Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

Press Release

VANFLYTA® Approved in the EU as the First FLT3 Inhibitor Specifically for Patients with Newly Diagnosed *FLT3*-ITD Positive AML

- Approval based on QuANTUM-First results demonstrating VANFLYTA added to chemotherapy improved overall survival
- Second innovative medicine from the oncology pipeline of Daiichi Sankyo approved in the EU

Tokyo and Munich – (November 9, 2023) – Daiichi Sankyo's (TSE: 4568) VANFLYTA® (quizartinib) has been approved in the European Union (EU) for use in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, followed by VANFLYTA single-agent maintenance therapy for adult patients with newly diagnosed acute myeloid leukemia (AML) that is *FLT3*-ITD positive.

VANFLYTA is the first FLT3 inhibitor approved in the EU specifically for the treatment of patients with newly diagnosed *FLT3*-ITD positive AML, which represents about 25 to 30% of all new AML cases.[1,2]

The authorization by the European Commission (EC) follows the positive opinion of the Committee for Medicinal Products for Human Use and is based on the results of the QuANTUM-First trial, which were published in *The Lancet.* In QuANTUM-First, VANFLYTA 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 VANFLYTA (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.

"This approval of VANFLYTA represents an important advancement for frontline treatment of patients with *FLT3*-ITD positive acute myeloid leukemia, an aggressive and historically difficult-to-treat subtype," said Richard F. Schlenk, MD, Professor and Head of the Trial Center of the National Center of Tumour Diseases, Heidelberg University Hospital and German Cancer Research Center, Germany. "VANFLYTA is a potent

and selective FLT3 inhibitor that significantly improved overall survival when added to standard chemotherapy and it will be a valuable treatment option for newly diagnosed *FLT3*-ITD positive AML."

"This approval of VANFLYTA is very welcome news for eligible patients diagnosed with *FLT3*-ITD positive AML each year," said Samantha Nier, Network Director, Acute Leukemia Advocates Network (ALAN). "New medicines and treatment approaches are needed to help patients with this difficult type of leukemia live longer, and we look forward to VANFLYTA becoming available in countries throughout the EU."

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

"With the approval of VANFLYTA in the European Union, patients diagnosed with *FLT3*-ITD positive acute myeloid leukemia may for the first time receive a targeted therapy developed and approved specifically for their disease subtype," said Ken Keller, Global Head of Oncology Business, and President and CEO, Daiichi Sankyo, Inc. "VANFLYTA is the second innovative medicine from our oncology pipeline approved in the EU and its successful development reflects our commitment to creating new standards of care for patients with cancer."

About QuANTUM-First

QuANTUM-First is a randomized, double-blind, placebo-controlled, global phase 3 study evaluating VANFLYTA in combination with standard induction and consolidation therapy, including hematopoietic stem cell transplant (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 VANFLYTA 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 also were 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.[3] AML accounts for 23.1% of total leukemia cases worldwide and is most common in adults.[4,5] 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.[6,7]

A number of gene mutations have been identified in AML and *FLT3* (FMS-like tyrosine kinase 3) mutations are the most common.[8] 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.[1,2] *FLT3*-ITD mutations occur in about 25% of all AML cases, with frequency reported as high as 30%.[1,2]

About VANFLYTA

VANFLYTA 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.[2]

VANFLYTA is approved in the EU in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, followed by VANFLYTA single-agent maintenance therapy for adult patients with newly diagnosed AML that is *FLT3*-ITD positive.

VANFLYTA 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. VANFLYTA is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT); improvement in overall survival with VANFLYTA in this setting has not been demonstrated.

VANFLYTA 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. VANFLYTA is an investigational medicine in all countries outside of Europe, Japan and the U.S.

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.

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

Media Contacts:

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

EU:
Simone Jendsch-Dowé
Daiichi Sankyo Europe GmbH
simone.dowe@daiichi-sankyo.eu
+49 (89) 78080 (office)

Japan:
Koji Ogiwara
Daiichi Sankyo Co., Ltd.
ogiwara.koji.ay@daiichisankyo.co.jp
+81 3 6225 1126 (office)

Investor Relations Contact:
DaiichiSankyoIR@daiichisankyo.co.jp

References:
[1] Daver N, et al. *Leukemia*. (2019) 33:299-312.
[2] Patel JP, et al *N Engl J Med*. (2012) Mar 22;366(12):1079-89.
[3] Global Cancer Observatory. Population Fact Sheet: World. Updated March 2021.
[4] American Cancer Society: Key Statistics for Acute Myeloid Leukemia. Updated January 2023.
[5] Dong Y, et al. *Exp Hematol Oncol*. (2020);9:14.
[6] Rodriguez-Abreu D, et al. *Ann Oncol* (2007);18 Suppl 1:i3-i8.
[7] Heuser M, et al. *Ann Oncol*. (2020) 31(6):697-712.
[8] Kennedy VE, et al. *Front Onc*. 23 December 2020;10. Volume 10 – 2020.