



Press Release

Daiichi Sankyo Initiates Clinical Trial with 5th DXd ADC, DS-6157, in Collaboration with Sarah Cannon Research Institute

- First-in-human phase 1 trial initiated with DS-6157, a GPR20 directed ADC, in patients with advanced gastrointestinal stromal tumor (GIST)
- GIST is a rare cancer of the digestive tract with limited treatment options available to patients who progress on standard TKI therapy
- DS-6157 is the fifth DXd ADC from the oncology pipeline of Daiichi Sankyo to enter clinical development and the second being developed with Sarah Cannon Research Institute

Tokyo, Munich and Basking Ridge, NJ and Nashville, Tenn. -- (May 22, 2020) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and Sarah Cannon Research Institute (Sarah Cannon) announced today that the first patient has been dosed in a first-in-human phase 1 study evaluating DS-6157, an investigational GPR20 directed antibody drug conjugate (ADC), in patients with advanced gastrointestinal stromal tumor (GIST) who have progressed on, or are intolerant to, standard treatment.

Treatment guidelines for patients with advanced GIST recommend surgery where possible and targeted therapy with tyrosine kinase inhibitors (TKIs).¹ For the majority of patients who eventually develop resistance to available therapies, there are few remaining options and new types of treatments may help address refractory disease.²

“We are proud to build upon our relationship with Sarah Cannon to initiate this trial evaluating the potential of DS-6157 as a new type of targeted therapy for patients with advanced GIST,” said Arnaud Lesegretain, Vice President Oncology R&D and Head, Alpha Portfolio, Daiichi Sankyo. “Based on preclinical assessments, biomarker research and the demonstrated portability of our DXd ADC technology, we believe that DS-6157 could potentially play a major role in the treatment of patients with GIST that is resistant to TKIs.”

DS-6157 is the fifth DXd ADC from the oncology pipeline of Daiichi Sankyo to enter clinical development and the second being evaluated in the strategic oncology collaboration between Daiichi Sankyo and Sarah Cannon. DS-6157 was designed utilizing Daiichi Sankyo’s proprietary and portable DXd ADC technology to target and deliver chemotherapy inside cancer cells that express GPR20, particularly gastrointestinal stromal tumors, which highly express this target.³

“Through the development of the DS-6157 targeted therapy, we are taking a critical step in finding more effective therapies for GIST patients,” said Johanna Bendell, MD, Chief Development Officer and Director of Drug Development, Sarah Cannon Research Institute. “In partnership with Daiichi Sankyo, we look forward to providing access to this novel therapy for patients who vitally need these treatment options.”

GIST is a rare soft tissue sarcoma that originates in the digestive tract, usually in the stomach. The annual worldwide incidence of GIST is estimated to be 10 to 15 cases per million, depending on the published series, and similar rates have been reported for Asian, European and Western countries.⁴

GPR20 (G protein-coupled receptor 20) is a seven-pass transmembrane protein, which is selectively and abundantly expressed in GIST.³ GPR20 expression is detected in more than 80% of all GIST tumor samples irrespective of the number of prior lines of TKI treatments received.⁵ In preclinical studies, DS-6157 demonstrated activity in GPR20 expressing tumor cells. No GPR20 directed therapies are currently approved for treatment of GIST or any cancer.

About the Study

The two-part, multicenter, open-label, first-in-human phase 1 study will investigate the safety, tolerability and efficacy of DS-6157 in adult patients with advanced/unresectable or metastatic GIST who have progressed on, or are intolerant to, standard treatment.

The first part of the study (dose escalation) will assess the safety and tolerability of increasing doses of DS-6157 to determine the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE). This part of the trial will enroll approximately 40 patients with advanced/unresectable or metastatic GIST who have progressed on or are intolerant to imatinib and other TKI treatments. Enrollment into Part 1 will not be restricted to patients with evidence of GPR20 expression. The second part of the study (dose expansion) will evaluate the safety, tolerability and efficacy of DS-6157 at the established RDE. This part of the trial will include two cohorts. Cohort 1 will include approximately 30 patients with GIST who have progressed on imatinib and at least one post-imatinib treatment. Cohort 2 will include approximately 30 patients with GIST who progressed on imatinib but have not received additional systemic therapies.

The study will evaluate safety endpoints that include adverse events and efficacy endpoints including objective response rate, duration of response, disease control rate, clinical benefit rate, time to response, progression-free survival, and best percent change in target lesion by RECIST Version 1.1.

Pharmacokinetic endpoints and exploratory biomarker endpoints will also be assessed.

A total of approximately 100 patients are expected to be enrolled in this study at approximately 10 sites in the U.S., Japan and other countries. For more information, please visit [ClinicalTrials.gov](https://clinicaltrials.gov).

About DS-6157

DS-6157 is a potential first-in-class GPR20 targeting ADC and the fifth DXd ADC in the oncology pipeline of Daiichi Sankyo to enter clinical development. 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 utilizing Daiichi Sankyo’s proprietary DXd ADC technology, DS-6157 is comprised of a humanized anti-GPR20 monoclonal antibody, which is attached to a novel topoisomerase I inhibitor payload by a tetrapeptide-based linker.

Preclinical studies have shown that DS-6157 specifically binds to GPR20 on the surface of individual tumor cells. It is proposed that DS-6157 is then brought inside the cancer cell where lysosomal enzymes break down the tetrapeptide-based linker and release the DXd payload.

DS-6157 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 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.

About Sarah Cannon Research Institute

Sarah Cannon Research Institute is one of the world's leading clinical research organizations conducting community-based clinical trials throughout the United States and United Kingdom. With a focus on advancing therapies for patients, the organization has led more than 400 first-in-man clinical trials since its inception in 1993 and has been a clinical trial leader in the majority of approved cancer therapies over the last 10 years.

Additionally, Sarah Cannon offers management, regulatory, and other research support services for drug development and industry sponsors through its oncology-focused contract research organization (CRO), Sarah Cannon Development Innovations. As the CRO of Sarah Cannon, it leverages expert physician leadership to design and implement clinical trials that effectively and efficiently lead to rapid clinical development decisions. For more information, visit sarahcannon.com.

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References:

¹ NCCN Guidelines Version 6.2019, Feb 10, 2020. Gastrointestinal Stromal Tumors (GIST). P GIST-5

² Mei L et al. *Front Oncol* 2018; 8: 135.

³ Allander SV et al. *Cancer Res* 2001;61:8624-8628

⁴ Søreide K et al. *Cancer Epidemiology* 2016;40:39-46

⁵ Data in-house at Daiichi Sankyo (to be reported at upcoming medical meeting)