Press Release

Gilteritinib as Maintenance Therapy Demonstrated Benefit in Subgroups of FLT3-ITD Acute Myeloid Leukemia Patients

Data from Phase 3 MORPHO trial selected for press briefing and to be presented as oral session during the 2023 European Hematology Association (EHA) Hybrid Congress

Exploratory results demonstrated improvement of relapse-free survival (RFS) in a subgroup of patients with measurable residual disease (MRD)

TOKYO and ROCKVILLE, Md., June 9, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") and the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) today presented data from the Phase 3 MORPHO clinical trial which demonstrated favorable results in subgroups of FMS-like tyrosine kinase 3 (FLT3)-internal tandem duplication (ITD) mutated acute myeloid leukemia (AML) patients, including a subgroup of patients with detectable measurable residual disease (MRD). The data were shared during the 2023 European Hematology Association (EHA) Hybrid Congress Press Briefing, taking place in Frankfurt, Germany, and will also be presented as an oral session on June 11.

These data from the Phase 3 MORPHO trial, which evaluated gilteritinib as a maintenance therapy following allogeneic hematopoietic stem cell transplantation (HSCT) for patients with FLT3-ITD AML, did not demonstrate statistically significant improvement of relapse-free survival (RFS) in the entire cohort (Hazard Ratio [HR] for gilteritinib versus placebo 0.68; P=0.0518). However, there was clinical improvement of RFS in a subgroup of patients with detectable MRD (gilteritinib [72.4%] vs placebo [57.4%] at 2 years with HR: 0.515; 95% Confidence Interval [CI], 0.316-0.838; nominal P=0.0065) compared to patients without detectable MRD (HR: 1.213; 95% CI, 0.616-2.387; nominal P=0.575). In exploratory analysis, gilteritinib showed favorable RFS for the approximate 50% of patients with detectable MRD pre- or post-HSCT, compared to those without detectable MRD. In addition, RFS in the North American sub-population showed a HR of 0.397 (P=0.0022) for gilteritinib versus placebo. Further analysis is being conducted to understand regional results across the study population.

"While we are continuing to conduct a thorough assessment of the full data set from our Phase 3 MORPHO trial, we are encouraged by these data which explore the potential of gilteritinib in a maintenance setting," said Ahsan Arozullah, M.D., M.P.H., Senior Vice President and Head of Oncology Development, Astellas. "AML patients with a FLT3-ITD mutation often face worse outcomes than those with other mutations and have restricted post-HSCT treatment options with unmet need. With these findings, we remain focused on sharing updates with the scientific community to inform continued innovation for the AML community."

"As the AML treatment landscape continues to evolve, the exploration of prognostic indicators like MRD, which may be used to guide the management of AML, is vital to

advance science and patient care," said Mary M. Horowitz, M.D., Principal Investigator of the BMT CTN Data and Coordinating Center. "We look forward to continuing our collaboration with Astellas to explore innovative approaches for those impacted by AML."

The Phase 3 MORPHO trial is a randomized, double-blind, placebo-controlled, multi-center trial that compares gilteritinib to placebo as maintenance therapy over a period of two years following HSCT in 356 patients with FLT3-ITD mutated AML and in remission after induction therapy. The study did not meet its pre-defined primary endpoint of RFS and key secondary endpoint of overall survival or patients treated with gilteritinib compared to placebo. The most frequent treatment-emergent adverse events (TEAEs) were decrease in neutrophil count, diarrhea and nausea, which were generally consistent with previous studies of gilteritinib. In FLT3-ITD AML patients, TEAEs associated with gilteritinib compared to placebo were neutrophil decrease (42.1% versus 15.8%) and increased incidence of chronic graft-versus-host disease (GVHD) (52.2% versus 42.1%). Additional data and sub-analyses will be submitted for publication and for consideration at upcoming medical meetings.

Gilteritinib is a FLT3 inhibitor with demonstrated activity against FLT3-ITD, a common driver mutation that presents with a high disease burden and poor prognosis, and FLT3-tyrosine kinase domain (TKD) mutations. Gilteritinib is available as XOSPATA® in the U.S., Japan, China and selected European countries for the treatment of adult patients who have relapsed or refractory FLT3+ AML.

About Gilteritinib
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 disease burden and poor prognosis, and FLT3-TKD mutations.[1] It was discovered through a research collaboration with Kotobuki Pharmaceutical Co., Ltd., and Astellas has exclusive global development, commercialization and manufacturing rights to gilteritinib.[2]

XOSPATA (gilteritinib) U.S. Indication & Important Safety Information

Indication

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.

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.

