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Press Release

Daiichi Sankyo Presents Phase 3 ENLIVEN Study of Pexidartinib, Demonstrating Statistically Significant Clinical Improvement Across Multiple Endpoints in Patients with Tenosynovial Giant Cell Tumor at 2018 American Society of Clinical Oncology (ASCO) Annual Meeting

- ENLIVEN, the first placebo-controlled study of a systemic investigational therapy in patients with tenosynovial giant cell tumor (TGCT), enrolled patients where surgery would be associated with potentially worsening functional limitation or severe morbidity.
- Oral pexidartinib significantly reduced tumor size (39 percent overall tumor response rate), compared to no tumor response in patients treated with placebo.
- TGCT is a debilitating tumor of the joint or tendon sheath - previously referred to as pigmented villonodular synovitis (PVNS) or giant cell tumor of the tendon sheath (GCT-TS), for which there is no approved therapy.
- Serious, nonfatal liver toxicity with increased bilirubin was observed in 4 percent of all 91 ENLIVEN patients treated with pexidartinib.
- Daiichi Sankyo will submit an NDA based upon the ENLIVEN study to the U.S. FDA for pexidartinib as a treatment for TGCT associated with severe morbidity or functional limitations, and for which surgery is not recommended.

Tokyo, Basking Ridge, NJ, and Munich – (June 4, 2018) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that the phase 3 ENLIVEN study showed a statistically significant 39 percent overall response rate (ORR) at week 25 based upon central review of MRI scans using Response Evaluation Criteria in Solid Tumors, version 1.1 (the primary endpoint) for patients treated with oral pexidartinib compared to no tumor response among patients who received placebo ($P<0.0001$). Patients enrolled in the trial were those with tenosynovial giant cell tumor (TGCT) for whom surgery would be associated with potentially worse function or severe morbidity. After a median six month follow-up (longest 17 months), no responders in the ENLIVEN study had progressed. The data will be presented during an oral abstract session on Monday, June 4, 2018 between 8:24 AM - 8:36 AM CDT (Abstract 11502) at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

“Current treatment options for TGCT are largely limited to surgery in order to remove as much of the tumor as possible. Despite the best surgical intervention, the recurrence rate of diffuse TGCT is high and the disease may advance to the point where surgery is no longer an option,” said William D. Tap, MD, lead investigator of the study and Chief of the Sarcoma Medical Oncology Service at Memorial Sloan Kettering Cancer Center in New York City. “Pexidartinib may offer a relevant treatment option for patients with TGCT, which is associated with severe morbidity or functional limitations, and for which surgery is not recommended.”

Pexidartinib is an investigational, oral small molecule that potently inhibits CSF1R (colony stimulating factor-1 receptor), a primary growth driver of abnormal cells in the synovium that cause TGCT.

In the ENLIVEN study, hepatic toxicities were more frequent with pexidartinib versus placebo (AST or ALT ≥3X ULN: 33 percent, total bilirubin ≥2X ULN: 5 percent, N=61). Eight patients discontinued pexidartinib due to hepatic adverse events (AEs); four were serious nonfatal AEs with increased bilirubin, one lasting ~7 months. In non-TGCT development studies using pexidartinib, two severe liver toxicity cases (one required liver transplant, one was associated with death) were observed.

Other AEs noted in ENLIVEN >10 percent and more common with pexidartinib included hair color changes, pruritus, rash, vomiting, abdominal pain, constipation, fatigue, dysgeusia, facial edema, peripheral edema, periorbital edema, decreased appetite and hypertension.

Secondary efficacy endpoints demonstrated that patients treated with pexidartinib had a 56 percent overall response rate (ORR) by Tumor Volume Score (TVS), compared to no response in patients who received placebo (P<0.0001). Clinically meaningful improvement versus placebo was observed in other secondary efficacy endpoints, including range of motion (+15% vs +6%, P=0.0043), PROMIS physical function (+4.1 vs -0.9, P=0.0019), and worst stiffness (-2.5 vs -0.3, P<0.0001). There was also a nonsignificant improvement in pain response (31% vs 15%).

