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Press Release

Daiichi Sankyo Initiates Phase 2 Study of Patritumab Deruxtecan in Patients with HER3 Expressing Advanced Colorectal Cancer

- Phase 2 study to evaluate patritumab deruxtecan, a potential first-in-class HER3 directed antibody drug conjugate, in previously treated patients with HER3 expressing advanced/metastatic colorectal cancer
- Initiation of third clinical study of patritumab deruxtecan demonstrates the commitment of Daiichi Sankyo to evaluate targeting of HER3 across a range of cancers including breast, non-small cell lung cancer and colorectal cancer
- There currently are no approved HER3 directed therapies for any type of cancer

Tokyo, Basking Ridge, N.J. and Munich – **(September 14, 2020**) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced today that the first patient has been dosed in a phase 2 study evaluating patritumab deruxtecan (U3-1402), a HER3 directed DXd antibody drug conjugate (ADC), in patients with advanced or metastatic colorectal cancer who are resistant, refractory, or intolerant to at least two prior lines of systemic therapy.

Standard treatment options for patients with advanced or metastatic colorectal cancer include surgery when possible, chemotherapy with or without targeted therapy, and radiation therapy.[1,2] However, many patients with advanced colorectal cancer will progress through multiple lines of therapy, and prognosis remains poor after failure of these therapies.[2,3] It is estimated that up to 83 percent of patients with colorectal cancer overexpress the HER3 protein, which can be associated with an increased incidence of metastases, reduced survival and resistance to standard cancer treatment.[4,5,6,7]

“The prognosis of patients with advanced or metastatic colorectal cancer remains poor, and there is a need to develop new treatment strategies, including targeting HER3,” said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Development, Oncology R&D, Daiichi Sankyo. “In this study, we are exploring whether the targeted delivery of cytotoxic chemotherapy with patritumab deruxtecan to cancer cells with varying levels of HER3 expression may be a potential treatment option for previously treated advanced or metastatic colorectal cancer.”

About the Study

The multi-center, open-label, two-cohort, two-part, phase 2 study will evaluate the safety and efficacy of patritumab deruxtecan in patients with advanced or metastatic colorectal cancer who are resistant, refractory, or intolerant to at least two prior approved systemic therapies. Prior treatments must include chemotherapy (fluoropyrimidine, irinotecan and a platinum agent), an anti-EGFR agent if clinically indicated, and an anti-VEGF agent, unless contraindicated. Patients with confirmed microsatellite instability-high (MSI-H) colorectal cancer must have received treatment with an immune checkpoint inhibitor, unless contraindicated.

The first part of the study will include two cohorts of patients with varying levels of HER3 expression. One cohort will include patients with HER3 high expression (IHC 3+ or 2+), and the second cohort will include patients with HER3 low/HER3 negative expression (IHC 1+ or 0). Based on a preliminary review of the data, specifically treatment response in both cohorts, additional patients may be enrolled into a second part of the study, which will further assess treatment with patritumab deruxtecan in patients with either HER3 high expression or both HER3 high and low expression.

The primary objective of the study is to assess the antitumor activity of patritumab deruxtecan, and will evaluate objective response rate (ORR), as assessed by Blinded Independent Central Review per RECIST v1.1, as the primary endpoint. Secondary objectives of the study include the assessment of antitumor activity (evaluated by assessing duration of response (DoR), investigator-assessed ORR, disease control rate (DCR), time to response (TTR), progression-free survival (PFS) and overall survival (OS)), safety and tolerability, level of HER3 protein expression in tumor tissue and its relationship with efficacy, pharmacokinetics and immunogenicity. Secondary efficacy assessments (ORR, DOR, DCR, TTR, and PFS) will be assessed by BICR and investigator per RECIST v1.1.

The study is expected to enroll up to approximately 80 patients in the U.S., Europe and Japan.

Unmet Need in Colorectal Cancer

Colorectal cancer is the third most common cancer and the second-leading cause of cancer-related deaths worldwide.[8] In 2020, there will be an estimated 147,950 new cases of colorectal cancer diagnosed in the U.S. and an estimated 53,200 deaths.[9] Approximately 25 percent of patients have metastatic disease at diagnosis, meaning the cancer has spread to distant organs, and about 50 percent will eventually develop metastases.[9,10] Only 14 percent of patients with metastatic colorectal cancer are expected to survive five years after they are diagnosed.[3]

Most patients with metastatic colorectal cancer receive surgery (when possible), chemotherapy with or without targeted therapy, and radiation therapy.[1,2] The introduction of EGFR targeting treatments and other

targeted therapies has helped prolong overall survival in advanced colorectal cancer compared to chemotherapy.[8,11] However, many patients eventually become resistant to these targeted treatments, underscoring the need for new treatment approaches for metastatic colorectal cancer.[2,4,5]

About HER3

HER3 is a member of the EGFR family of tyrosine kinase receptors, which are associated with aberrant cell proliferation and survival.[12] The HER3 protein is overexpressed in as many as 83 percent of colorectal cancers, and it is associated with an increased incidence of metastases and reduced survival.[4,5,6,7] Currently, no HER3 directed therapies are approved for any cancer.

About Patritumab Deruxtecan (U3-1402)

Patritumab deruxtecan (U3-1402) is one of three lead DXd antibody drug conjugates (ADC) in the oncology pipeline of Daiichi Sankyo.

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. Patritumab deruxtecan is comprised of a human anti-HER3 antibody attached to a topoisomerase I inhibitor payload by a tetrapeptide-based linker. It is designed to target and help deliver chemotherapy to cancer cells that express HER3 on the surface of tumor cells.

Patritumab deruxtecan is currently being evaluated in a phase 1 study in previously treated patients with metastatic or unresectable non-small cell lung cancer (NSCLC) and a phase 1/2 study in patients with HER3 expressing metastatic breast cancer.

Patritumab 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 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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