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Press Release

Quizartinib Marketing Authorization Application Validated by EMA for Treatment of Adult Patients with Newly Diagnosed *FLT3*-ITD Positive Acute Myeloid Leukemia

- Submission based on QuANTUM-First results showing quizartinib plus chemotherapy significantly improved overall survival compared to chemotherapy alone

Tokyo & Munich –August 23, 2022 – Daiichi Sankyo (TSE: 4568) today announced that the European Medicines Agency (EMA) has validated the marketing authorization application (MAA) for quizartinib in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, and as continuation monotherapy following consolidation, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FMS-like tyrosine kinase 3 internal tandem duplication (*FLT3*-ITD) positive.

AML is one of the most common forms of leukemia in adults, representing about one-third of all cases.[1] In Europe, approximately 18,000 people are diagnosed with AML each year and the five-year survival rate is reported at 17% for adult patients.[2,3] Of all newly diagnosed cases of AML, approximately 25% carry the *FLT3*-ITD gene mutation, which is associated with a particularly unfavorable prognosis including increased risk of relapse and shorter overall survival.[4]

"There is a need to improve survival for the majority of patients with acute myeloid leukemia, particularly those with the *FLT3*-ITD subtype, which is aggressive and difficult to treat," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "We look forward to working with the EMA to support their review of quizartinib as a potential option for patients with newly diagnosed *FLT3*-ITD positive acute myeloid leukemia."

Validation confirms that the application is complete and commences the scientific review process by the EMA's Committee for Medicinal Products for Human Use (CHMP). The application is based on data from the QuANTUM-First phase 3 trial recently presented at the European Hematology Association (#EHA2022) Congress. In QuANTUM-First, quizartinib combined with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, and continued as monotherapy following consolidation, demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS) in adult patients with newly diagnosed *FLT3*-ITD positive AML

compared to chemotherapy alone. The safety of quizartinib combined with intensive chemotherapy and as continuation monotherapy in QuANTUM-First was generally manageable and consistent with previous clinical trials. The incidence of Grade ≥3 QT prolongation was low, with uncommon ventricular arrythmia events. Overall, the risk of QT prolongation was manageable with ECG monitoring, quizartinib dose modification and correction/elimination of additional risk factors.

About QuANTUM-First

QuANTUM-First is a randomized, double-blind, placebo-controlled global phase 3 study evaluating quizartinib in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, and as continuation monotherapy following consolidation, in adult patients aged 18-75 with newly diagnosed *FLT3*-ITD positive AML. Patients were randomized 1:1 into two treatment groups to receive quizartinib or placebo combined with anthracycline- and cytarabine-based regimens. Eligible patients, including those who underwent hematopoietic stem cell transplant (HSCT), continued with quizartinib or placebo for up to 36 cycles.

The primary study endpoint was OS. Secondary endpoints include event-free survival (EFS), post-induction rates of complete remission (CR) and composite complete remission (CRc), and the percentage of patients who achieve CR or CRc with *FLT3*-ITD minimal residual disease negativity. Safety and pharmacokinetics, along with exploratory efficacy and biomarker endpoints, also were evaluated. QuANTUM-First enrolled 539 patients at 193 study sites across Asia, Europe, North America, Oceania and South America. For more information, visit Clinicaltrialsregister.eu or ClinicalTrials.gov.

About Acute Myeloid Leukemia (AML)

More than 474,500 new cases of leukemia were reported globally in 2020 with more than 311,500 deaths.[5] AML is one of the most common types of leukemia in adults, representing about one-third of all cases, and the average age of diagnosis is 68 years old.[1] In Europe, approximately 18,000 people are diagnosed with AML each year and the five-year survival rate is reported at 17% for adult patients.[2,3] The conventional treatment for newly diagnosed AML is intensive induction and consolidation chemotherapy with HSCT for eligible patients.[6,3]

About *FLT3*-ITD

FLT3 (FMS-like tyrosine kinase 3) is a tyrosine kinase receptor protein normally expressed by hematopoietic stem cells that plays an important role in cell development, promoting cell survival, growth and differentiation through various signaling pathways.[4] Mutations of the FLT3 gene, which occur in approximately 30% of AML patients, can drive oncogenic signaling.[4] *FLT3*-ITD (internal tandem

duplication) is the most common type of FLT3 mutation in AML, occurring in about 25% of all newly diagnosed patients, and is associated with increased risk of relapse and shorter overall survival.[4]

About Quizartinib

Quizartinib is an oral, selective type II FLT3 inhibitor currently in clinical development for treatment of *FLT3*-ITD positive AML. In addition to QuANTUM-First, the quizartinib development program includes a phase 1/2 trial in pediatric and young adult patients with relapsed/ refractory *FLT3*-ITD positive AML in Europe and North America. Several phase 1/2 combination studies with quizartinib are also underway at The University of Texas MD Anderson Cancer Center as part of a strategic research collaboration focused on accelerating development of Daiichi Sankyo pipeline therapies for AML.

Quizartinib, which is currently not approved in Europe, has been granted Orphan Drug Designation for the treatment of AML in Europe, Japan and the U.S. Quizartinib has received Fast Track Designation from the U.S. Food and Drug Administration for the treatment of adult patients with newly diagnosed AML that is *FLT3*-ITD positive, in combination with standard cytarabine and anthracycline induction and cytarabine consolidation chemotherapy. Quizartinib is currently approved for use in Japan for the treatment of adult patients with relapsed/refractory *FLT3*-ITD AML, as detected by an approved test. Quizartinib is an investigational medicine in all countries outside of Japan.

About Daiichi Sankyo

Daiichi Sankyo is dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose "to contribute to the enrichment of quality of life around the world." In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases with high unmet medical needs. With more than 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 to realize our 2030 Vision to become an "Innovative Global Healthcare Company Contributing to the Sustainable Development of Society." For more information, please visit www.daiichisankyo.com.

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