

Press Release

Daiichi Sankyo Presents Phase 1 Data for EZH1/2 Dual Inhibitor DS-3201 in Patients with Non-Hodgkin Lymphomas at the 59th Annual Meeting of the American Society of Hematology

- Preliminary exploratory efficacy results from phase 1 study show an overall response rate of 58.8 percent with single agent DS-3201, an investigational and potential first-in-class EZH1/2 dual inhibitor, in patients with relapsed or refractory non-Hodgkin lymphomas
- In subgroup analyses, an overall response rate of 45.5 percent with DS-3201 was observed in patients with B-cell lymphomas and 83.3 percent in patients with T-cell lymphomas
- Separate study of DS-3201 also underway in U.S. in patients with acute myeloid leukemia and acute lymphocytic leukemia, underscoring Daiichi Sankyo Cancer Enterprise commitment to advancing science for blood cancers

Tokyo, Basking Ridge, NJ, and Munich – (December 11, 2017) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that preliminary safety and efficacy data from a phase 1 study of DS-3201, an investigational and potential first-in-class EZH1/2 dual inhibitor, in patients with relapsed or refractory non-Hodgkin lymphomas (NHLs) were presented during a poster session at the 59th Annual Meeting of the American Society of Hematology in Atlanta, Georgia.

Preliminary exploratory efficacy results from an ongoing phase 1 dose escalation study showed that an overall response rate of 58.8 percent (10 of 17 patients) was observed with single agent DS-3201 in 17 evaluable patients with NHLs, including B-cell and T-cell lymphomas, who were relapsed from or refractory to standard treatment or for whom no standard treatment was available. Among the 10 patients with response, there were one complete remission and nine partial remissions. Additionally, four patients experienced stable disease and three patients experienced progressive disease.

An overall response rate of 45.5 percent (5 of 11 patients) was observed with DS-3201 in 11 evaluable patients with B-cell lymphomas, including follicular lymphoma (5 patients), diffuse large B-cell lymphoma (3 patients), extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (2 patients) and lymphoplasmacytic lymphoma (1 patient). An overall response rate of 83.3 percent (5 of 6 patients) was observed with DS-3201 in six evaluable patients with T-cell lymphomas, including peripheral T-cell lymphoma not otherwise specified (2 patients), angioimmunoblastic T-cell lymphoma (2 patients) and adult T-cell leukemia-lymphoma (2 patients).

“Based on these preliminary safety and efficacy data on DS-3201 in a clinical setting, further evaluation of DS-3201 is warranted,” said Dai Maruyama, MD, PhD, Department of Hematology, National Cancer Center Hospital, Tokyo, Japan. “As the first dual inhibitor of EZH1 and EZH2 in clinical development, DS-3201 may represent a new epigenetic approach to treating blood cancers. We look forward to reviewing additional data as it becomes available to evaluate the potential of this approach.”

Following observation of dose-limiting toxicities (DLTs) in three of 18 evaluable patients, dose expansion is ongoing to determine a conclusive recommended phase 2 dose. Four DLTs were observed in three patients who received either the 200 mg or 300 mg dose: there were three cases of temporary grade 4 platelet count decreases (one patient in the 200 mg cohort and two patients in the 300 mg cohort) and one case of grade 3 anemia requiring transfusion in a patient in the 300 mg cohort. Preliminary safety data from 18 evaluable patients in the study also were reported. The most common treatment emergent hematologic adverse events of any grade seen in all patients included decreased platelet count (77.8 percent), anemia (55.6 percent), decreased lymphocyte count (50.0 percent) and decreased neutrophil count (44.4 percent). The most common treatment emergent non-hematologic adverse events were dysgeusia (50.0 percent), alopecia (33.3 percent), diarrhea (22.2 percent), decreased appetite (22.2 percent), nasopharyngitis (22.2 percent), alanine aminotransferase increased (22.2 percent), rash (16.7 percent), aspartate aminotransferase increased (16.7 percent) and dry skin (16.7 percent). One serious adverse event of grade 3 pneumocystis jirovecii pneumonia (PJP) led to discontinuation from the study. There was one additional non-serious case of PJP observed, leading to the institution of prophylactic treatment for all subsequent patients enrolled into the study.

