

## Press Release

# Phase 3 QuANTUM-R Study Demonstrates Daiichi Sankyo's Quizartinib Significantly Prolongs Overall Survival as Single Agent Compared to Chemotherapy in Patients with Relapsed/Refractory AML with *FLT3*-ITD Mutations

- Data from QuANTUM-R presented as a late-breaking oral presentation during plenary session at 23<sup>rd</sup> Congress of the European Hematology Association (EHA)
- Quizartinib is the first *FLT3* inhibitor to prolong overall survival as a single agent compared to chemotherapy in patients with relapsed/refractory AML with *FLT3*-ITD mutations, a very aggressive form of the disease associated with poor prognosis
- There is high unmet medical need in relapsed/refractory AML as available treatment options are limited; currently, there are no approved targeted therapies for patients with relapsed/refractory *FLT3*-ITD-mutated AML
- Results of the global QuANTUM-R study will form the basis of regulatory submissions for quizartinib, the lead investigational agent in the AML Franchise of Daiichi Sankyo

**Tokyo, Munich, and Basking Ridge, NJ – (June 16, 2018)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that positive results from the pivotal QuANTUM-R phase 3 study of single agent quizartinib were presented today as a late-breaking oral presentation in the plenary program at the 23<sup>rd</sup> Congress of the European Hematology Association (EHA) in Stockholm, Sweden.

QuANTUM-R study results showed that patients with relapsed/refractory acute myeloid leukemia (AML) with *FLT3*-ITD mutations who received single agent quizartinib had a 24 percent reduction in the risk of death compared to patients who received salvage chemotherapy (hazard ratio [HR] = 0.76, P=0.0177, 95 percent CI 0.58-0.98). The median overall survival was 6.2 months (two-sided 95 percent CI 5.3-7.2) for patients treated with quizartinib and 4.7 months (two-sided 95 percent CI 4.0-5.5) for patients treated with salvage chemotherapy. The estimated survival probability at 1 year was 27 percent for patients who received quizartinib and 20 percent for patients who received salvage chemotherapy.

“*FLT3*-ITD mutated AML represents a high unmet need entity as patients with this aggressive form of the disease have an overall dismal prognosis as evidenced by low response rates to current available therapies, high risk of relapse and a shorter overall survival than those without this mutation,” said Jorge E. Cortes, MD, Deputy Chair of the Department of Leukemia in the Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center. “In relapsed/refractory AML with *FLT3*-ITD mutations, these findings represent the first reported clinical data demonstrating that a single agent can significantly improve overall survival, suggesting that quizartinib could potentially help these patients live longer. Additionally, in the study, a higher

proportion of patients received a stem cell transplant in the quizartinib arm compared to the chemotherapy arm.”

Secondary and key exploratory analyses including composite complete remission (CRc) are consistent and supportive of the primary analysis.

“Results of this study are consistent with previous phase 2 studies of quizartinib and demonstrate the value of targeting the *FLT3*-ITD driver mutation. We are encouraged by these data, which will form the basis of regulatory submissions to health authorities. If approved, quizartinib has the potential to redefine the treatment of patients with relapsed/refractory AML with *FLT3*-ITD mutations,” said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo. “These results also build on our understanding of this difficult-to-treat type of AML as we continue to explore the potential role of quizartinib in combination with chemotherapy and other novel mechanisms to further advance the treatment of patients with relapsed/refractory and newly-diagnosed AML with *FLT3*-ITD mutations.”

The safety profile observed in QuANTUM-R appears consistent with that observed at similar doses in the quizartinib clinical development program. The median treatment duration with quizartinib was 4 cycles of 28 days (97 days; range: 1-1,182 days) versus 1 cycle (range: 1-2) in the salvage chemotherapy arm. The median relative dose intensity for quizartinib was 89 percent. Incidence of treatment-emergent adverse events were comparable between patients who received single agent quizartinib (n=241) and those who received salvage chemotherapy (n=94). The most common adverse events (>30 percent, any Grade) in patients treated with quizartinib versus chemotherapy, respectively, included nausea (48 vs 42 percent), thrombocytopenia (39 vs 34 percent), fatigue (39 vs 29 percent), musculoskeletal pain (37 vs 28 percent), pyrexia (38 vs 45 percent), anemia (37 vs 32 percent), neutropenia (34 vs 26 percent), febrile neutropenia (34 vs 28 percent), vomiting (33 vs 21 percent) and hypokalemia (32 vs 28 percent). The most common adverse events Grade  $\geq 3$  (>10 percent of patients) were thrombocytopenia (35 vs 34 percent), anemia (30 vs 29 percent), neutropenia (32 vs 25 percent), febrile neutropenia (31 vs 21 percent), leukopenia (17 vs 16 percent), sepsis/septic shock (16 vs 18 percent), hypokalemia (12 vs 9 percent) and pneumonia (12 vs 9 percent). 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 (Torsade de Pointe, sudden death or cardiac arrest) in the quizartinib arm.

### **About the QuANTUM-R Study**

QuANTUM-R is a pivotal, global, phase 3, open-label randomized study that enrolled 367 patients with *FLT3*-ITD-mutated AML who were refractory to or in relapse following (with duration of remission of six months or less) standard first-line AML therapy with or without hematopoietic stem cell transplantation (HSCT). Patients were randomized in a 2:1 ratio to receive either single agent oral quizartinib (60 mg, with 30 mg lead-in) or salvage chemotherapy. The primary objective of the study was to determine whether single agent quizartinib prolonged overall survival compared to salvage chemotherapy.

### **About Quizartinib**

Quizartinib, the lead investigational agent in the AML Franchise of the Daiichi Sankyo Cancer Enterprise, is an oral selective FLT3 inhibitor currently in global phase 3 development for relapsed/refractory ([QuANTUM-R](#)) and newly-diagnosed ([QuANTUM-First](#)) AML with *FLT3*-ITD mutations, and phase 2 development for relapsed/refractory AML with *FLT3*-ITD mutations in Japan.

Quizartinib has been granted Fast Track designation by the U.S. Food and Drug Administration (FDA) for the treatment of relapsed/refractory AML. Quizartinib also has been granted Orphan Drug designation by the FDA and European Medicines Agency (EMA) for the treatment of AML. Quizartinib is an investigational agent that has not been approved for any indication in any country. Safety and efficacy have not been established.

### **About Acute Myeloid Leukemia with *FLT3*-ITD Mutations**

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> The five-year survival rate of AML reported from 2005 to 2011 was approximately 26 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>2</sup> The *FLT3*-ITD mutation is the most common *FLT3* mutation, affecting approximately one in four patients with AML.<sup>3,4,5,6</sup> Patients with *FLT3*-ITD-mutated 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 HSCT as compared to those without this mutation.<sup>7,8</sup>

### **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: DS-8201, 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 acute myeloid leukemia (AML) with *FLT3*-ITD mutations; 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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