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Daiichi-Sankyo

Press Release

Quizartinib Granted Priority Review in the U.S. for 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 and Basking Ridge, NJ – (October 24, 2022) – Daiichi Sankyo (TSE: 4568) received notification of acceptance by the U.S. Food and Drug Administration (FDA) of 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 application has been granted Priority Review.

The FDA grants Priority Review to applications for medicines that, if approved, would offer significant improvements over available options by demonstrating safety or efficacy improvements, preventing serious conditions or enhancing patient compliance. The Prescription Drug User Fee Act date (PDUFA), the FDA action date for their regulatory decision, is April 24, 2023. The Priority Review follows receipt of Fast Track Designation, granted by the FDA in March 2022 for quizartinib in newly diagnosed *FLT3*-ITD positive AML.

AML is one of the most common forms of leukemia in adults.[1] An estimated 20,050 new cases of AML will be diagnosed in the U.S. in 2022, and the five-year overall survival rate is reported at 30.5%.[1,2] Of all newly diagnosed cases of AML, approximately 25% have the *FLT3*-ITD mutation, which is associated with particularly unfavorable prognosis including increased risk of relapse and shorter overall survival.[3]

"There is a need for new targeted therapy options for patients with acute myeloid leukemia and the results of the QuANTUM-First trial showed that quizartinib in combination with standard chemotherapy has potential to change the current standard of care for newly diagnosed patients with the historically difficult-to-treat *FLT3*-ITD subtype," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "The FDA's prioritization of this application reflects the importance of the data, and we will continue to work with the FDA and other global regulatory authorities to support the review of quizartinib for the treatment of patients with newly diagnosed *FLT3*-ITD positive acute myeloid leukemia."

The NDA is based on data from the QuANTUM-First phase 3 trial presented at the Presidential Symposium of the European Hematology Association (EHA) 2022 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 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 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 Acute Myeloid Leukemia

More than 474,500 new cases of leukemia were reported globally in 2020 with more than 311,500 deaths.[4] In 2017, AML accounted for 23.1% of total leukemia cases worldwide, and it is one of the most common types of leukemia in adults.[5,1] In the U.S., an estimated 20,050 new cases of AML will be diagnosed in 2022 with the five-year survival rate reported at 30.5%.[1,6]

The conventional treatment for newly diagnosed AML is intensive induction and consolidation chemotherapy with HSCT for eligible patients.[7] The introduction of new targeted therapies in recent years

has added to the standard of care and improved outcomes for some patients with molecularly defined AML subtypes.[8] However, there remains a need to improve survival for the majority of patients with AML.[7]

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.[3] Mutations of the FLT3 gene, which occur in approximately 30% of AML patients, can drive oncogenic signaling.[3] *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.[3]

About Quizartinib

Quizartinib is an oral, highly potent and selective type II FLT3 inhibitor currently in clinical development for treatment of *FLT3*-ITD positive AML.[3] 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 also are 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.

In addition to U.S. FDA Priority Review, quizartinib has received Fast Track Designation from the FDA 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.

Regulatory applications are currently under review in Europe and Japan for quizartinib in 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, and as continuation monotherapy following consolidation, based on the results of the QuANTUM-First trial.

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.

Media Contacts:

Global/US:
Jennifer Brennan
Daiichi Sankyo, Inc.
jbrennan2@dsi.com
+1 908 992 6631 (office)
+1 908 900 3183 (mobile)

Japan:
Masashi Kawase
Daiichi Sankyo Co., Ltd.
kawase.masashi.a2@daiichisankyo.co.jp
+81 3 6225 1126 (office)

Investor Relations Contact:
DaiichiSankyoIR@daiichisankyo.co.jp

References

[1] American Cancer Society: Key Statistics for Acute Myeloid Leukemia. Updated January 2022.
[2] National Cancer Institute SEER Program. Cancer Stat Facts: Acute Myeloid Leukemia
[3] Daver N et al. *Leukemia*. (2019) 33:299–312.
[4] Global Cancer Observatory. Population Fact Sheet: World. Updated March 2021.
[5] Dong Y et al. *Exp Hematol Oncol.* 2020;9:14.
[6] National Cancer Institute SEER Program. Cancer Stat Facts: Acute Myeloid Leukemia
[7] Daver et al. *Blood Cancer J.* 2020;10(10):107.
[8] Short et al. *Cancer Discov.* 2020;10:506–25.