Press Release

# Astellas' XOSPATA® (gilteritinib) Meets Overall Survival Endpoint in COMMODORE Trial of Patients with Relapsed or Refractory Acute Myeloid Leukemia with a FLT3 Mutation

*- Confirmatory Phase 3 trial in China, other countries stopped early due to positive results at planned interim analysis -*

**TOKYO, March 30, 2021** – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced that a Phase 3 confirmatory trial of XOSPATA® (gilteritinib) in patients with relapsed (disease that has returned) or refractory (resistant to treatment) FLT3 mutation-positive (FLT3mut+) acute myeloid leukemia (AML) met its primary endpoint of overall survival (OS) compared to chemotherapy at a planned interim analysis.

COMMODORE is an open-label, randomized study of gilteritinib versus salvage chemotherapy in adult patients who have relapsed or refractory AML in China and other countries. Astellas has stopped enrollment in the trial and patients in the chemotherapy arm will be offered the opportunity to receive gilteritinib.

Earlier this year, the China National Medical Products Administration (NMPA) granted conditional approval to gilteritinib for the treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation detected by a fully validated test. Approval was granted under an expedited pathway, following NMPA's acceptance of gilteritinib for priority review in July 2020[1] and its inclusion in the third batch of overseas new drugs urgently needed in clinical settings in November 2020.[2]

Astellas plans to submit results of COMMODORE to the NMPA in support of full approval. Detailed results will also be submitted to a peer-reviewed journal and/or scientific congress.

"In COMMODORE, patients receiving gilteritinib lived longer than those receiving salvage chemotherapy, confirming the overall survival benefit seen in the Phase 3 ADMIRAL trial," said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Global Therapeutic Area Head, Oncology Development. "For these patients, who have limited treatment options, the new findings provide additional evidence supporting gilteritinib as a treatment option."

AML is a cancer that impacts the blood and bone marrow,[3] and its incidence increases with age.[4] It is one of the most common types of leukemia in adults.[5] Every year, it is estimated that more than 85,000 people in China are diagnosed with leukemia.[6]

In previous clinical trials, the safety of gilteritinib was evaluated in 319 patients with relapsed or refractory AML who had received at least one dose of 120 mg gilteritinib daily.[7] The most frequent all-grade adverse reactions (frequency ≥ 10%) with

gilteritinib were alanine aminotransferase (ALT) increased (25.4%), aspartate aminotransferase (AST) increased (24.5%), anemia (20.1%), thrombocytopenia (13.5%), febrile neutropenia (12.5%), platelet count decreased (12.2%), diarrhea (12.2%), nausea (11.3%), blood alkaline phosphatase increased (11%), fatigue (10.3%), white blood cell count decreased (10%), and blood creatine phosphokinase increased (10%). One fatal adverse reaction of differentiation syndrome occurred in patients receiving gilteritinib. The most frequent (frequency ≥3%) serious adverse reactions were febrile neutropenia (7.5%), ALT increased (3.4%), and AST increased (3.1%). Other clinically significant serious adverse reactions included electrocardiogram QT prolonged (0.9%) and posterior reversible encephalopathy syndrome (0.3%).

**About the COMMODORE Trial**
The Phase 3 COMMODORE trial (NCT03182244) is an open-label, multicenter, randomized study of gilteritinib versus salvage chemotherapy in adult patients who have relapsed or refractory AML in China, as well as in other countries. The primary endpoint of the trial is OS. The study also evaluated safety and determined the overall efficacy in event-free survival (EFS) and complete remission (CR) rate of gilteritinib compared to salvage chemotherapy. Subjects were randomized in a 1:1 ratio to receive gilteritinib (120 mg) or salvage chemotherapy.[8]

**About the ADMIRAL Trial**
The Phase 3 ADMIRAL trial (NCT02421939) was an open-label, multicenter, randomized study of gilteritinib versus salvage chemotherapy in adult patients with FLT3mut+ who are refractory to or have relapsed after first-line AML therapy. The co-primary endpoints of the trial were OS and CR/CRh rates; OS was the primary endpoint at the trial's final analysis. The study enrolled 371 patients with relapsed or refractory AML and FLT3mut+ present in bone marrow or whole blood. Subjects were randomized in a 2:1 ratio to receive gilteritinib (120 mg) or salvage chemotherapy.[9]

**About Gilteritinib**
Gilteritinib was discovered through a research collaboration with Kotobuki Pharmaceutical Co., Ltd., and Astellas has exclusive global rights to develop, manufacture and commercialize gilteritinib. Gilteritinib is available as XOSPATA® in the U.S., Japan and selected European countries, among others, for the treatment of adult patients who have relapsed or refractory FLT3mut+ AML.[10] Gilteritinib is an FMS-like tyrosine kinase 3 (FLT3) inhibitor with demonstrated activity against FLT3-ITD, a common driver mutation that presents with a high burden and poor prognosis, and FLT3-TKD mutations.[11]

**About Astellas**
Astellas Pharma Inc. is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at https://www.astellas.com/en.

**Cautionary Notes**
In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties.

Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

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**References:**

[1] Center for Drug Evaluation, NMPA. List of priority review varieties. Available at: http://www.cde.org.cn/news.do?method=changePage&pageName=service&frameStr=21. Last accessed March 2021.

[2] Center for Drug Evaluation, NMPA. Notice on the release of the third batch of clinically urgently needed overseas new drugs. Available at: http://www.cde.org.cn/news.do?method=viewInfoCommon&id=5ed6430be031fc66. Last accessed March 2021.

[3] American Cancer Society. What is Acute Myeloid Leukemia (AML)? Available at https://www.cancer.org/cancer/acute-myeloid-leukemia/about/what-is-aml.html. Last accessed March 2021.

[4] American Cancer Society. Risk Factors for Acute Myeloid Leukemia (AML). Available at: www.cancer.org/cancer/acute-myeloid-leukemia/causes-risks-prevention/risk-factors.html. Last accessed March 2021.

[5] American Cancer Society. Key Statistics for Acute Myeloid Leukemia (AML). Available at https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html. Last accessed March 2021.

[6] GLOBOCAN Cancer Today Database, International Agency for Research on Cancer, World Health Organisation. Population Fact Sheets in 2020. Available at: http://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf. Last accessed March 2021.

[7] Perl A, et al. Gilteritinib or Chemotherapy for Relapsed or Refractory FLT3-mutated AML. N Engl J Med 2019; 381:1728-40.

[8] ClinicalTrials.gov. A Study of ASP2215 Versus Salvage Chemotherapy in Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML) With FLT3 Mutation. Available at: https://clinicaltrials.gov/ct2/show/NCT03182244. Last accessed March 2021.

[9] ClinicalTrials.gov. A Study of ASP2215 Versus Salvage Chemotherapy in Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML) With FMS-like Tyrosine Kinase (FLT3) Mutation. Available at: https://clinicaltrials.gov/ct2/show/NCT02421939. Last accessed March 2021.

[10] Data on file. Northbrook, IL. Astellas Pharma Inc.

[11] Daver N, Schlenk RF, Russel NH, Levis MJ. (2019). Targeting FLT3 mutations in AML: review of current knowledge and evidence. Leukemia 33: 299-312.