Press Release

Astellas' XOSPATA® (gilteritinib) Receives Conditional Approval by China's National Medical Products Administration for Relapsed or Refractory Acute Myeloid Leukemia with a FLT3 Mutation

- *Accelerated approval follows priority review designation and inclusion in overseas new drugs urgently needed in clinical settings*

- *XOSPATA® is the first and only FLT3 inhibitor approved by the NMPA for patients with relapsed or refractory AML*

TOKYO, February 4, 2021 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced that the China National Medical Products Administration (NMPA) has granted conditional approval to XOSPATA® (gilteritinib) for the treatment of adult patients who have relapsed (disease that has returned) or refractory (resistant to treatment) acute myeloid leukemia (AML) with a FLT3 mutation (FLT3mut+) detected by a fully validated test. Gilteritinib has been approved 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]

"Patients with relapsed or refractory AML with a FLT3 mutation are in urgent need of new treatment options," said Professor Ma Ju, Director of the Harbin Institute of Hematology, China. "As the first approved targeted therapy agent to treat relapsed or refractory AML with a FLT3 mutation in China, gilteritinib, which was approved under an expedited pathway, has enabled patients in China to have rapid access to a novel treatment option."

Gilteritinib has shown itself to be effective against two types of FLT3 mutation – FLT3 internal tandem duplication (FLT3-ITD) and FLT3 tyrosine kinase domain (FLT3-TKD). Impacting approximately 30% of AML patients,[3] the FLT3-ITD mutation is associated with higher risk of relapse and shorter overall survival compared to wild-type FLT3.[4,5] FLT3-TKD mutations impact approximately 7% of AML patients.[3] The status of FLT3 mutation can change over the course of AML treatment, including after relapse. Confirming patients' FLT3 mutation status at the time of relapse can help inform an appropriate and potentially targeted treatment approach.[6]

"Having a FLT3 mutation has a highly negative impact on prognosis for people living with AML," said Professor Wang Jianxiang, Vice Director of Institute of Hematology, Chinese Academy of Medical Sciences. "The approval of gilteritinib provides an important new option for Chinese patients that have relapsed or refractory AML with a FLT3 mutation, backed by substantial safety and efficacy data."

AML is a cancer that impacts the blood and bone marrow,[7] and its incidence increases with age.[8] It is one of the most common types of leukemia in adults.[9] Every

year, it is estimated that around 80,000 people in China are diagnosed with leukemia.[10]

“There is an urgent unmet need among FLT3-mutated relapsed or refractory AML patients, whose median survival is currently less than six months with chemotherapy,” said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Global Therapeutic Area Head, Oncology Development. “The expedited approval of gilteritinib is an important step in offering a new treatment option for doctors and patients in China. We look forward to offering gilteritinib as part of our commitment to developing innovative solutions for patients with hard-to-treat cancers with limited treatment options.”

The approval was based on results from the Phase 3 ADMIRAL trial, published in the *New England Journal of Medicine*. Patients treated with gilteritinib had significantly longer overall survival (OS) than those who received salvage chemotherapy. Median OS for patients who received gilteritinib was 9.3 months, compared to 5.6 months for patients who received salvage chemotherapy (Hazard Ratio = 0.64 (95% CI 0.49, 0.83), P=0.0004).[11] Additional Chinese patient pharmacokinetics data from the ongoing Phase 3 COMMODORE trial were also reviewed.

The safety of gilteritinib was evaluated in 319 patients with relapsed or refractory AML who have received at least one dose of 120 mg gilteritinib daily.[11] 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%).

Astellas has already reflected the impact from this approval in its financial forecast of the current fiscal year ending March 31, 2021.

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.[12]

About the COMMODORE Trial
The Phase 3 COMMODORE trial (NCT03182244) is an open-label, multicenter, randomized ongoing 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 will also evaluate safety as well as determine the overall efficacy in event-free survival (EFS) and complete remission (CR) rate of gilteritinib compared to salvage chemotherapy. Subjects are being randomized in a 1:1 ratio to receive gilteritinib (120 mg) or salvage chemotherapy.[13]

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.[14] 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.[15]

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 December 2020.

[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 December 2020.

[3] Patel JP, Gönen M, Figueroa ME, et al. Prognostic relevance of integrated genetic profiling in acute myeloid leukemia. N Engl J Med. 2012;366(12):1079-89.

[4] Whitman SP, Archer KJ, Feng L, et al. Absence of the wild-type allele predicts poor prognosis in adult de novo acute myeloid leukemia with normal cytogenetics and the internal tandem duplication of FLT3: a Cancer and Leukemia Group B study. Cancer Res. 2001;61(19):7233-7239.

[5] Whitman SP, Maharry K, Radmacher MD, et al. FLT3 internal tandem duplication associates with adverse outcome and gene- and microRNA-expression signatures in patients 60 years of age or older with primary cytogenetically normal acute myeloid leukemia: a Cancer and Leukemia Group B study. Blood. 2010;116(18):3622-3626.

[6] Warren M, et al. Clinical impact of change of FLT3 mutation status in acute myeloid leukemia patients. Mod Pathol. 2012;25(10):1405-12.

[7] 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 December 2020.

[8] 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 December 2020.

[9] 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 December 2020.

[10] GLOBOCAN Cancer Today Database, International Agency for Research on Cancer, World Health Organisation. Population Fact Sheets in 2018. Available at: http://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf. Last accessed December 2020.

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

[12] 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 December 2020.

[13] 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 December 2020.

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

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