# Press Release

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

- Approval based on pivotal phase 2 trial where EZHARMIA® demonstrated an objective response rate of 48% in previously treated patients
- Fifth innovative oncology medicine approved in Japan over the past three years for Daiichi Sankyo

**Tokyo – September 26, 2022 –** Daiichi Sankyo (TSE:5468) today announced that the Japan Ministry of Health, Labour and Welfare (MHLW) has approved EZHARMIA® (valemetostat tosilate), a first-in-class dual inhibitor of EZH1 and EZH2, for the treatment of patients with relapsed or refractory adult T-cell leukemia/lymphoma (ATL).

EZHARMIA previously received Orphan Drug Designation (ODD) from the MHLW for this indication and is now the first dual inhibitor of EZH1 and EZH2 to be approved for treatment of ATL. A rare and aggressive hematologic malignancy that can manifest as either leukemia or lymphoma, ATL occurs with higher frequency in certain regions of Japan and is associated with a five-year overall survival rate of approximately 14%.[1,2]

The approval of EZHARMIA by the MHLW is based on results of an open-label, single-arm pivotal phase 2 study evaluating efficacy and safety in 25 patients with three aggressive subtypes of relapsed or refractory ATL in Japan. The study demonstrated an objective response rate (ORR) of 48% (95% CI: 27.8%-68.7%), as evaluated by an independent efficacy assessment committee. Complete responses (CR) were seen in 20% of patients (n=5) and partial responses (PR) in 28% of patients (n=7).

“As the first dual inhibitor of EZH1 and EZH2 to receive regulatory approval anywhere in the world, EZHARMIA represents an important advancement in the treatment of patients with relapsed or refractory adult T-cell leukemia/lymphoma, who have very few options beyond intensive chemotherapy,” said Wataru Takasaki, PhD, Executive Officer, Head of R&D Division in Japan, Daiichi Sankyo. “We are proud to have successfully translated the science behind dual EZH1 and EZH2 inhibition into a new and novel therapy for these patients, who face a poor prognosis and represent one of the most significant unmet medical needs in Japan. We will continue to pioneer the approach in the global development of EZHARMIA, our fifth new oncology medicine approved in Japan in the past three years.”

EZHARMIA was generally well-tolerated in the phase 2 study. Drug-related treatment emergent adverse events occurred in 24 of 25 patients (96%) with the most common including platelet count decrease (80%), anemia (44%), alopecia (40%), dysgeusia (36%), lymphocyte count decrease (20%), neutrophil count decrease (20%) and white blood cell count decrease (20%).

**About Adult T-Cell Leukemia/Lymphoma**

Adult T-cell leukemia/lymphoma (ATL) is a rare and aggressive type of T-cell hematologic malignancy that is caused by human T-cell lymphotropic virus type 1 (HTLV-1).[1] Incidence of ATL is higher in regions where the HTLV-1 virus is endemic including southwest Japan, Central and South America, the Far East, central Australia and Romania.[3] Approximately 3,000 new cases of ATL are diagnosed each year worldwide.[4] In Japan, there are approximately 1,000 new ATL cases and 1,000 deaths due to ATL annually.[5]

ATL has a five-year overall survival rate reported at 14%.[2] A median survival time of approximately eight months (252 days) was observed for patients in Japan with acute ATL, the most common subtype of the disease.[6]

Treatment of ATL is based on subtype and consists primarily of intensive multi-drug chemotherapy regimens.[3] Nearly 90% of patients relapse after completing first-line therapy, often within months, at which point there are few options available.[1,7] Additional therapies are needed to improve the prognosis of ATL in Japan and worldwide.[3]

**About the Pivotal Phase 2 Study**

The pivotal, open-label, multi-center, single-arm phase 2 study evaluated efficacy and safety of EZHARMIA (200 mg dose daily) as monotherapy in patients with relapsed/refractory ATL who were previously treated with mogamulizumab or at least one systemic chemotherapy in case of intolerance/ contraindication for mogamulizumab and with no history of allogenic hematopoietic stem cell transplant.

The primary endpoint is ORR assessed by independent efficacy assessment committee. Secondary endpoints include investigator-assessed ORR, best response in tumor lesions, complete remission rate, tumor control rate, time to response, duration of response, progression-free survival, overall survival and safety. A total of 25 patients were enrolled in the study in Japan. The data were presented at the 2021 American Society of Hematology (ASH) Annual Meeting. For more information, visit ClinicalTrials.gov.

**About EZHARMIA**

EZHARMIA (valemetostat tosilate) is a first-in-class dual inhibitor of EZH1 and EZH2 currently in clinical development for treatment of several types of non-Hodgkin lymphoma. The EZH1 (enhancer of zeste homolog 1) and EZH2 (enhancer of zeste homolog 2) enzymes are part of the polycomb protein complex and act through histone methylation to help regulate the expression of genes involved in maintaining hematopoietic stem cells.[8] Both enzymes are recurrently mutated or overexpressed in hematologic malignancies including some T-cell lymphomas, and research shows they can contribute to the silencing of tumor suppressor genes and drive oncogenic growth.[9,10]

The EZHARMIA development program in lymphoma also includes VALENTINE-PTCL01, a global pivotal phase 2 trial in patients with relapsed/refractory peripheral T-cell lymphoma (PTCL) including ATL, and VALYM, a phase 2 trial in patients with relapsed/refractory B-cell lymphomas being conducted under a strategic research collaboration with the French LYSA-LYSARC-CALYM group in Europe.

EZHARMIA received ODD from the U.S. Food & Drug Administration for the treatment of PTCL in December 2021, ODD from the Japan MHLW for the treatment of relapsed/refractory ATL in November 2021, and SAKIGAKE Designation from the Japan MHLW for the treatment of adult patients with relapsed/refractory PTCL in April 2019.

EZHARMIA is approved in Japan for the treatment of patients with relapsed or refractory adult T-cell leukemia/lymphoma and 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.

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