Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

Press Release

Valemetostat New Drug Application Submitted in Japan for Treatment of Patients with Adult T-Cell Leukemia/Lymphoma

- Submission of Orphan Drug designated valemetostat based on pivotal phase 2 trial in patients with relapsed/refractory ATL
- Fifth potential medicine from the innovative oncology pipeline of Daiichi Sankyo to be submitted to Japan MHLW in past three years

Tokyo and Basking Ridge, NJ – December 28, 2021 – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that it has submitted a New Drug Application (NDA) to Japan's Ministry of Health, Labour and Welfare (MHLW) for valemetostat, a potential first-in-class dual inhibitor of EZH1 and EZH2, for the treatment of patients with relapsed/refractory adult T-cell leukemia/lymphoma (ATL).

ATL is a rare and aggressive type of peripheral T-cell lymphoma that occurs with greater frequency in parts of Japan and other regions.[1,2] Patients with ATL face a poor prognosis with current therapies.[3] Nearly 90% of patients relapse after completing intensive first-line treatment, at which point there are few options available.[1,4]

The Japan NDA submission of valemetostat is based on pivotal phase 2 study results in Japanese patients with three aggressive subtypes of relapsed/refractory ATL, recently presented at the 2021 American Society of Hematology (ASH) Annual Meeting. Valemetostat previously received Orphan Drug designation (ODD) from the Japan MHLW for treatment of patients with relapsed/refractory ATL.

"Valemetostat would potentially be the first dual inhibitor of EZH1 and EZH2 to be approved anywhere in the world and could provide a new type of targeted therapy option for patients with relapsed/refractory ATL, which represents one of the most significant unmet medical needs in Japan," said Wataru Takasaki, PhD, Executive Officer, Head of R&D Division in Japan, Daiichi Sankyo. "Valemetostat is the fifth innovative oncology medicine from our pipeline to be submitted for regulatory approval in Japan in the past three years."

About Adult T-Cell Leukemia/Lymphoma

Adult T-cell leukemia/lymphoma (ATL) is a rare and aggressive type of peripheral T-cell lymphoma (PTCL) that is caused by human T-cell lymphotropic virus type 1 (HTLV-1).[1] More than 3,000 new cases of ATL are diagnosed each year worldwide.[5] ATL occurs with greater frequency in regions where the

HTLV-1 virus is endemic including southwest Japan, Central and South America and central Australia.[3] Cases are also observed in North America and Europe, and incidence of ATL is rising in non-endemic areas.[3] In Japan, there are approximately 1,000 new ATL cases and over 1,000 deaths due to ATL annually.[6]

ATL has the poorest prognosis compared to other types of PTCL, with a five-year overall survival rate of about 14%.[7] A median survival time of approximately eight months (252 days) was reported for patients in Japan with the most common acute ATL subtype.[5]

Treatment of ATL is based on subtype and consists primarily of intensive multi-drug chemotherapy regimens.[3] Nearly 90% of patients relapse after completing intensive first-line treatment, at which point there are few options available.[1,4] Additional therapies are needed to improve the prognosis of ATL in Japan and worldwide.[1,3]

About Valemetostat

Valemetostat is a potential first-in-class dual inhibitor of EZH1 and EZH2 currently in clinical development in the Alpha portfolio of Daiichi Sankyo. A potent and selective small molecule inhibitor, valemetostat is designed to counter epigenetic dysregulation by targeting both the EZH1 and EZH2 enzymes.[8]

The valemetostat development program includes VALENTINE-PTCL01, a global pivotal phase 2 trial in patients with relapsed/refractory PTCL and ATL; a pivotal phase 2 trial in patients with relapsed or refractory ATL in Japan; and, a phase 1 study in patients with relapsed/refractory NHL in the U.S. and Japan. Valemetostat 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.

Valemetostat is an investigational medicine that has not been approved for any indication in any country. Safety and efficacy have not been established.

About the Pivotal Phase 2 Study

The pivotal, open-label, multi-center, single-arm phase 2 study evaluated efficacy and safety of valemetostat (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 objective response rate (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 Daiichi Sankyo Oncology

The oncology portfolio of Daiichi Sankyo is powered by our team of world-class scientists that push beyond traditional thinking to create transformative medicines for people with cancer. Anchored by our DXd antibody drug conjugate (ADC) technology, our research engines include biologics, medicinal chemistry, modality and other research laboratories in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in the U.S. We also work alongside leading academic and business collaborators to further advance the understanding of cancer as Daiichi Sankyo builds towards our ambitious goal of becoming a global leader in oncology by 2025.

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.

Media Contacts:

Global/US:
Jennifer Brennan
Daiichi Sankyo, Inc.
jbrennan2@dsi.com
+1 908 992 6631 (office)
+1 908 900 3183 (mobile)

Japan:
Masashi Kawase
Daiichi Sankyo Co., Ltd.
kawase.masashi.a2@daiichisankyo.co.jp
+81 3 6225 1126 (office)

EU:
Lydia Worms
Daiichi Sankyo Europe GmbH
lydia.worms@daiichi-sankyo.eu
+49 (89) 7808751 (office)
+49 176 11780861 (mobile)

Investor Relations Contact:
DaiichiSankyoIR@daiichisankyo.co.jp

References

[1] Hermine O et al. *Adv Ther*. 2018 Feb; 35(2): 135–152.
[2] Vose JM et al. *J Clin Onc*. 2008;26:4124-4130.
[3] Cook et al. *J Clin Onc*. 2019 Mar 10;37(8):677-687
[4] Mehta-Shah N, et al. *Oncol Pract*. 2017;13:487-493
[5] Imazumi et al *Cancer Science*. 2020;111:4567–4580.
[6] Iwanaga M et al. *Front Microbiol*. 2012 Sep 10;3:322
[7] Phillips A et al. *Haematologica*. 2019; 104:5
[8] Ishitsuka K et al. *Hematological Oncology*. 2021;39:S2