TOGETHER AGAINST LYMPHOMA

# Press Release

## Daiichi Sankyo and LYSA-LYSARC-CALYM Enter Research Collaboration for Valemetostat in Patients with Relapsed/Refractory B-Cell Lymphoma

- Phase 2 trial to evaluate valemetostat in patients with five disease subtypes along with a planned robust translational research program

**Tokyo, Basking Ridge, N.J., Munich and Lyon** – (February 24, 2021) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and LYSA-LYSARC-CALYM today announced that they have entered a strategic research collaboration to study valemetostat (DS-3201), Daiichi Sankyo's potential first-in-class EZH1/2 dual inhibitor, in B-cell malignancies starting with a phase 2 study in patients with five subtypes of relapsed/refractory B-cell lymphoma.

The collaboration brings together Daiichi Sankyo's innovative science and the multidisciplinary expertise of the Lymphoma Study Association (LYSA), the Lymphoma Academic Research Organization (LYSARC) and the CALYM research consortium to conduct clinical and translational research that will build upon the ongoing phase 1 study of valemetostat in patients with relapsed/refractory non-Hodgkin lymphoma.[1]

Lymphoma is a heterogenous disease with more than 90 different subtypes and while new treatment advances have improved outcomes for some patients, management of relapsed/refractory B-cell lymphoma remains a major challenge.[2] There are currently no dual EZH1/2 directed therapies approved for cancer treatment.

"We are pleased to join forces with Europe's largest lymphoma research organization to advance and strengthen the development of valemetostat as a potential novel precision medicine for patients with relapsed/refractory B-cell lymphoma," said Arnaud Lesegretain, Vice President, Global Oncology Development, Alpha Portfolio, Daiichi Sankyo. "LYSA-LYSARC-CALYM together with Daiichi Sankyo have designed a phase 2 study that will enroll patients based on disease subtype and biomarkers in order to further evaluate safety and efficacy, and we are planning a comprehensive translational research program to answer important scientific questions relating to clinical utility, optimal patient selection and mechanisms of resistance."

"We are very happy to engage our cooperative group in a collaboration with Daiichi Sankyo for this promising development program with valemetostat targeting relevant epigenetic factors EZH2 and EZH1 in B-cell lymphomas," said Franck Morschhauser, Professor of Hematology in Lille, France and President of LYSA-LYSARC. "We believe that our extensive multidisciplinary and international expertise will help advance the science behind the novel mechanism of action and we look forward to playing a role in bringing this potential new medicine to patients with lymphoma."

**About the Collaboration**

Under the agreement, LYSA-LYSARC will execute a multi-center, non-randomized, open-label phase 2 study to evaluate the safety and efficacy of valemetostat in six cohorts of patients with relapsed/refractory B-cell lymphoma.

The study will enroll patients with diffuse large B-cell lymphoma (with and without an EZH2 mutation) that has progressed on at least one prior treatment; follicular lymphoma (EZH2 mutant and EZH2 wild-type), mantle cell lymphoma, and marginal zone lymphoma/other indolent lymphomas that have progressed on two or more prior treatments; and Hodgkin lymphoma that has progressed on three or more prior treatments including checkpoint inhibitors.

The primary endpoint of the study is best overall response rate determined by investigator assessment. Secondary endpoints include complete response rate, progression-free survival, duration of response, time to response and safety measures including adverse events. Exploratory endpoints include overall survival and measures of biomarker expression and treatment response. Pharmacokinetic endpoints will also be assessed.

The study will include approximately 140 patients at 22 sites in France and Belgium and is anticipated to initiate in 2021.

**About EZH1 and EZH2**

EZH1 (enhancer of zeste homolog 1) and EZH2 (enhancer of zeste homolog 2) enzymes are part of polycomb protein complexes that act through histone methylation to regulate gene expression.[3] EZH1 and EZH2 are recurrently highly expressed or mutated in many hematologic malignancies.[4] Epigenetic dysregulation of the methylation process is associated with suppression of genes that regulate cancer cell growth and proliferation.[4] Research shows that both EZH1 and EZH2 have a role in hematologic cancer progression and that simultaneous inhibition would be effective in targeting the cancers.[5] There are no dual EZH1/2 directed therapies approved for treatment of cancer.

