

## Press Release

### **Astellas Launches XOSPATA<sup>®</sup> (gilteritinib) in the U.S. for the Treatment of Adult Patients with Relapsed/Refractory Acute Myeloid Leukemia (AML) with a FLT3 Mutation**

**TOKYO – December 11, 2018** – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D. “Astellas”) today announced that XOSPATA<sup>®</sup> (generic name: gilteritinib) is now available for prescription in the United States for the treatment of adult patients who have relapsed or refractory (resistant to treatment) Acute Myeloid Leukemia (AML) with a FLT3 mutation as detected by an FDA-approved test.<sup>1</sup> An oral monotherapy, XOSPATA is the first and only FLT3-targeting agent approved by the FDA for the treatment of relapsed or refractory FLT3 mutation-positive (FLT3mut+) AML.

XOSPATA was approved by the U.S. Food and Drug Administration (FDA) on November 28, 2018. Health professionals, patients and their caregivers can learn more about XOSPATA and support services provided through Astellas at <https://www.xospata.com/>.

“Astellas aims to pursue cutting-edge science that provides value to patients,” said Mark Reisenauer, senior vice president, oncology business unit, Astellas. “XOSPATA is an excellent example of how we are continuing to advance on this promise to patients.”

Astellas is providing a full range of patient support services for XOSPATA in the U.S. XOSPATA Support Solutions<sup>SM</sup> offers access and reimbursement support to help patients access XOSPATA as prescribed by their healthcare providers. XOSPATA Support Solutions<sup>SM</sup> also provides information regarding patient healthcare coverage options and financial assistance programs that may be available to help eligible patients with financial needs. Patients, caregivers and healthcare providers can visit [www.xospatasupportsolutions.com](http://www.xospatasupportsolutions.com) or call 844-632-9272 to learn more.

Astellas reflected the impact from this launch in its financial forecasts of the current fiscal year ending March 31, 2019.

#### **About Acute Myeloid Leukemia**

Acute Myeloid Leukemia (AML) is a cancer that impacts the blood and bone marrow,<sup>2</sup> and its incidence increases with age.<sup>3</sup> The American Cancer Society estimates that in 2018, approximately 19,000 people will be diagnosed with AML in the U.S.<sup>3</sup>

#### **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.<sup>1</sup> XOSPATA is also approved by the

Japan Ministry of Health, Labor and Welfare (MHLW) for relapsed or refractory AML with FLT3 mutations. It is launched as XOSPATA® 40 mg Tablets in Japan.

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

Astellas is currently investigating gilteritinib in various FLT3 mutation-positive AML patient populations through several Phase 3 trials. Visit [AstellasAMLTrials.com](http://AstellasAMLTrials.com) to learn more about ongoing gilteritinib clinical trials.

## **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 ( $\geq 20\%$ ) 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  $\leq 10\%$  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  $\geq 3$  that occurred  $\geq 10\%$  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.

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<sup>1</sup> XOSPATA [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

<sup>2</sup> American Cancer Society. What is acute myeloid leukemia? (02-22-2016).  
<https://www.cancer.org/cancer/acute-myeloid-leukemia/about/what-is-aml.html>. Accessed 05-10-2018.

<sup>3</sup> American Cancer Society. Key statistics for acute myeloid leukemia (01-04-2018).  
<https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html>. Accessed 03-12-2018.