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Daiichi-Sankyo

Press Release

VANFLYTA® First FLT3 Inhibitor Approved in Japan for Patients with Newly Diagnosed *FLT3*-ITD Positive AML

- First FLT3 inhibitor approved in newly diagnosed setting based on QuANTUM-First results demonstrating VANFLYTA added to standard chemotherapy improved overall survival
- Second indication approved for VANFLYTA in Japan

Tokyo – May 25, 2023 – Daiichi Sankyo (TSE:4568) today announced that VANFLYTA® (quizartinib) has been approved in Japan for the treatment of acute myeloid leukemia (AML) that is *FLT3*-ITD mutation positive.

VANFLYTA is now approved to treat patients with newly diagnosed *FLT3*-ITD positive AML in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy and as maintenance monotherapy, making it the first and only FLT3 inhibitor in Japan approved for newly diagnosed AML treatment. VANFLYTA was first approved in 2019 as a monotherapy in the relapsed/refractory setting.

AML is one of the most common leukemias in adults.[1] Approximately 7,000 new cases of AML are diagnosed each year in Japan where the five-year survival rate has been reported at 21.1% for adult patients.[2,3] Up to 37% of newly diagnosed cases of AML have a *FLT3* gene mutation and 80% of these have *FLT3*-ITD mutations, which contribute to particularly unfavorable prognosis including increased risk of relapse and shorter overall survival.[4,5]

The approval by Japan's Ministry of Health, Labour and Welfare (MHLW) is based on results of the QuANTUM-First trial recently published in *The Lancet*.[6] In QuANTUM-First, VANFLYTA combined with standard cytarabine and anthracycline induction and standard cytarabine consolidation, and continued as maintenance monotherapy following consolidation, resulted in a 22.4% 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 VANFLYTA (n=268; 95% CI: 21.0-NE) compared to 15.1 months for patients receiving chemotherapy (n=271; 95% CI: 13.2-26.2) after a median follow-up of 39.2 months.

"Patients with newly diagnosed *FLT3*-ITD positive acute myeloid leukemia now will have the opportunity to receive targeted therapy with VANFLYTA," said Wataru Takasaki, PhD, Executive Officer, Head of R&D Division in Japan, Daiichi Sankyo. "VANFLYTA is the only medicine developed and approved specifically for treatment of newly diagnosed *FLT3*-ITD positive AML in Japan and has demonstrated improved overall survival for this patient population."

The most common adverse reactions in 265 patients who received VANFLYTA in the QuANTUM-First trial were neutropenia (25.0%), thrombocytopenia (22.7%), nausea (20.6%) and electrocardiogram QT prolonged (19.3%). The safety profile of VANFLTYA in QuANTUM-First was consistent with previous use and no new safety concerns were identified.

About QuANTUM-First

QuANTUM-First is a randomized, double-blind, placebo-controlled, global phase 3 study evaluating VANFLYTA 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 VANFLYTA or placebo combined with anthracycline- and cytarabine-based regimens. Eligible patients, including those who underwent hematopoietic stem cell transplant (HSCT), continued with VANFLYTA 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 measurable 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.[7] AML accounts for 23.1% of total leukemia cases worldwide and is most common in adults.[1,8] In Japan, approximately 7,000 new cases of AML are diagnosed each year, and the five-year overall survival rate has been reported at 21.1% for adult patients.[2,3]

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.[4,5] Approximately 80% of *FLT3*

mutations in AML are *FLT3*-ITD (internal tandem duplications), an oncogenic driver mutation that presents with a high leukemic burden.[5,9] Patients with *FLT3*-ITD positive AML tend to have a particularly unfavorable prognosis including increased risk of relapse and shorter overall survival.[5]

The conventional treatment for fit/eligible patients with newly diagnosed AML is intensive induction and consolidation chemotherapy with or without HSCT, and maintenance therapy is recommended in some cases.[10,11]

About VANFLYTA

VANFLYTA (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.[5]

VANFLYTA 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. VANFLYTA is an investigational medicine in all countries outside of Japan.

About the VANFLYTA Clinical Development Program

The VANFLYTA 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.

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

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 17,000 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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