**About Valemetostat**

Valemetostat (DS-3201) is a potential first-in-class small molecule oral EZH1/2 dual inhibitor currently in clinical development in the Alpha portfolio of Daiichi Sankyo for several hematologic cancers. Valemetostat targets epigenetic regulation by inhibiting both the EZH1 and EZH2 enzymes. Valemetostat has displayed antitumor activity in various hematological malignancies in preclinical models.[5,6]

The development program of valemetostat includes a pivotal phase 2 trial in patients with relapsed or refractory adult T-cell leukemia/lymphoma (ATL) in Japan; a phase 1 study in patients with several types of non-Hodgkin lymphomas (NHL) including B-cell lymphoma, adult T-cell leukemia-lymphoma (ATL) and peripheral T-cell lymphoma (PTCL) in the U.S. and Japan; and a phase 1 study in patients with acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML) in the U.S.

In April 2019, valemetostat received SAKIGAKE Designation for the treatment of adult patients with relapsed or refractory PTCL by the Japan Ministry of Health, Labour and Welfare (MHLW).

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

**About B-Cell Lymphoma**

Lymphoma is the most common type of blood cancer.[7] There were more than 627,000 new cases of lymphoma diagnosed globally and more than 283,000 deaths from the disease in 2020.[8]

There are more than 90 different lymphoma subtypes, which occur in varying frequencies in different geographic regions around the world.[7] Most lymphomas originate in B-cell lymphocytes, with the most common types being diffuse large B-cell lymphoma (about 33 percent), follicular lymphoma (about 20 percent), mantle cell lymphoma (about 5 percent) and marginal zone lymphoma (5 to10 percent).[9] Treatment recommendations and prognosis vary for different subtypes of B-cell lymphoma.[10] New treatment advances have improved outcomes for some patients with certain types of B-cell lymphoma, but management of relapsed or refractory lymphoma remains a major challenge and new and novel treatments are needed.[2]

**About LYSA-LYSARC-CALYM, A Multidisciplinary Research Ecosystem**

LYSA-LYSARC-CALYM form a multidisciplinary community of more than 800 professionals committed to lymphoma research in France and Belgium. Their shared missions are the following: fighting against lymphomas, researching better treatments and improving the patients' quality of life. The origin of LYSA-LYSARC dates back to the 1980s and 90s. European lymphoma research experts have coordinated their

efforts and competences over the years to create a premiere multidisciplinary ecosystem at the international level.

**LYSA - A Network of Clinical Research Professionals**

The Lymphoma Study Association, or LYSA, is the internationally leading cooperative group for lymphoma research in Europe, conducting clinical studies ranging from the first tests of new medicines in humans to the establishment of reference therapeutic strategies. LYSA includes in its network more than 120 care centers distributed throughout four countries (France, Belgium, Portugal, Israel), and collaborates with many scientific teams at the international level.

**LYSARC - An Academic Research Organization Linked to the LYSA**

The Lymphoma Academic Research Organization, or LYSARC, is the LYSA operational structure that conducts clinical research projects on lymphomas at the international level. LYSARC has all the integrated functions and dedicated platforms for pathology, biology and imagery to conduct as sponsor many phase 1 to 4 clinical studies or registries every year in lymphoma.

**CALYM CARNOT INSTITUTE - A Consortium of Experts Dedicated to Partnership-Based Research**

The purpose of the Carnot Institute CALYM, a consortium for the acceleration of innovation and its transfer to the field of lymphoma research, is to promote the development of diagnostic and care solutions for lymphomas, in partnership with the public and private socio-economic sector. It consists of 20 complementary research organizations: 18 public research laboratories, and LYSA and LYSARC.
For more information about LYSA-LYSARC-CALYM visit lymphoma-research-experts.org

**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 our DXd antibody drug conjugate (ADC) technology, our powerful 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 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.

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