WARNING: DIFFERENTIATION SYNDROME
Patients treated with XOSPATA have experienced symptoms of differentiation syndrome, which can be fatal or life-threatening if not treated. Symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, or renal dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

Warnings and Precautions

Differentiation Syndrome (See BOXED WARNING) 3% of 319 patients treated with XOSPATA in the clinical trials experienced differentiation syndrome. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells and may be life-threatening or fatal if not treated. Symptoms and other clinical findings of differentiation syndrome in patients treated with XOSPATA included fever, dyspnea, pleural effusion, pericardial effusion, pulmonary edema, hypotension, rapid weight gain, peripheral edema, rash, and renal dysfunction. Some cases had concomitant acute febrile neutrophilic dermatosis. Differentiation syndrome occurred as early as 1 day and up to 82 days after XOSPATA initiation and has been observed with or without concomitant leukocytosis. If differentiation syndrome is suspected, initiate dexamethasone 10 mg IV every 12 hours (or an equivalent dose of an alternative oral or IV corticosteroid) and hemodynamic monitoring until improvement. Taper corticosteroids after resolution of symptoms and administer corticosteroids for a minimum of 3 days. Symptoms of differentiation syndrome may recur with premature discontinuation of corticosteroid

treatment. If severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids, interrupt XOSPATA until signs and symptoms are no longer severe.

Posterior Reversible Encephalopathy Syndrome (PRES) 1% of 319 patients treated with XOSPATA in the clinical trials experienced posterior reversible encephalopathy syndrome (PRES) with symptoms including seizure and altered mental status. Symptoms have resolved after discontinuation of XOSPATA. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). Discontinue XOSPATA in patients who develop PRES.

Prolonged QT Interval XOSPATA has been associated with prolonged cardiac ventricular repolarization (QT interval). 1% of the 317 patients with a post-baseline QTc measurement on treatment with XOSPATA in the clinical trial 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 4% of 319 patients treated with XOSPATA in the clinical trials experienced pancreatitis. Evaluate patients who develop signs and symptoms of pancreatitis. Interrupt and reduce the dose of XOSPATA in patients who develop pancreatitis.

Embryo-Fetal Toxicity 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 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 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
Fatal adverse reactions occurred in 2% of patients receiving XOSPATA. These were cardiac arrest (1%) and one case each of differentiation syndrome and pancreatitis. The most frequent (≥5%) nonhematological serious adverse reactions reported in patients were fever (13%), dyspnea (9%), renal impairment (8%), transaminase increased (6%) and noninfectious diarrhea (5%).

7% discontinued XOSPATA treatment permanently due to an adverse reaction. The most common (>1%) adverse reactions leading to discontinuation were aspartate aminotransferase increased (2%) and alanine aminotransferase increased (2%).

The most frequent (≥5%) grade ≥3 nonhematological adverse reactions reported in patients were transaminase increased (21%), dyspnea (12%), hypotension (7%), mucositis (7%), myalgia/arthralgia (7%), and fatigue/malaise (6%).

Other clinically significant adverse reactions occurring in ≤10% of patients included: electrocardiogram QT prolonged (9%), hypersensitivity (8%), pancreatitis (5%), cardiac failure (4%), pericardial effusion (4%), acute febrile neutrophilic dermatosis (3%), differentiation syndrome (3%), pericarditis/myocarditis (2%), large intestine perforation (1%), and posterior reversible encephalopathy syndrome (1%).

Lab Abnormalities Shifts to grades 3-4 nonhematologic laboratory abnormalities in XOSPATA treated patients included phosphate decreased (14%), alanine aminotransferase increased (13%), sodium decreased (12%), aspartate aminotransferase increased (10%), calcium decreased (6%), creatine kinase increased (6%), triglycerides increased (6%), creatinine increased (3%), and alkaline phosphatase increased (2%).

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.

P-gp, BCRP, and OCT1 Substrates Based on in vitro data, gilteritinib is a P-gp, breast cancer resistant protein (BCRP), and organic cation transporter 1 (OCT1) inhibitor. Coadministration of gilteritinib may increase the exposure of P-gp, BCRP, and OCT1 substrates, which may increase the incidence and severity of adverse reactions of these substrates. For P-gp, BCRP, or OCT1 substrates where small concentration changes may lead to serious adverse reactions, decrease the dose or modify the dosing frequency of such substrate and monitor for adverse reactions as recommended in the respective prescribing information.

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, including BOXED WARNING for additional safety information.

