

## Press Release

# **Daiichi Sankyo Announces Outcome of FDA Oncologic Drugs Advisory Committee Meeting to Review FLT3 Inhibitor Quizartinib for the Treatment of Patients with Relapsed/Refractory *FLT3*-ITD AML**

**Tokyo and Basking Ridge, NJ – (May 14, 2019)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced the outcome of the U.S. Food and Drug Administration (FDA) Oncologic Drugs Advisory Committee (ODAC) to discuss the company’s New Drug Application (NDA) for quizartinib for the treatment of adults with relapsed/refractory *FLT3*-ITD acute myeloid leukemia (AML).

Three committee members voted yes and 8 committee members voted no when asked if the results from the pivotal phase 3 QuANTUM-R study demonstrated that treatment with quizartinib provides a benefit that outweighs the safety risks for patients with relapsed/refractory *FLT3*-ITD AML.

“While we are disappointed by the outcome of today’s ODAC vote, we will work closely with the FDA as it completes the review of our submission,” said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. “Patients with relapsed/refractory *FLT3*-ITD AML are facing a very aggressive disease with poor prognosis, and we continue to believe that quizartinib could offer an important additional treatment option that specifically targets *FLT3*-ITD, a driver mutation in AML.”

The FDA is not bound by the recommendations of the advisory committee. The NDA for quizartinib is currently under Priority Review in the U.S., and the FDA is expected to make a decision on approval by the Prescription Drug User Fee Act (PDUFA) date of August 25, 2019. The NDA submission of quizartinib is based on the results of the pivotal phase 3 QuANTUM-R study, which was the first randomized phase 3 study to show that a *FLT3* inhibitor prolonged overall survival as an oral, single agent compared to chemotherapy in patients with relapsed/refractory *FLT3*-ITD AML.

In the quizartinib QuANTUM-R study, the median treatment duration with quizartinib was 4 cycles of 28 days each versus 1 cycle in the salvage chemotherapy arm. Incidence of treatment-emergent adverse events was comparable between patients who received single agent quizartinib and those who received salvage chemotherapy. The most common adverse drug reactions (>30 percent, any Grade) in patients treated with quizartinib included infections, bleeding, nausea, asthenic conditions, pyrexia, febrile neutropenia, and

vomiting, and the most common Grade  $\geq 3$  adverse drug reactions (>20 percent) were infection and febrile neutropenia. The most common laboratory adverse reactions (incidence >50 percent) were decreased white blood cell count, decreased lymphocyte count, decreased hemoglobin, decreased neutrophil count, and decreased platelet count. QTcF >500 msec occurred in 8 patients (3.3 percent) and 2 out of 241 patients discontinued quizartinib due to QTcF prolongation. There were no reported events of Grade 4 QTcF prolongation (Torsades de Pointes, sudden death or cardiac arrest) in the quizartinib arm. The safety profile observed in QuANTUM-R appears consistent with that observed at similar doses in the quizartinib clinical development program.

### **About *FLT3*-ITD AML**

AML is an aggressive blood and bone marrow cancer that causes uncontrolled growth and accumulation of malignant white blood cells that fail to function normally and interfere with the production of normal blood cells.<sup>1</sup> In the U.S. this year, it is estimated that there will be more than 19,000 new diagnoses of AML and more than 10,000 deaths from AML.<sup>2</sup> The five-year survival rate of AML reported from 2007 to 2013 was approximately 27 percent, which was the lowest of all leukemias.<sup>1</sup>

*FLT3* gene mutations are one of the most common genetic abnormalities in AML.<sup>3</sup> *FLT3*-ITD is the most common *FLT3* mutation, affecting approximately one in four patients with AML.<sup>4,5,6,7</sup> *FLT3*-ITD is a driver mutation that presents with high leukemic burden and has poor prognosis and a significant impact on disease management for patients with AML.<sup>5,8</sup> Patients with *FLT3*-ITD AML have a worse overall prognosis, including an increased incidence of relapse, an increased risk of death following relapse and a higher likelihood of relapse following hematopoietic stem cell transplantation as compared to those without this mutation.<sup>9,10</sup>

### **About Quizartinib**

Quizartinib, the lead investigational agent in the AML Franchise of the Daiichi Sankyo Cancer Enterprise, is an oral selective type II *FLT3* inhibitor currently under regulatory review with the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Japan Ministry of Health, Labour and Welfare (MHLW) for the treatment of adult patients with relapsed/refractory AML which is *FLT3*-ITD positive. Quizartinib has been granted Priority Review and Breakthrough Therapy designation for the treatment of adult patients with relapsed/refractory *FLT3*-ITD AML, and Fast Track designation for the treatment of relapsed/refractory AML by the FDA. Quizartinib also has been granted Orphan Drug designation by both the FDA and the European Commission (EC) for the treatment of AML and by the Japan MHLW for the treatment of *FLT3*-mutated AML.

Quizartinib is also in phase 3 development in combination with standard chemotherapy in newly-diagnosed *FLT3*-ITD AML ([QuANTUM-First](#)) in the U.S., EU and Japan; phase 1/2 development for pediatric and young adult relapsed/refractory *FLT3*-ITD AML in North America and the EU; and phase 1 development in combination with an investigational MDM2 inhibitor, milademetan, for relapsed/refractory *FLT3*-ITD AML and newly-diagnosed *FLT3*-ITD AML unfit for intensive chemotherapy in the U.S. and Japan.

Quizartinib and milademetan are investigational agents that have 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. Compounds in pivotal stage development include: [fam-] trastuzumab deruxtecan, an antibody drug conjugate (ADC) for HER2 expressing breast, gastric and other cancers; quizartinib, an oral selective *FLT3* inhibitor, for newly-diagnosed and relapsed/refractory *FLT3*-ITD acute myeloid leukemia (AML); and pexidartinib, an oral CSF1R inhibitor, for tenosynovial giant cell tumor (TGCT). For more information, please visit: [www.DSCancerEnterprise.com](http://www.DSCancerEnterprise.com).

### **About Daiichi Sankyo**

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 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 hypertension and thrombotic disorders, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo research and development is primarily focused on bringing forth novel therapies in oncology, including immuno-oncology, with additional focus on new horizon areas, such as pain management, neurodegenerative diseases, heart and kidney diseases, and other rare diseases. For more information, please visit: [www.daiichisankyo.com](http://www.daiichisankyo.com). Daiichi Sankyo, Inc., headquartered in Basking Ridge, New Jersey, is a

member of the Daiichi Sankyo Group. For more information on Daiichi Sankyo, Inc., please visit:

[www.dsi.com](http://www.dsi.com).

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