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Press Release

Daiichi Sankyo Presents Phase 1 Data for MDM2 Inhibitor DS-3032 in Acute Myeloid Leukemia and Myelodysplastic Syndrome at the 58th Annual Meeting of the American Society of Hematology

- Preliminary results of phase 1 study demonstrate once-daily oral dosing of DS-3032 appears to be promising approach to treat relapsed/refractory acute myeloid leukemia (AML) and high-risk myelodysplastic syndrome (MDS)
- Single-agent activity of DS-3032 observed after one four-week cycle of treatment including two complete remissions
- Evaluation of additional dosing schedules of DS-3032 underway and combination studies currently being planned, emphasizing Daiichi Sankyo commitment to AML

Tokyo, Japan and Parsippany, NJ – (December 5, 2016) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced preliminary safety and efficacy data from a phase 1 study of DS-3032, an investigational oral selective MDM2 inhibitor, suggesting that DS-3032 may be a promising treatment for hematological malignancies including relapsed/refractory acute myeloid leukemia (AML) and high-risk myelodysplastic syndrome (MDS). Preliminary results from the dose escalation part of the phase 1 study of DS-3032 were presented in an oral presentation at the 58th Annual Meeting of the American Society of Hematology (ASH).

A total of 38 patients with relapsed/refractory AML or high-risk MDS were enrolled into the study. Five dose levels of DS-3032 (60 mg, 90 mg, 120 mg, 160 mg and 210 mg) were given. The maximum tolerated dose of DS-3032 was determined to be 160 mg once daily for 21 days in a 28 day cycle based on results from 37 patients who received at least one dose of DS-3032.

Clinical activity of DS-3032 was observed by a reduction of bone marrow blasts at the end of the first cycle of treatment in 15 out of 26 patients who had at least one post-dose bone marrow evaluation. Complete remission was seen in two patients with relapsed/refractory AML receiving 120 mg and 160 mg of DS-3032 with a duration of approximately four months and 13 months, respectively. One patient with high-risk MDS receiving the 120 mg dose of DS-3032 achieved marrow complete remission with platelet improvement for four months. Each of the three patients experiencing a complete response showed a TP53 gene mutation while receiving treatment, which was not identified at the start of the study.

“MDM2 inhibitors such as DS-3032 represent a promising approach in cancer therapy as they have the potential to restore the tumor suppressor protein function of p53 via release from the inhibitory effects of MDM2. Wild-type p53 plays an important role in preventing the uncontrolled growth of cancer cells,” said Courtney DiNardo, MD, MSCE, Assistant Professor, Department of Leukemia, Division of Cancer

Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX. "While these findings are encouraging in that single-agent clinical activity in refractory hematologic malignancies was demonstrated with DS-3032, further study with optimized dosing regimens including combination strategies is needed."

Five patients experienced dose limiting toxicities including two patients in the 160 mg cohort (grade 3 hypokalemia and diarrhea) and three patients in the 210 mg cohort (grade 3 nausea/vomiting, grade 3 anorexia/fatigue and grade 2 creatinine elevation/renal insufficiency leading to early discontinuation of treatment). The most common treatment-emergent adverse events (TEAEs) of any grade (greater than 20 percent) included nausea (73 percent), diarrhea (57 percent), vomiting (33 percent), fatigue (37 percent), anemia (33 percent), thrombocytopenia (33 percent), neutropenia (20 percent), hypotension (30 percent), hypokalemia (23 percent), and hypomagnesemia (20 percent).

"Additional research is currently underway to further explore the appropriate dose and treatment schedule of DS-3032 as well as determine how it can be combined with other therapies," said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. "We are committed to investigating novel approaches to treat AML and MDS in hopes of changing the standard of care for these patients."

About the Study

The primary objectives of the dose escalation part of the phase l study are to assess the safety, tolerability, and maximum tolerated dose or the tentative recommended phase 2 dose of DS-3032 in several hematological malignancies including refractory or relapsed acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML) in blast phase, and myelodysplastic syndrome (MDS). Secondary objectives include evaluating the pharmacokinetics and pharmacodynamic effects of DS-3032. Exploratory objectives include evaluating the efficacy of DS-3032. Further evaluation of alternative dosing schedules of DS-3032 is currently underway. For more information about the study visit ClinicalTrials.gov.

About DS-3032

DS-3032 is an investigational oral selective inhibitor of the murine double minute 2 (MDM2) protein currently being investigated in three phase 1 clinical trials for solid and hematological malignancies including acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML) in blast phase, lymphoma and myelodysplastic syndrome (MDS). DS-3032 has not been approved by any regulatory authority for uses under investigation.

MDM2 is a ubiquitously expressed protein that plays an important role in tissue development and tightly regulates p53, a protein that functions as a tumor suppressor.[1] Overexpression or oncogenic activation of

MDM2 can disrupt the balanced MDM2 and p53 interaction, blocking the tumor suppressor activity and leading to solid tumors and hematological malignancies.[1,2] Small molecules designed to block the MDM2-p53 interaction, reactivating p53 to suppress tumors, may be a promising therapeutic approach for the treatment of wild-type (non-mutant) p53 cancer.[1]

Unmet Need in AML and MDS

Acute myeloid leukemia (AML) is the most common type of acute leukemia, accounting for about 33 percent of all new cases of leukemia.[3] The five-year survival rate of AML is approximately 26 percent, which is the lowest of all leukemias.[3] In the U.S., each year there are about 13,000 new cases of myelodysplastic syndrome (MDS), a type of cancer that can occur when the blood-forming cells in the bone marrow are damaged.[4] In about one in three patients, MDS progresses to AML.[4] Currently, there are no approved targeted treatments for AML, with little progress in approval of new drugs for AML over the past 30 years.[5,6]

About Daiichi Sankyo Cancer Enterprise

The vision of Daiichi Sankyo Cancer Enterprise is to push beyond traditional thinking to align world-class science to create innovative treatments for patients with cancer. The oncology pipeline of Daiichi Sankyo continues to grow and currently includes more than 20 small molecules, monoclonal antibodies and antibody drug conjugates with novel targets in both solid and hematological cancers. Compounds in development include: quizartinib, an oral FLT3 inhibitor, for newly-diagnosed and relapsed/refractory FLT3-ITD+ acute myeloid leukemia (AML); pexidartinib, an oral CSF-1R inhibitor, for tenosynovial giant cell tumor (TGCT), also known as pigmented villonodular synovitis (PVNS) and giant cell tumor of the tendon sheath (GCT-TS), which also is being investigated in combination with anti-PD1 immunotherapy, pembrolizumab, in a range of solid tumors; tivantinib, an oral MET inhibitor, for second-line treatment of patients with MET-high hepatocellular carcinoma in partnership with ArQule, Inc.; and DS-8201, a HER2 targeting antibody drug conjugate, for HER2-expressing breast or gastric cancer or other HER2-expressing solid tumors.

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 16,000 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 a 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 Parsippany, 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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