About MORPHO Phase 3 Clinical Trial
The Phase 3 MORPHO Study is a two-arm, randomized, double-blind, placebo-controlled, multi-center trial in 356 patients with a diagnosis of AML harboring a FLT3/ITD mutation. Participants must be in first complete remission prior to transplant, as defined by less than five percent blasts in the bone marrow (BM) with no morphologic characteristics of acute leukemia in the BM with no evidence of extra-medullary leukemia. After undergoing transplantation, participants will be randomized to receive gilteritinib (120 mg) or placebo beginning after the time of engraftment for a two-year period. Participants will be stratified according to: 1) conditioning regimen intensity (myeloablative vs. reduced intensity/non-myeloablative), 2) time from first day of hematopoietic cell infusion to randomization (30-60 days vs. 61-90 days) and 3) presence vs. absence of or unknown minimal residual disease from the most recent pre-registration BM aspirate. The primary endpoint of the trial is RFS. The study is being conducted in countries across North America, Europe and the Asia-Pacific region, including Japan. For more information about this trial, please visit www.clinicaltrials.gov under trial identifier NCT02997202.

About Acute Myeloid Leukemia (AML)
Acute myeloid leukemia (AML) is an aggressive cancer that affects the bone marrow and blood, and its incidence increases with age.[3,4] Of patients newly diagnosed with AML and tested for FLT3 mutations, approximately one-third have an alteration to the FLT3 gene. FLT3-ITD mutations have been associated with worsened disease-free survival and overall survival, and a higher risk of getting the disease more than once. FLT3 mutation status can change over the course of AML treatment, even after relapse.[5-8]

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.

About the Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
The Blood and Marrow Transplant Clinical Trials Network (BMT CTN) conducts rigorous multi-institutional clinical trials of high scientific merit, focused on improving survival for patients undergoing hematopoietic cell transplantation and/or receiving cellular therapies. The BMT CTN has completed accrual to 52 Phase II and III trials at more than 100 transplant centers and enrolled over 16,600 study participants. BMT CTN is funded by the National Heart, Lung, and Blood Institute and the National Cancer Institute, both parts of the National Institutes of Health (NIH), and is a collaborative effort of 20 Core Transplant Centers/Consortia, The Center for International Blood and Marrow Transplant Research (CIBMTR), the National Marrow Donor Program (NMDP)/Be The Match and the Emmes Company, LLC, a clinical research organization. CIBMTR is a research collaboration between the NMDP/Be The Match and the Medical College of Wisconsin. Together with MCW/CIBMTR and NMDP, Emmes has been providing research support to the BMT CTN since 2001, as a key member of the data coordinating center. More information about the BMT CTN can be found at www.bmtctn.net

About National Marrow Donor Program® (NMDP)/Be The Match®
The National Marrow Donor Program® (NMDP)/Be The Match® is the leading global partner working to save lives through cellular therapy. With 35 years of experience managing the most diverse registry of potential unrelated blood stem cell donors and cord blood units in the world, NMDP/Be The Match is a proven partner in providing cures to patients with life-threatening blood and marrow cancers and diseases. Through their global network, they connect centers and patients to their best cell therapy option—from blood stem cell transplant to a next-generation therapy—and collaborate with cell and gene therapy companies to support therapy development and delivery through Be The Match BioTherapies®. NMDP/Be The Match is a tireless advocate for the cell therapy community, working with hematologists/oncologists to remove barriers to consultation and treatment, and supporting patients through no-cost programs to eliminate non-medical obstacles to cell therapy. In addition, they are a global leader in research through the CIBMTR® (Center for International Blood and Marrow Transplant

Research®)—a collaboration with Medical College of Wisconsin, investing in and managing research studies that improve patient outcomes and advance the future of care.

About the Medical College of Wisconsin
With a history dating back to 1893, The Medical College of Wisconsin is dedicated to leadership and excellence in education, patient care, research, and community engagement. More than 1,500 students are enrolled in MCW's medical school and graduate school programs in Milwaukee, Green Bay, and Central Wisconsin. MCW's School of Pharmacy opened in 2017. A major national research center, MCW is the largest research institution in the Milwaukee metro area and second largest in Wisconsin. In the last 10 years, faculty received more than $1.5 billion in external support for research, teaching, training, and related purposes. This total includes highly competitive research and training awards from the National Institutes of Health (NIH). Annually, MCW faculty direct or collaborate on more than 3,100 research studies, including clinical trials. Additionally, more than 1,650 physicians provide care in virtually every specialty of medicine for more than 2.8 million patients annually.

About Emmes
Founded more than 45 years ago, Emmes is a global, full-service Clinical Research Organization dedicated to excellence in supporting the advancement of public health and biopharmaceutical innovation. The company's clients include numerous agencies and institutes of the U.S. federal government and a wide range of biotechnology, pharmaceutical and medical device companies throughout the world. To learn more about how our research is making a positive impact on human health, go to the Emmes website at www.emmes.com.

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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