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Daiichi-Sankyo

Press Release

EZHARMIA® Supplemental New Drug Application Submitted in Japan for Patients with Peripheral T-Cell Lymphoma

- Submission for second indication of SAKIGAKE-designated EZHARMIA based on VALENTINE-PTCL01 results in patients with relapsed or refractory PTCL

Tokyo – (January 31, 2024) – Daiichi Sankyo (TSE: 4568) has submitted a supplemental New Drug Application (sNDA) to Japan's Ministry of Health, Labour and Welfare (MHLW) for EZHARMIA® (valemetostat tosilate), a first-in-class dual inhibitor of EZH1 and EZH2, for the treatment of adult patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).

PTCL is a group of rare and aggressive blood cancers, which represent about 10 to 15% of all non-Hodgkin lymphomas (NHL).[1] A majority of patients with PTCL experience disease progression following initial treatment with a multi-drug chemotherapy-based regimen and median overall survival following relapse is approximately 5.8 months.[1]

The sNDA for EZHARMIA is based on VALENTINE-PTCL01 phase 2 trial results, which were recently presented at the 2023 American Society of Hematology (ASH) Annual Meeting. EZHARMIA had previously received SAKIGAKE designation from the Japan MHLW for treatment of patients with relapsed or refractory PTCL, and the sNDA represents the first submission for this potential indication globally.

"EZHARMIA has the potential to become a new treatment for patients in Japan with relapsed or refractory peripheral T-cell lymphoma, where there remains a need for additional options to improve outcomes," said Wataru Takasaki, PhD, Executive Officer, Head of R&D Division in Japan, Daiichi Sankyo. "EZHARMIA is the only dual inhibitor of EZH1 and EZH2 approved anywhere in the world, and we look forward to working with the Japan Health Authority to bring a second indication of this novel medicine to patients."

About VALENTINE-PTCL01 Trial

VALENTINE-PTCL01 is a global, open-label, single-arm, two-cohort phase 2 study evaluating the efficacy and safety of EZHARMIA in patients with relapsed or refractory PTCL and adult T-cell leukemia/lymphoma (ATLL) who received at least one systemic therapy and were ineligible for

hematopoietic stem cell transplant at the time of screening. One cohort enrolled patients with PTCL and a second cohort enrolled patients with ATLL.

The primary endpoint of VALENTINE-PTCL01 is objective response rate (ORR) based on CT-assessed blinded independent central review (BICR). Secondary endpoints include duration of response, complete response (CR), partial response, duration of CR and progression-free survival – all assessed by both BICR and investigator assessment – as well as ORR assessed by investigator, overall survival, safety and pharmacokinetics. Exploratory endpoints include PET-CT-based BICR and biomarker mutational status. Patients were enrolled at approximately 60 sites in Asia, Europe, North America and Oceania. For more information about this study, visit ClinicalTrials.gov.

About Peripheral T-Cell Lymphoma

PTCL is a group of rare and aggressive blood cancers, which represent 10 to 15% of all NHLs.[1] Approximately 544,000 new cases of NHL were diagnosed worldwide in 2020.[2] There are at least 29 recognized subtypes of PTCL, which occur with significant geographic variation.[3] PTCL is more frequent in Asia compared to Western countries.[4]

Prognosis of PTCL is generally poor, with a five-year overall survival rate of 32% in PTCL not otherwise specified (PTCL-NOS) and angioimmunoblastic T-cell lymphoma (AITL) and 7% or lower in certain subtypes.[4] A majority of patients with PTCL experience disease progression after standard first-line treatment with a multi-drug chemotherapy-based regimen and median overall survival following relapse is 5.8 months.[1] Development of more effective medicines for PTCL continues to be an unmet clinical need, particularly in the relapsed or refractory setting.[1]

About EZH1 and EZH2

The EZH1 (enhancer of zeste homolog 1) and EZH2 (enhancer of zeste homolog 2) enzymes help regulate the expression of genes involved in maintaining healthy hematopoietic stem cells (immature blood cells).[5] Both enzymes are recurrently mutated or overexpressed in hematologic malignancies, including T-cell lymphomas, and research shows they contribute to the silencing of tumor suppressor genes and drive oncogenic growth.[6,7]

About EZHARMIA

EZHARMIA (valemetostat tosilate) is a first-in-class dual inhibitor of EZH1 and EZH2 and one of two medicines in the hematology portfolio of Daiichi Sankyo. EZHARMIA is approved in Japan for the treatment of patients with relapsed or refractory ATLL. It is an investigational medicine in all countries outside of Japan.

EZHARMIA Clinical Development Program

In addition to VALENTINE-PTCL01, the EZHARMIA development program includes VALYM, a phase 2 trial in patients with relapsed or refractory B-cell lymphomas being conducted under a strategic research collaboration with the LYSA-LYSARC-CALYM group in Europe. Plans are underway to evaluate EZHARMIA in combination with other anti-cancer medicines in various solid tumors.

EZHARMIA has received SAKIGAKE Designation for the treatment of adult patients with relapsed or refractory PTCL by the Japan MHLW.

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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