Press Release

Daiichi Sankyo's Pexidartinib Demonstrated Further Improvement with Continued Treatment of Tenosynovial Giant Cell Tumor Patients in New Long-Term Analysis Presented at 2019 ASCO Annual Meeting

- New pooled data demonstrated continued treatment with pexidartinib increased tumor response rate in patients with tenosynovial giant cell tumor (TGCT)
- TGCT, also referred to as pigmented villonodular synovitis (PVNS) or giant cell tumor of the tendon sheath (GCT-TS), is a debilitating tumor of the joint or tendon sheath for which there is no approved systemic therapy
- Updated results show that the safety profile remained similar, with no new mixed or cholestatic hepatotoxicity
- Earlier this year, ASCO recognized pexidartinib as one of five significant advancements in rare disease treatment, calling it the first promising investigational therapy for TGCT

Munich and Basking Ridge, NJ – (June 1, 2019) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo), today announced that new data from a pooled analysis of the phase 3 ENLIVEN study and phase 1 extension study showed continued treatment with pexidartinib resulted in an increased tumor response rate in TGCT patients. The data will be presented during a Poster Session on Saturday, June 1, at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago (Abstract #11042; 8:00-11:00 a.m. CDT).

The long-term pooled results showed the best overall response with pexidartinib at a median treatment duration of 17 months was 54 percent by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 and 64 percent by Tumor Volume Score (TVS). The median duration of response was not reached.

The safety profile of pexidartinib in the long-term follow-up was consistent with what has been seen in previous analyses. Across the studies, the most frequent adverse events were hair color change (75%), fatigue (60%), nausea (45%), arthralgia (38%), aspartate aminotransferase (AST) increase (30%) and diarrhea (30%). Pexidartinib was associated with two clinically distinct types of hepatic adverse reactions. The first was frequent dose-dependent aminotransferase elevations that may be a pharmacologic effect of CSF1R inhibition. The second hepatic adverse reaction was an idiosyncratic serious mixed or cholestatic hepatotoxicity. Across the pexidartinib clinical program, there were two irreversible cases of cholestatic liver injury, both in non-TGCT study populations. One patient died with advanced cancer and ongoing liver toxicity and one patient required a liver transplant.[1]

"Looking across the longer-term findings from both the pivotal phase 3 trial and phase 1 extension study, the results demonstrated continued and improved effect of pexidartinib in reducing tumor size in TGCT patients," said A.J. Gelderblom, MD, Chair of the Department of Medical Oncology at the Leiden University Medical Center and an ENLIVEN investigator. "This is important because TGCT is often a chronic disease, and we do not have effective treatment options for patients whose TGCT is inoperable or for which surgery would likely be associated with severe morbidity or functional limitations, like those enrolled in the studies."

Additional data published online ahead of ASCO (Abstract #e22527) further highlight the need for new treatment options, showing that TGCT patients missed more time from work due to disability and medical visits. The disability burden seen was greater in patients receiving surgery.

"We are pleased to share additional data that reinforce the potential of pexidartinib to offer clinically meaningful improvement for select patients with TGCT associated with severe morbidity or functional limitations and not amenable to improvement with surgery," said Dale Shuster, Ph.D., Executive Director, Global Oncology R&D, Daiichi Sankyo. "We look forward to working with regulatory authorities and delivering on our goal to help address the significant unmet need that exists in the treatment of this rare and debilitating tumor."

About the Phase 1 Extension Study

Patients enrolled in this phase 1 single-arm, multi-center, extension cohort study included those with a histologically confirmed diagnosis of TGCT with demonstrated tumor progression within the past year that was recurrent, inoperable or resectable but requiring extensive surgery. Following baseline assessment, the efficacy of pexidartinib was assessed radiologically every two months utilizing RECIST 1.1 criteria and TVS. Patients remained on treatment until disease progression or drug intolerance.

Interim data from the phase 1 study were published in *The New England Journal of Medicine.*[2]

About the ENLIVEN Study

ENLIVEN, a double-blind, randomized, global multi-center, 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/day for 2 weeks followed by 800 mg/day 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)

TGCT, also referred to as pigmented villonodular synovitis (PVNS) or giant cell tumor of the tendon sheath (GCT-TS), is a rare, nonmalignant tumor that can be locally aggressive. TGCT affects the synovium-lined joints, bursae and tendon sheaths, resulting in swelling, pain, stiffness and reduced mobility in the affected joint or limb.[3, 4, 5]

While the exact incidence of TGCT is not known, it is estimated that the incidence of TGCT is 11 to 50 cases per million person-years, based on studies from three countries.[6, 7, 8] TGCT is subcategorized into two types: localized, which is more common and accounts for 90 percent of cases, and diffuse, which accounts for 10 percent of cases.[7,8] The current standard of care for TGCT is surgical resection.[3,4] However, in patients with a recurrent, difficult-to-treat or diffuse form where the tumor can wrap around bone, tendons, ligaments and other parts of the joint, it is more difficult to remove or might not be amenable to improvement with surgery due to the risk of morbidity and potential recurrence. Additional surgeries for more severe cases can lead to significant joint damage, debilitating functional impairments and reduced quality of life, and amputation may be considered.[9, 10, 11]

Recurrence rates for localized TGCT are estimated to be up to 15 percent following complete resection.[4,12,13,14] Diffuse TGCT recurrence rates are estimated to be about 20 to 50 percent following complete resection.[5,12,15] TGCT affects all age groups; the diffuse type, on average, occurs most often in people below the age of 40, and the localized type typically occurs in people between 30 and 50 years old. [3,6,7,8]

About Pexidartinib

Pexidartinib is an investigational, novel, oral small molecule that potently inhibits the colony stimulating factor-1 receptor (CSF1R), 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 is currently under regulatory review with the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of for adult patients with symptomatic TGCT associated with severe morbidity or functional limitations and not amenable to improvement with surgery. In addition to Priority Review designation, pexidartinib has been granted Breakthrough Therapy designation for the treatment of patients with pigmented villonodular synovitis (PVNS) or giant cell tumor of the 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 FDA. Pexidartinib also has received Orphan Drug designation from the European Commission for the treatment of TGCT.

Pexidartinib is an investigational compound 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 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: [fam-] trastuzumab deruxtecan, 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 *FLT3*-ITD acute myeloid leukemia (AML); and pexidartinib, an oral CSF1R inhibitor, for 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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