

Press Release

Daiichi Sankyo Initiates Pivotal Phase 2 Trial in Japan with Valemetostat in Patients with Adult T-Cell Leukemia-Lymphoma

- Study to evaluate valemetostat, potential first-in-class EZH1/2 dual inhibitor, in patients with relapsed/refractory ATL in Japan
- Valemetostat is only dual inhibitor in clinical development for ATL, a rare and aggressive non-Hodgkin's lymphoma (NHL) with high incidence in Japan
- Trial initiated based on results from ongoing phase 1 study in several types of NHL

Tokyo - (December 10, 2019) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced today that the first patient has been dosed in a pivotal phase 2 study in Japan evaluating valemetostat (DS-3201), an investigational EZH1/2 dual inhibitor, in patients with relapsed/refractory adult T-cell leukemia-lymphoma (ATL).

ATL is one of the most aggressive forms of non-Hodgkin's lymphoma (NHL) and although rare, occurs with greater frequency in certain regions including Japan. Treatments for ATL, a complex and heterogeneous disease, are largely limited to systemic chemotherapy combinations, and patients often face a difficult prognosis, especially for relapsed disease.¹

“Valemetostat is a novel targeted therapy that has demonstrated preliminary potential in several types of NHL including ATL, which represents one of the greatest areas of need among lymphoma patients, particularly in Japan,” said Kaszushi Araki, DVM, PhD, Valemetostat Global Team Leader, Oncology Clinical Development Department, Oncology Function, Daiichi Sankyo. “Valemetostat is the only EZH1/2 dual inhibitor in clinical development, and our program includes translational research to improve understanding of underlying disease mechanisms and treatment response.”

The pivotal phase 2 trial with valemetostat was initiated based on preliminary findings from an ongoing phase 1 study in patients with several types of NHL, which were presented on December 9th at the 2019 annual meeting of the American Society of Hematology (ASH).²

About the Study

The pivotal, open-label, multi-center, single-arm phase 2 study will evaluate efficacy and safety of valemetostat as monotherapy in patients with relapsed/refractory ATL previously treated with mogamulizumab or at least one systemic chemotherapy.

The primary efficacy endpoint is overall response rate (ORR). Secondary efficacy endpoints include investigator-assessed ORR, complete remission rate, time to response, duration of response, progression-free survival and overall survival. The study will evaluate safety endpoints including adverse events and a number of pharmacokinetic, pharmacodynamic and biomarker endpoints. Approximately 25 patients are expected to be enrolled in the study in Japan. For more information, please visit [ClinicalTrials.gov](https://clinicaltrials.gov).

About Adult T-Cell Leukemia/Lymphoma

Adult T-cell leukemia/lymphoma (ATL), an often fast-growing form of T-cell lymphoma, is associated with human T-cell lymphotropic virus type 1 (HTLV-1).³ While ATL is rare in most parts of the world, it is endemic in several regions of the world with Japan having the highest prevalence of both HTLV-1 and ATL. Although the majority of an estimated one million people in Japan that are carriers of the HTLV-1 virus remain asymptomatic during their lifetime, it is estimated that the annual incidence of developing ATL is approximately 60 per 100,000 carriers resulting in 1,000 deaths annually.⁴ The lifetime risk of ATL for HTLV-1 carriers is approximately 5 percent for men and 3 percent for women in Japan.⁴

Treatment options for ATL vary based on the subtype of the disease. Since there are no optimal standard treatments to manage this type of cancer, enrollment in a clinical trial is a recommended treatment option for all patients with ATL.⁵

About Valemetostat

Valemetostat (DS-3201) is an investigational and potential first-in-class EZH1/2 dual inhibitor that targets epigenetic regulation by inhibiting both the EZH1 (enhancer of zeste homolog 1) and EZH2 (enhancer of zeste homolog 2) enzymes, which act through histone methylation to regulate gene expression.⁶

Research has shown that EZH1 and EZH2 are recurrently highly expressed or mutated in many hematologic cancers and are involved in suppression of genes that control tumor cell growth and proliferation.⁷ Valemetostat has displayed preliminary activity in various hematological malignancies in preclinical models.^{8, 9}

In addition to the pivotal phase 2 trial in relapsed/refractory ATL, valemetostat is in phase 1 clinical development for several types of NHLs including ATL, peripheral T-cell lymphoma (PTCL) and B-cell lymphomas, and the trial is now enrolling patients in the U.S. as well as Japan ([ClinicalTrials.gov](https://clinicaltrials.gov)). A phase 1 study is also underway with valemetostat in other hematologic cancers including acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL) ([ClinicalTrials.gov](https://clinicaltrials.gov)). Valemetostat has received SAKIGAKE Designation for the treatment of adult patients with relapsed/refractory PTCL by the Ministry of Health, Labour and Welfare (MHLW) in Japan.

There are no dual EZH1/2 targeting treatments approved for treatment of any cancer. Valemetostat is an investigational agent that has not been approved for any indication in any country. Safety and efficacy have not been established.

About Daiichi Sankyo Cancer Enterprise

The mission of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do.

Anchored by three pillars including our investigational Antibody Drug Conjugate Franchise, Acute Myeloid Leukemia Franchise and Breakthrough Science, we aim to deliver seven distinct new molecular entities over eight years during 2018 to 2025. Our powerful research engines include two laboratories for biologic/immuno-oncology and small molecules in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley, CA. For more information, please visit: www.DSCancerEnterprise.com.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical therapies to improve standards of care and address diversified, unmet medical needs of people globally by leveraging our world-class science and technology. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for cardiovascular diseases, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo is primarily focused on providing novel therapies in oncology, as well as other research areas centered around rare diseases and immune disorders. For more information, please visit: www.daiichisankyo.com.

Media Contacts

Japan:

Koji Ogiwara
Daiichi Sankyo, Co., Ltd
ogiwara.koji.ay@daiichisankyo.co.jp
+81 3 6225 1126 (office)

Global and US

Jennifer Brennan
Daiichi Sankyo, Inc.
jbrennan2@dsi.com
+1 908 992 6631 (office)
+1 201 709 9309 (mobile)

Investor Relations:

DaiichiSankyoIR@daiichisankyo.co.jp

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