Press Release

Phase 3 ADMIRAL Trial Data Show XOSPATA® (gilteritinib) Significantly Prolongs Overall Survival in Adult Patients with FLT3 Mutation-Positive Relapsed/Refractory Acute Myeloid Leukemia Compared with Salvage Chemotherapy

- Study results will be presented at American Association for Cancer Research Annual Meeting 2019 -

TOKYO – April 1, 2019 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D. "Astellas") today announced results from the Phase 3 ADMIRAL clinical trial comparing XOSPATA® (gilteritinib) to salvage chemotherapy in adult patients with relapsed or refractory (resistant to treatment) Acute Myeloid Leukemia (AML) with a FLT3 mutation. The results show that patients treated with XOSPATA had significantly longer Overall Survival (OS) than those who received standard salvage chemotherapy. The data were shared today by Alexander Perl, M.D., Abramson Cancer Center, University of Pennsylvania, in a press conference at the American Association for Cancer Research (AACR) Annual Meeting. The data will also be presented during the AACR Clinical Trials Plenary Session (#CT184), which takes place April 2, 2019, 10:30 a.m. – 12:45 p.m. at the Georgia World Congress Center, Marcus Auditorium, Bldg A-GWCC.

Results from the ADMIRAL trial show the median OS for patients who received XOSPATA was 9.3 months compared to 5.6 months for patients who received salvage chemotherapy (Hazard Ratio = 0.637 (95% CI 0.490, 0.830), P=0.0007); one-year survival rates were 37% for patients who received XOSPATA compared to 17% for patients who received salvage chemotherapy.

The most common treatment-emergent adverse events (TEAEs) of any grade occurring in ≥10% of patients during the first 30 days of treatment with gilteritinib were anemia (33%), increased alanine aminotransferase (24%), increased aspartate aminotransferase (24%), febrile neutropenia (21%), thrombocytopenia (19%), constipation (17%), pyrexia (15%), fatigue (15%), decreased neutrophil count (14%), increased blood alkaline phosphatase (13%), nausea (13%), hypokalemia (11%), cough (11%), headache (10%), and diarrhea (10%). The most common TEAEs of any grade occurring in ≥10% of patients during the first 30 days of treatment with salvage chemotherapy were anemia (33%), febrile neutropenia (32%), nausea (30%), diarrhea (28%), hypokalemia (27%), pyrexia (26%), decreased appetite (17%), decreased white blood cell count (17%), thrombocytopenia (16%), constipation (14%), abdominal pain (14%), hyperglycemia (13%), headache (13%), stomatitis (13%), fatigue (11%), decreased neutrophil count (11%), increased aspartate aminotransferase (10%), vomiting (10%), peripheral edema (10%), and hypomagnesemia (10%).

“We are very encouraged by the findings of the ADMIRAL trial,” said Alexander Perl, M.D., an associate professor of Hematology-Oncology in Penn’s Perelman School of Medicine. “Patients with relapsed/refractory FLT3 mutation-positive AML generally have a poor prognosis and short survival. Until just recently, they had few treatment options. These findings change the treatment paradigm for this patient population.”

XOSPATA was approved by the U.S. Food and Drug Administration (FDA) in November 2018 for the treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation as detected by an FDA-approved test.[1]

XOSPATA was discovered through a research collaboration with Kotobuki Pharmaceutical Co., Ltd., and Astellas has exclusive global rights to develop, manufacture and commercialize XOSPATA.

XOSPATA was approved by the Japan Ministry of Health, Labor and Welfare (MHLW) for relapsed or refractory AML with FLT3 mutations and launched as XOSPATA® 40 mg Tablets in 2018.[2] In February 2019, a marketing authorization application (MAA) for the oral once-daily therapy XOSPATA for the treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation was accepted by the European Medicines Agency for regulatory review.[3]

Astellas is currently investigating gilteritinib in various FLT3 mutation-positive AML patient populations through several Phase 3 trials. Visit http://www.clinicaltrials.gov to learn more about ongoing gilteritinib clinical trials.

About the ADMIRAL Trial[4]
The Phase 3 ADMIRAL trial (NCT02421939) was an open-label, multicenter, randomized study of gilteritinib versus salvage chemotherapy in adult patients with FLT3 mutations who are refractory to or have relapsed after first-line AML therapy. The primary endpoint of the trial was Overall Survival (OS). The study enrolled 371 patients with relapsed or refractory AML and positive for FLT3 mutations present in bone marrow or whole blood. Subjects were randomized in a 2:1 ratio to receive gilteritinib (120 mg)[5] or salvage chemotherapy.

About XOSPATA® (gilteritinib)
XOSPATA is indicated for the treatment of adult patients who have relapsed or refractory Acute Myeloid Leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test.[1]

Important Safety Information

Contraindications
XOSPATA is contraindicated in patients with hypersensitivity to gilteritinib or any of the excipients. Anaphylactic reactions have been observed in clinical trials.

Warnings and Precautions
Posterior Reversible Encephalopathy Syndrome (PRES) There have been rare reports of PRES with symptoms including seizure and altered mental status with XOSPATA. Symptoms have resolved after discontinuation of XOSPATA. A diagnosis

of PRES requires confirmation by brain imaging, preferably MRI. Discontinue XOSPATA in patients who develop PRES.

