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Press Release

EZHARMIA® Approved in Japan as First Dual EZH1 and EZH2 Inhibitor Therapy for Patients with Peripheral T-Cell Lymphoma

- Approval based on VALENTINE-PTCL01 results showing a clinically meaningful objective response rate of 43.7% in patients with relapsed or refractory PTCL
- Second indication approved for EZHARMIA in Japan

Tokyo – (June 24, 2024) – Daiichi Sankyo's (TSE: 4568) EZHARMIA® (valemetostat tosilate) has been approved in Japan for the treatment of adult patients with relapsed or refractory peripheral T-cell lymphoma (PTCL). EZHARMIA is now the first dual inhibitor of EZH1 and EZH2 to be approved for PTCL after receiving SAKIGAKE designation for this indication.

PTCL is a group of rare and often aggressive blood cancers, which represent about 10 to 15% of all non-Hodgkin lymphomas (NHL).[1] PTCL is more common in Asia, including in Japan, compared to other parts of the world.[2] 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 approval of EZHARMIA by the Japan Ministry of Health, Labour and Welfare (MHLW) is based on results of the VALENTINE-PTCL01 phase 2 trial, which were presented at the 2023 American Society of Hematology (ASH) Annual Meeting. In VALENTINE-PTCL01, an objective response rate (ORR) of 43.7% (n=52, 95% CI: 34.6-53.1) was observed for EZHARMIA in 119 efficacy evaluable patients with relapsed or refractory PTCL as assessed by CT-based blinded independent central review (BICR). Seventeen complete responses (CRs) and 35 partial responses (PRs) were observed. Responses were seen across a variety of PTCL subtypes including angioimmunoblastic T-cell lymphoma (AITL), PTCL not otherwise specified (PTCL-NOS) and other PTCL subtypes.

"This second indication for EZHARMIA in Japan is an important advance for the treatment of relapsed or refractory peripheral T-cell lymphoma, as new and effective treatment options are needed to improve patient outcomes," said Toshinori Agatsuma, PhD, Executive Officer, Head of R&D Division in Japan, Daiichi Sankyo. "EZHARMIA exemplifies the innovative research being conducted by Daiichi Sankyo aimed at creating new medicines with potential to change the standard of care for patients with cancer."

The safety profile of EZHARMIA in VALENTINE-PTCL01 was consistent with previous clinical trials. Treatment-related adverse events occurred in 106 of 133 patients (79.7%) with the most common including platelet count decrease (44.4%), anemia (27.1%), dysgeusia (24.8%) and neutrophil count decrease (21.1%).

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 ORR assessed by CT-based BICR. Secondary endpoints include duration of response, CR, PR, 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. Responses were evaluated based on Lugano 2014 response criteria. VALENTINE-PTCL01 enrolled 133 patients at multiple 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 often aggressive blood cancers, which represent 10 to 15% of all NHLs.[1] Approximately 553,000 new cases of NHL were diagnosed worldwide in 2022.[3] There are at least 29 recognized subtypes of PTCL, which occur with significant geographic variation.[4] PTCL is more common in Asia, including in Japan, compared to other parts of the world.[2]

Prognosis of PTCL is generally poor, with a five-year overall survival rate of 32% in AITL and PTCL-NOS, and 7% or lower in certain subtypes.[5] 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] 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).[6] 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.[7,8]

About EZHARMIA

EZHARMIA (valemetostat tosilate) is first-in-class dual inhibitor of EZH1 and EZH2 that was discovered by Daiichi Sankyo. EZHARMIA is approved in Japan for the treatment of patients with relapsed or refractory PTCL and for the treatment of patients with relapsed or refractory ATLL. It is an investigational medicine in all countries outside of Japan.

About EZHARMIA Clinical Development Program

A global clinical development program is underway for EZHARMIA in hematologic and solid cancers. In addition to VALENTINE-PTCL01, EZHARMIA is being evaluated in the VALYM phase 2 trial in patients with relapsed or refractory B-cell lymphomas, which is being conducted under a strategic research collaboration with the LYSA-LYSARC-CALYM group in Europe, and a phase 1b study in combination with DXd antibody drug conjugates ENHERTU® (trastuzumab deruxtecan) and datopotamab deruxtecan (Dato-DXd) in patients with solid cancers.

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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