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Press Release

Quizartinib Recommended for Approval in EU by CHMP for Patients with Newly Diagnosed *FLT3*-ITD Positive AML

- Positive opinion based on QuANTUM-First results demonstrating quizartinib combined with standard chemotherapy improved overall survival

Tokyo and Munich – (September 15, 2023) – Daiichi Sankyo (TSE: 4568) announced that quizartinib has been recommended for approval in the European Union (EU) in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, followed by quizartinib single-agent maintenance therapy, for adult patients with newly diagnosed acute myeloid leukemia (AML) that is *FLT3*-ITD positive.

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on results from the phase 3 QuANTUM-First trial, which were published in *The Lancet*. The recommendation will now be reviewed by the European Commission, which has the authority to grant marketing authorizations for medicines in the EU.

In QuANTUM-First, quizartinib combined with standard cytarabine and anthracycline induction and standard cytarabine consolidation, and continued as maintenance monotherapy following consolidation, demonstrated a 22% reduction in the risk of death compared to standard chemotherapy alone (HR = 0.78 [95% CI: 0.62-0.98; p=0.032]) in patients with newly diagnosed *FLT3*-ITD positive AML. Median overall survival was 31.9 months for patients receiving quizartinib (n=268; 95% CI: 21.0-NE) compared to 15.1 months for patients in the control arm (n=271; 95% CI: 13.2-26.2) at a median follow-up of 39.2 months.

“Today’s positive CHMP opinion for quizartinib is an important step towards translating the clinical benefit observed in QuANTUM-First into an approved treatment option for patients in the EU with the difficult-to-treat *FLT3*-ITD subtype of acute myeloid leukemia,” said Mark Rutstein, MD, Global Head, Oncology Clinical Development, Daiichi Sankyo. “If approved, quizartinib would be the first FLT3 inhibitor approved specifically for patients with newly diagnosed *FLT3*-ITD positive AML.”

The safety profile of quizartinib in QuANTUM-First was consistent with previous clinical trials with no new safety signals observed. The most common grade 3 or 4 treatment emergent adverse events (occurring in ≥ 10% of patients) were febrile neutropenia (43%), hypokalemia (19%), neutropenia (18%) and pneumonia (11%). QTcF > 500 ms occurred in 2.3% of patients receiving quizartinib and 0.8% of patients discontinued

quizartinib due to QT prolongation. Ventricular arrhythmia events with quizartinib were uncommon. Two (0.8%) patients receiving quizartinib experienced cardiac arrest with recorded ventricular fibrillation on ECG (one with fatal outcome), both in the setting of severe hypokalemia.

About QuANTUM-First

QuANTUM-First is a randomized, double-blind, placebo-controlled, global phase 3 study evaluating quizartinib in combination with standard induction and consolidation therapy, including HSCT, and as maintenance monotherapy, in adult patients aged 18-75 with newly diagnosed *FLT3*-ITD positive AML. Patients were randomized 1:1 to receive quizartinib or placebo combined with cytarabine and anthracycline induction and cytarabine consolidation chemotherapy followed by up to three years of treatment with single-agent maintenance.

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 measurable residual disease negativity. Safety and pharmacokinetics, along with exploratory efficacy and biomarker endpoints including duration of CR were also evaluated.

QuANTUM-First enrolled 539 patients at 193 study sites in 26 countries 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.[1] AML accounts for 23.1% of total leukemia cases worldwide and is most common in adults.[2,3] 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.[4,5]

A number of gene mutations have been identified in AML, and *FLT3* (FMS-like tyrosine kinase 3) mutations are the most common.[6] Approximately 80% of FLT3 mutations are *FLT3*-ITD mutations, which drive cancer growth and contribute to particularly unfavorable prognosis including increased risk of relapse and shorter overall survival.[6,7] *FLT3*-ITD mutations occur in about 25% of all AML cases, with frequency reported as high as 30%.[6,7]

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]

Quizartinib is approved in the U.S. in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed AML that is *FLT3*-ITD positive as detected by an FDA-approved test. Quizartinib is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT); improvement in overall survival with quizartinib in this setting has not been demonstrated.

Quizartinib also is approved in Japan for the treatment of AML that is *FLT3*-ITD mutation positive, including for use in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy and as maintenance monotherapy for adult patients with newly diagnosed *FLT3*-ITD positive AML, and as a monotherapy for 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 and the U.S.

About the Quizartinib Clinical Development Program

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 an innovative global healthcare company contributing to the sustainable development of society that discovers, develops and delivers new standards of care to enrich the quality of life around the world. With more than 120 years of experience, Daiichi Sankyo leverages its world-class science and technology to create new modalities and innovative medicines for people with cancer, cardiovascular and other diseases with high unmet medical need. For more information, please visit www.daiichisankyo.com.

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