“We are encouraged by the results from the ENLIVEN study and we look forward to submitting an NDA to the U.S. FDA and engaging European regulators for review of pexidartinib,“ said Gideon Bollag, PhD, CEO, Plexxikon, a member of the Daiichi Sankyo Group.”

About the ENLIVEN Study

ENLIVEN, a double-blind, randomized, global multi-cener, pivotal phase 3 study, evaluated pexidartinib in patients with symptomatic advanced TGCT for whom surgical removal of the tumor would be associated with potentially worsening functional limitation or severe morbidity. The first part of the study, the double-blind phase, enrolled 120 patients who were randomized (1:1) to receive either pexidartinib or placebo at 1000 mg/d for 2 weeks followed by 800 mg/d for 22 weeks in order to evaluate the efficacy and safety of pexidartinib versus placebo. The primary endpoint of the study was the percentage of patients achieving a complete or partial response after 24 weeks of treatment (Week 25), as assessed with centrally-read MRI scans using RECIST 1.1 criteria. Key secondary endpoints included range of motion, response by tumor volume score, PROMIS physical function, stiffness and measures of pain reduction.

After completing the first part of the study, patients randomized to either pexidartinib or placebo were eligible to take part in the second part of ENLIVEN, a long-term, open-label part where patients could

continue to receive or start to receive pexidartinib. In October 2016, following two reported cases of serious, non-fatal liver toxicity in the ENLIVEN study, the data monitoring committee (DMC) recommended that patients receiving placebo in the first part of the study should no longer be eligible to start pexidartinib in the second part of the study. A total of 120 patients who were enrolled prior to the DMC recommendation continued with the study according to the revised protocol.

About TGCT (PVNS/GCT-TS)

Tenosynovial giant cell tumor (TGCT), previously referred to as pigmented villonodular synovitis (PVNS) or giant cell tumor of the tendon sheath (GCT-TS), is a rare, usually non-cancerous tumor that affects the synovium-lined joints, bursae, and tendon sheaths, resulting in swelling, pain, stiffness and reduced mobility in the affected joint or limb.[1,2] It has been estimated that the incidence of TGCT is 11 to 50 cases per million, based on studies from three countries.[3-5] Patients are commonly diagnosed in their 20s to 50s, and depending on the type of TGCT, women can be up to twice as likely to develop a tumor as men.[6,7]

Primary treatment of TGCT includes surgery to remove the tumor. However, in patients with a diffuse form where the tumor can wrap around bone, tendons, ligaments and other parts of the joint, it is more difficult to remove and may require multiple surgeries or joint replacement, eventually advancing to the point where surgical resection is no longer an option and amputation may be considered. It is estimated that the rate of recurrence for diffuse TGCT can be 20 to 55 percent.[8]

About Pexidartinib

Pexidartinib is an investigational, novel, oral small molecule that potently inhibits CSF1R (colony stimulating factor-1 receptor), which is a primary growth driver of abnormal cells in the synovium that cause TGCT. Pexidartinib also inhibits c-kit and FLT3-ITD. Pexidartinib was discovered by Plexxikon Inc., the small molecule structure-guided R&D center of Daiichi Sankyo.

Pexidartinib has been granted Breakthrough Therapy Designation for the treatment of patients with pigmented villonodular synovitis (PVNS) or giant cell tumor of tendon sheath (GCT-TS), where surgical resection may result in potentially worsening functional limitation or severe morbidity and Orphan Drug Designation for PVNS/GCT-TS by the U.S. Food and Drug Administration (FDA). Pexidartinib also has received Orphan Designation from the European Commission for the treatment of TGCT. Pexidartinib is not 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 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 three pillars including our investigational Antibody Drug Conjugate Franchise, Acute Myeloid Leukemia Franchise and Breakthrough Science, we aim to deliver seven distinct new molecular entities over eight years during 2018 to 2025. Our powerful research engines include 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 pivotal stage development include: DS-8201, an antibody drug conjugate (ADC) for HER2-expressing breast, gastric and other cancers; quizartinib, an oral selective FLT3 inhibitor, for newly-diagnosed and relapsed/refractory acute myeloid leukemia (AML) with *FLT3*-ITD mutations; and pexidartinib, an oral CSF1R inhibitor, for tenosynovial giant cell tumor (TGCT). 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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