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Press Release

EZHARMIA® Showed Clinically Meaningful and Durable Responses in Patients with Relapsed or Refractory Peripheral T-Cell Lymphoma in VALENTINE-PTCL01 Phase 2 Trial

- An objective response rate of 43.7% and median duration of response of 11.9 months were observed with EZHARMIA in previously treated patients
- A supplemental NDA is planned for SAKIGAKE-designated EZHARMIA in Japan for second half of fiscal year 2023

Tokyo – (December 9, 2023) – Results from the VALENTINE-PTCL01 phase 2 trial of Daiichi Sankyo's (TSE: 4568) EZHARMIA® (valemetostat tosilate) showed clinically meaningful and durable responses in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL). The data were presented today in an oral session (#302) at the 2023 American Society of Hematology (#ASH23) Annual Meeting.

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]

An objective response rate (ORR) of 43.7% (95% CI: 34.6-53.1) was observed with EZHARMIA in 119 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 seen. Median duration of response (DoR) of 11.9 months (95% CI: 7.8-NE) was observed after a median follow-up of 9.7 months. Responses were observed across all PTCL subtypes.

Median progression-free survival (PFS) of 5.5 months (95% CI: 3.5-8.3) was seen after a median follow-up of 11.3 months (95% CI: 11.1-13.8) and median overall survival (OS) of 17.0 months (95% CI: 13.5-NE) was observed after a median follow-up time of 12.3 months.

An exploratory analysis evaluating responses using PET-CT-based BICR assessment showed an ORR of 52.1% (n=62; 95% CI: 42.8-61.3) with 32 complete metabolic responses (CMRs).

"The high response rates and durability of responses observed with valemetostat in patients with relapsed or refractory peripheral T-cell lymphoma are very encouraging," said Steven M. Horwitz, MD,

Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York. "Relapse is too frequent in PTCL and there is an acute need for new medicines beyond standard chemotherapy to better control the disease in the relapsed or refractory setting and improve patient outcomes."

The safety profile of EZHARMIA in VALENTINE-PTCL01 (n=133) was consistent with previous clinical trials. Grade 3 or higher treatment emergent adverse events (TEAEs) occurred in 57.9% of patients. The most common grade 3 or higher TEAEs occurring in ≥ 10% of patients were thrombocytopenia (23.3%), anemia (18.8%) and neutropenia (17.3%).

"The results of VALENTINE-PTCL01 support the potential of EZHARMIA as a novel single agent therapy across subtypes of previously treated peripheral T-cell lymphomas," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "The response rate reported and duration of response of nearly one year seen in the study is impressive for this historically difficult-to-treat blood cancer with limited available treatment options."

Patients with PTCL enrolled in the study had received a median of two prior treatments (range, 1-12) and 35 patients (26.3%) received prior hematopoietic cell transplant (HCT). At the time of data cut-off of May 5, 2023, 32 patients (24.1%) remained on treatment.

Summary of VALENTINE-PTCL01 Results

Efficacy Measure [1]	**All Patients**[2] **(n=119)**
ORR (%) (95% CI) CT-based BICR	43.7% (34.6–53.1)
CR[3]	14.3%
PR	29.4%
Median DoR, months (95% CI) CT-based BICR	11.9 months (7.8-NE)
ORR (%) (95% CI) PET-CT-based BICR	52.1% (42.8-61.3)
CMR	26.9%
Median PFS, months (95% CI) CT-based BICR	5.5 months (3.5-8.3)
Median OS (95% CI)	17.0 months (13.5-NE)

CR, complete response; CMR, complete metabolic response; DoR, duration of response; NE, not evaluable; ORR, objective response rate; PFS, progression-free survival; PR, partial response; OS, overall survival

[1] Efficacy endpoints were evaluated based on Lugano 2014 response criteria

[2] Includes PTCL subtypes angioimmunoblastic T-cell lymphoma (AITL), PTCL not otherwise specified (PTCL-NOS), T-peripheral helper (PTCL-TFH), anaplastic large cell lymphoma (ALCL) and "other" PTCL

[3] Eight patients with a CR and 10 patients in total proceeded to HCT

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 are ineligible for HCT 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 based on CT-assessed BICR. Secondary endpoints include DoR, CR, PR, duration of CR and PFS – all assessed by both BICR and investigator assessment – as well as ORR assessed by investigator, OS, 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, at which time treatment options are very limited and median overall survival 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 the pivotal phase 2 trial in relapsed or refractory ATLL in Japan and the phase 1 study in relapsed or refractory NHL in North America and Asia. VALYM, a phase 2 trial in patients with relapsed or refractory B-cell lymphomas, is being conducted under a strategic research collaboration with the LYSA-LYSARC-CALYM group in Europe.

EZHARMIA has received SAKIGAKE Designation for the treatment of adult patients with relapsed or refractory PTCL by the Japan Ministry of Health, Labour and Welfare (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.

Disclosure: Dr. Horwitz has financial interests related to Daiichi Sankyo.

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