Japan have the first and third highest incidence rates of gastric cancer worldwide, respectively; in 2018, the age-standardized rate in Japan was 27.5 per 100,000 and in South Korea it was 39.6 per 100,000.⁵

Approximately one in five gastric cancers are HER2 positive.⁶ Gastric cancer is usually diagnosed in the advanced stage, but even when diagnosed in earlier stages of the disease the survival rate remains modest.⁷ Recommended first-line treatment for HER2 positive advanced or metastatic gastric cancer is combination chemotherapy plus trastuzumab, an anti-HER2 agent, which has been shown to improve outcomes when added to chemotherapy.⁸ For gastric cancer that progresses on trastuzumab, there are no other approved HER2 targeting therapies and subsequent treatment options are limited.⁹

About DS-8201

DS-8201 (trastuzumab deruxtecan in Japan and other regions of world; fam-trastuzumab deruxtecan-nxki in U.S. only), a HER2 directed antibody drug conjugate (ADC), is the lead product in the ADC Franchise of the Daiichi Sankyo Cancer Enterprise and the most advanced program in AstraZeneca's ADC scientific platform. 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-8201 is comprised of a HER2 monoclonal antibody attached to a topoisomerase I inhibitor payload by a tetrapeptide-based linker.

DS-8201 is an investigational agent that has not been approved for any indication in the EU and Japan. DS-8201 is an investigational agent globally for various indications. Safety and effectiveness has not been established for the subject proposed use.

About the Collaboration between Daiichi Sankyo and AstraZeneca

In March 2019, Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize DS-8201, except in Japan where Daiichi Sankyo maintains exclusive rights. Daiichi Sankyo is solely responsible for the manufacturing and supply.

About the DS-8201 Clinical Development Program

A comprehensive development program for DS-8201 is underway globally with five pivotal trials in HER2 expressing metastatic breast and gastric cancer, including a trial in patients with metastatic breast cancer and low levels of HER2 expression (HER2 low). Phase 2 trials are underway for HER2 expressing advanced colorectal cancer as well as metastatic non-squamous HER2 overexpressing or HER2 mutated non-small cell lung cancer. Trials in combination with other anticancer treatments, such as immunotherapy, also are underway.

A regulatory submission to the Japan MHLW for DS-8201 for the treatment of HER2 positive metastatic breast occurred in September 2019, and DS-8201 has previously received SAKIGAKE designation for the treatment of advanced HER2 positive gastric or gastroesophageal junction cancer by Japan's MHLW.

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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References:

¹ Shitara K et al. *Lancet Oncol.* 2019;S1470-2045 (19):30088-9

² Iqbal and Iqbal. *Mol Biol Int.* 2014; 2014: 852748

³ NCCN Guidelines® Gastric Cancer. Version 4.2019. December 20, 2019: GAST-B 3

⁴ Bray F et al. *GLOBOCAN CA CANCER J CLIN* 2018;68:394–424

⁵ World Cancer Research Fund International. Stomach Cancer Statistics. 2018. Accessed January 6, 2019:

<https://www.wcrf.org/dietandcancer/cancer-trends/stomach-cancer-statistics>

⁶ American Cancer Society. Tests for Stomach Cancer. 2017 . Accessed January 6, 2019: <https://www.cancer.org/cancer/stomach-cancer/treating/targeted-therapies.html>.

⁷ Curea et al. *Cancer Biotherapy & Radiopharmaceuticals.* 2017;32 (10): Review.

⁸ NCCN Guidelines® Gastric Cancer. Version 4.2019. December 20, 2019: MS-22

⁹ NCCN Guidelines® Gastric Cancer. Version 4.2019. December 20, 2019: MS-36