DS-3201 targets epigenetic regulation by inhibiting both the EZH1 (enhancer of zeste homolog 1) and EZH2 (enhancer of zeste homolog 2) enzymes, which may reactivate various genes that have been silenced by the protein H3K27me3.¹ Reactivation of the silenced genes has been shown to result in decreased proliferation of EZH2-expressing cancer cells. Preclinical research has shown that DS-3201 suppressed trimethylation of H3K27 in cells (IC₅₀: 0.55 nM) more potently than EZH2 selective inhibitors.¹

“Targeting epigenetic regulation is an approach to treating cancer that aims to reverse aberrant epigenetic changes that contribute to cancer cell growth and to maintain normal gene expression. The dual inhibition of EZH1/2 is theoretically able to provide a different spectrum of activity compared to EZH2-specific inhibitors already in the clinic. Our phase 1 program is designed to address the question of the potential benefit for this dual mode of action,” said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. “In addition to the phase 1 study in non-Hodgkin lymphomas, we also are evaluating targeting epigenetic regulation with DS-3201 in patients with acute myeloid leukemia and acute lymphocytic leukemia.”

About Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma (NHL) is a form of cancer that originates in lymphocytes, a type of white blood cell.² The two main types of NHL are B-cell lymphomas and T-cell lymphomas, which are classified into subtypes based on the origin and stage of the cancer.² There were an estimated 386,000 new cases and about 200,000 deaths globally from NHL in 2012.³ In Japan, there were nearly 21,000 new cases of NHL in 2012, accounting for around five percent of cases worldwide.³ While recent treatment advances have led to improved outcomes for patients with certain types of NHL, patients with aggressive NHL subtypes or relapsed or refractory disease still face a poor prognosis.^{2,4}

About the DS-3201 Phase 1 Study

A multicenter, non-randomized, open-label phase 1 dose escalation trial in Japan is enrolling adult patients with non-Hodgkin lymphomas (NHL) who have relapsed from or are refractory to standard treatment or for whom no standard treatment is available. The primary objectives are to evaluate the safety and pharmacokinetics of multiple-dose monotherapy of DS-3201 and to determine the recommended phase 2 dose. Secondary objectives are to determine the maximum tolerated dose of DS-3201 and to conduct exploratory evaluations of DS-3201-related biomarkers and the efficacy of DS-3201. For more information about the clinical trial, visit ClinicalTrials.gov.

About DS-3201

Part of the AML Franchise of the Daiichi Sankyo Cancer Enterprise, DS-3201 is an investigational and potential first-in-class EZH1/2 dual inhibitor in phase 1 clinical development for hematologic cancers including acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL) and non-Hodgkin lymphoma (NHL). DS-3201 is an investigational agent that has not been approved by the FDA or any other regulatory agency worldwide as a treatment for any indication. Safety and efficacy have not been established.

About Daiichi Sankyo Cancer Enterprise

The vision of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking in order 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 Antibody Drug Conjugate (ADC) and Acute Myeloid Leukemia (AML) Franchises, our cancer pipeline includes more than 20 small molecules, monoclonal antibodies and ADCs stemming from our powerful research engines: our 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 development include: quizartinib, an oral FLT3 inhibitor, for newly-diagnosed and relapsed or refractory AML with FLT3-ITD mutations; DS-8201, an ADC for HER2-expressing breast and gastric cancer, and

other HER2-expressing solid tumors; and pexidartinib, an oral CSF-1R inhibitor, for tenosynovial giant cell tumor (TGCT), which is also being explored in a range of solid tumors in combination with the anti-PD1 immunotherapy pembrolizumab. 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.

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References

1. Honma D, et al. ASH Annual Meeting. Abstract #2073. 2017.
2. American Cancer Society. Non-Hodgkin's Lymphoma. 2017.
3. Ferlay J, et al. GLOBOCAN 2012 v1.0. Cancer Incidence and Mortality Worldwide; IARC CancerBase No. 11. 2013.
4. Chao M. Cancer Manag Res. 2013;5:251-269.