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Daiichi-Sankyo

Press Release

Quizartinib NDA Review for Patients with Newly Diagnosed *FLT3*-ITD Positive AML Extended by FDA

Tokyo and Basking Ridge, NJ – (April 20, 2023) – Daiichi Sankyo (TSE: 4568) today announced that the U.S. Food and Drug Administration (FDA) has extended the review period for the New Drug Application (NDA) of 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 *FLT3*-ITD positive.

The FDA has extended the Prescription Drug User Fee Act (PDUFA) action date by three months to July 24, 2023 to allow additional time to review requested updates to the proposed Risk Evaluation and Mitigation Strategies (REMS) included in this application. No additional efficacy or safety data has been requested.

"We are continuing to work with the FDA to facilitate completion of their review of the quizartinib new drug application in order to bring this important medicine to patients as soon as possible," said Mark Rutstein, MD, Global Head, Oncology Clinical Development, Daiichi Sankyo. "Quizartinib was shown to improve overall survival when added to standard chemotherapy and continued as monotherapy and has potential to change the standard of care for patients with newly diagnosed *FLT3*-ITD positive AML."

The NDA is based on results from the QuANTUM-First trial, which demonstrated that quizartinib combined with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, and continued as monotherapy following consolidation, resulted in a statistically significant and clinically meaningful improvement in overall survival in adult patients with newly diagnosed *FLT3*-ITD positive AML compared to chemotherapy alone. The results of QuANTUM-First were presented at the 2022 European Hematology Association (EHA) Congress.[1]

The safety of quizartinib combined with intensive chemotherapy and as continuation monotherapy in QuANTUM-First was generally manageable with no new safety signals observed. The incidence of grade ≥3 QT prolongation events 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 overall survival. Secondary endpoints include event-free survival, 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 ClinicalTrials.gov.

About *FLT3*-ITD Positive Acute Myeloid Leukemia

More than 474,500 new cases of leukemia were reported globally in 2020 with more than 311,500 deaths.[2] AML accounts for 23.1% of total leukemia cases worldwide and is most common in adults.[3,4] In the U.S., an estimated 20,380 new cases of AML will be diagnosed in 2023 with the five-year survival rate reported at 30.5%.[4,5]

A number of gene mutations have been identified in AML, and FLT3 (FMS-like tyrosine kinase 3) mutations are the most common, observed in up to 37% of all newly diagnosed patients.[6,7] Approximately 80% of *FLT3* mutations in AML are *FLT3*-ITD (internal tandem duplications), an oncogenic driver mutation that presents with a high leukemic burden.[7,6] Patients with *FLT3*-ITD positive AML tend to have a particularly unfavorable prognosis including increased risk of relapse and shorter overall survival.[6] The five-year survival rate for patients with *FLT3*-ITD positive AML has been reported at approximately 20%.[8]

The conventional treatment for fit patients with newly diagnosed AML is intensive induction and consolidation chemotherapy, with or without targeted therapy, and HSCT for eligible patients.[9]

About Quizartinib

Quizartinib is an oral, highly potent type II FLT3 inhibitor that selectively targets *FLT3*-ITD mutations and has been specifically developed for patients with *FLT3*-ITD positive AML.[6]

Regulatory applications for quizartinib in newly diagnosed *FLT3*-ITD positive AML are currently under review in Europe, Japan and the U.S. based on the results of the QuANTUM-First trial. The FDA has granted Priority Review and Fast Track Designation to quizartinib 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. Orphan Drug Designation has been granted to quizartinib for the treatment of AML in Europe, Japan and the U.S.

Quizartinib is approved for use in Japan for the treatment of adult patients with relapsed/refractory AML that is *FLT3*-ITD positive, as detected by an approved test. Quizartinib is an investigational medicine in all countries outside of Japan. The quizartinib clinical 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 and several phase 1/2 combination studies as part of a strategic collaboration with The University of Texas MD Anderson Cancer Center.

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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