Prolonged QT Interval XOSPATA has been associated with prolonged cardiac ventricular repolarization (QT interval). Of the 292 patients treated with XOSPATA in the clinical trial, 1.4% were found to have a QTc interval greater than 500 msec and 7% of patients had an increase from baseline QTc greater than 60 msec. Perform electrocardiogram (ECG) prior to initiation of treatment with XOSPATA, on days 8 and 15 of cycle 1, and prior to the start of the next two subsequent cycles. Interrupt and reduce XOSPATA dosage in patients who have a QTcF >500 msec. Hypokalemia or hypomagnesemia may increase the QT prolongation risk. Correct hypokalemia or hypomagnesemia prior to and during XOSPATA administration.

Pancreatitis There have been rare reports of pancreatitis in patients receiving XOSPATA in clinical studies. Evaluate patients who develop signs and symptoms of pancreatitis. Interrupt and reduce the dose of XOSPATA in patients who develop pancreatitis.

Embryo-Fetal Toxicity Based on findings in animals and its mechanism of action, XOSPATA can cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with XOSPATA and for at least 6 months after the last dose of XOSPATA. Advise males with female partners of reproductive potential to use effective contraception during treatment with XOSPATA and for at least 4 months after the last dose of XOSPATA. Pregnant women, patients becoming pregnant while receiving XOSPATA or male patients with pregnant female partners should be apprised of the potential risk to the fetus.

Adverse Reactions
The most frequent non-hematological serious adverse reactions (≥5%) reported in patients were pneumonia (19%), sepsis (13%), fever (13%), dyspnea (7%) and renal impairment (5%).

Overall, 22 of 292 patients (8%) discontinued XOSPATA treatment permanently due to an adverse reaction. The most common adverse reactions (>1%) leading to discontinuation were pneumonia (2%), sepsis (2%) and dyspnea (1%). The most common adverse reactions (≥20%) were myalgia/arthralgia (42%), transaminase increased (41%), fatigue/malaise (40%), fever (35%), non-infectious diarrhea (34%), dyspnea (34%), edema (34%), rash (30%), pneumonia (30%), nausea (27%), stomatitis (26%), cough (25%), headache (21%), hypotension (21%), dizziness (20%) and vomiting (20%).

Other clinically significant adverse reactions occurring in ≤10% of patients included: electrocardiogram QT prolonged (7%), cardiac failure (grouped terms) (4%), pericardial effusion (3%), pericarditis (2%), differentiation syndrome (1%), anaphylactic reaction (1%) and posterior reversible encephalopathy syndrome (1%).

Lab Abnormalities: The most common lab abnormalities (>20%) that were Grade ≥3 that occurred ≥10% were: hypophosphatemia (12%), alanine aminotransferase increased (12%), hyponatremia (12%), aspartate aminotransferase increased (10%).

Drug Interactions

Combined P-gp and Strong CYP3A Inducers: Concomitant use of XOSPATA with a combined P-gp and strong CYP3A inducer decreases XOSPATA exposure which may decrease XOSPATA efficacy. Avoid concomitant use of XOSPATA with combined P-gp and strong CYP3A inducers.

Strong CYP3A inhibitors: Concomitant use of XOSPATA with a strong CYP3A inhibitor increases XOSPATA exposure. Consider alternative therapies that are not strong CYP3A inhibitors. If the concomitant use of these inhibitors is considered essential for the care of the patient, monitor patient more frequently for XOSPATA adverse reactions. Interrupt and reduce XOSPATA dosage in patients with serious or life-threatening toxicity.

Drugs that Target 5HT2B Receptor or Sigma Nonspecific Receptor: Concomitant use of XOSPATA may reduce the effects of drugs that target the 5HT2B receptor or the sigma nonspecific receptor (e.g., escitalopram, fluoxetine, sertraline). Avoid concomitant use of these drugs with XOSPATA unless their use is considered essential for the care of the patient.

Specific Populations

Lactation: Advise women not to breastfeed during treatment with XOSPATA and for 2 months after the last dose.

Please see Full Prescribing Information for additional safety information.

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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[1] XOSPATA [package insert]. Northbrook, IL: Astellas Pharma US, Inc.
[2] Astellas Pharma Inc. Astellas Announces Approval in Japan for XOSPATA® 40 mg Tablets for the Treatment of FLT3mut+ Relapsed or Refractory AML (09-21-2018). https://www.astellas.com/en/news/14271. Accessed 03-14-2019.
[3] Astellas Pharma Inc. Astellas Announces Acceptance of XOSPATA™ (gilteritinib) for Regulatory Review by the European Medicines Agency (02-28-2019). https://www.astellas.com/us/news/14631. Accessed 03-14-2019.
[4] ClinicalTrials.gov. A study of ASP2215 versus salvage chemotherapy in patients with relapsed refractory acute myeloid leukemia (AML) with FMS-like tyrosine kinase (FLT3) mutation (02-01-2019). https://clinicaltrials.gov/ct2/show/NCT02421939. Accessed 02-05-2019.
[5] Gorcea CM, Burthem J, Tholouli E. ASP2215 in the treatment of relapsed/refractory acute myeloid leukemia with FLT3 mutation: background and design of the ADMIRAL trial. Future Oncol (Epub) 03-02-2018.