Press Release

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

- EZHARMIA is the fifth innovative oncology medicine to be launched in Japan by Daiichi Sankyo in the past three years

Tokyo – December 20, 2022 – Daiichi Sankyo (TSE:4568) today announced the launch of EZHARMIA® (valemetostat tosilate), a first-in-class dual inhibitor of EZH1 and EZH2, in Japan for the treatment of patients with relapsed or refractory adult T-cell leukemia-lymphoma (ATLL).

Marketing approval of EZHARMIA was granted by Japan's Ministry of Health, Labor and Welfare (MHLW) in September 2022 based on results of an open-label, single-arm pivotal phase 2 study in 25 patients with three aggressive subtypes of relapsed or refractory ATLL in Japan. Data from the trial demonstrated an objective response rate (ORR) of 48% (95% CI: 27.8%-68.7%).

"Patients in Japan with relapsed or refractory adult T-cell leukemia-lymphoma, who have had limited treatment options beyond intensive chemotherapy, now have access to EZHARMIA, the first dual inhibitor of EZH1 and EZH2 to be approved for treatment of ATLL," said Yoshinori Kaneshima, Corporate Officer, Head of Marketing Division, Japan Business Unit, Daiichi Sankyo. "EZHARMIA is a new and novel therapy discovered by Daiichi Sankyo and is the fifth innovative oncology medicine we have launched in Japan in the past three years."

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

About Adult T-Cell Leukemia-Lymphoma

Adult T-cell leukemia-lymphoma (abbreviated ATLL or ATL) is a rare and aggressive hematologic malignancy that is caused by human T-cell lymphotropic virus type 1 (HTLV-1).[1] Incidence of ATLL is higher in regions where the HTLV-1 virus is endemic including southwest Japan, Central and South America, Asia, central Australia and Romania.[2] Sporadic cases are observed in non-endemic regions

including North America and parts of Europe.[2] Approximately 3,000 new cases of ATLL are diagnosed each year worldwide.[3] In Japan, there are approximately 1,000 new ATLL cases and 1,000 deaths due to ATLL annually.[4]

The five-year overall survival rate for people with ATLL is reported at 14%.[5] A median survival time of approximately eight months (252 days) was observed for patients in Japan with acute ATLL, the most common of four ATLL subtypes.[6] Treatment of ATLL is based on subtype and consists primarily of intensive multi-drug chemotherapy regimens.[2] Nearly 90% of patients relapse after completing first-line therapy, often within months, at which point there are few options available.[1,7]

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 ATLL 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. 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 the treatment of several types of non-Hodgkin lymphoma. The EZH1 (enhancer of zeste homolog 1) and EZH2 (enhancer of zeste homolog 2) enzymes help regulate the expression of genes involved in maintaining hematopoietic stem cells.[8] Both enzymes are recurrently mutated or overexpressed in blood cancers including T-cell lymphomas, and research shows they can drive oncogenic growth.[9,10] EZHARMIA binds to EZH1 and EZH2 to inhibit their activity and alter gene expression to counter cancer cell growth and proliferation.[11,12]

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 ATLL, 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 Orphan Drug Designation (ODD) from the Japan MHLW for the treatment of relapsed/refractory ATLL in November 2021. EZHARMIA also received ODD from the U.S. Food & Drug Administration for the treatment of PTCL in December 2021 and SAKIGAKE Designation from the Japan MHLW for the treatment of 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/regions 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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