Press release

European Commission Approves Astellas' XOSPATA™ (gilteritinib) as a Monotherapy for Patients with Relapsed or Refractory Acute Myeloid Leukemia with a FLT3 Mutation

Approval follows accelerated assessment, orphan designation by European Medicines Agency

TOKYO, Oct. 25, 2019 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") announced today that the European Commission (EC) has approved the oral once-daily therapy XOSPATA™ (gilteritinib) as a monotherapy for the treatment of adult patients with relapsed or refractory (resistant to treatment) acute myeloid leukemia (AML) with a FLT3 mutation (FLT3mut+). Gilteritinib has the potential to improve treatment outcomes for AML patients with two forms of the most common mutation—FLT3 internal tandem duplication (ITD) and FLT3 tyrosine kinase domain (TKD) mutation.[1,2]

This approval is based on results from the Phase 3 ADMIRAL trial, which investigated gilteritinib versus salvage chemotherapy in patients with relapsed or refractory FLT3mut+ AML. 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). Rates of one-year survival were 37% for patients who received gilteritinib, compared to 17% for patients who received salvage chemotherapy.[3,4]

"AML is a rare cancer and patients with a FLT3 mutation have a particularly poor prognosis, with a median survival of less than six months following treatment with salvage chemotherapy," said Giovanni Martinelli, M.D., Institute of Hematology, S.Orsola-Malpighi University Hospital, Bologna, Italy, an investigator in the ADMIRAL trial. "Gilteritinib is a new and clinically meaningful treatment option that provides a welcome advance for patients and health care professionals across the European Union."

The EC marketing authorization for gilteritinib in relapsed or refractory FLT3mut+ AML is applicable to the European Union (EU) member countries, and is also valid in Iceland, Norway and Liechtenstein. Gilteritinib has been designated an orphan medicinal product and also received accelerated assessment from the European Medicines Agency earlier this year, which reduced the timeframe for approval.[5,6,7]

"Today's approval marks a significant advance for patients living with relapsed or refractory, FLT3 mutation-positive acute myeloid leukemia," said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Global Therapeutic Area Head, Oncology Development, Astellas. "We look forward to working with health authorities across the EU to bring gilteritinib to patients who need it the most, as soon as possible."

Patients' FLT3mut+ status can change over the course of AML treatment, even after relapse. Due to the poor outcomes associated with FLT3mut+ AML, patients' FLT3 mutation status may be confirmed to help inform the best treatment approach.[8,9,10]

Astellas reflected the impact from this approval in its financial forecast of the current fiscal year ending March 31, 2020.

About XOSPATA™ (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 was approved in the U.S. and Japan in 2018 for the treatment of adult patients who have relapsed or refractory FLT3mut+ AML.[11,12]

Astellas is currently investigating gilteritinib in various FLT3 mutation-positive AML patient populations through several clinical trials. Visit http://www.clinicaltrials.gov to learn more about ongoing gilteritinib clinical trials.

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, the primary endpoint at the trial's final analysis, was the basis of EC approval. 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.[13]

The most common adverse events (AEs) across both treatment arms of the ADMIRAL trial were febrile neutropenia (43.7%), anemia (43.4%), and pyrexia (38.6%). Common grade ≥3 AEs related to gilteritinib were anemia (19.5%), febrile neutropenia (15.4%), thrombocytopenia (12.2%), and decreased platelet count (12.2%). Adjusted for exposure duration, serious treatment-emergent AEs per patient year were less common with gilteritinib (7.1%) than salvage chemotherapy (9.2%).[3]

About Astellas
Astellas Pharma Inc., based in Tokyo, Japan, is a company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. 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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