Press Release

Astellas and BMT CTN Announce Topline Results from Phase 3 MORPHO Trial of Gilteritinib

TOKYO and ROCKVILLE, Md., March 9, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") and the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) today announced topline results from the Phase 3 MORPHO clinical trial evaluating gilteritinib as a maintenance therapy following allogeneic hematopoietic stem cell transplantation (HSCT) for patients with FMS-like tyrosine kinase 3 (FLT3)-internal tandem duplication (ITD) mutated acute myeloid leukemia (AML). Based on the data, the study did not meet its pre-defined primary endpoint of relapse-free survival (RFS) for patients treated with gilteritinib compared to placebo. The study was conducted in collaboration with BMT CTN.

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 most frequent treatment-emergent adverse events (TEAEs) were decrease in neutrophil count, diarrhea and nausea, which were generally consistent with previous studies of gilteritinib. Detailed results will be submitted for publication and for consideration at upcoming medical meetings. Since RFS was not statistically significant at the primary analysis, the study, including follow-up, will be stopped as per the study protocol.

"While we are disappointed by these results, we remain committed to providing AML patients with treatment options throughout the disease continuum," said Ahsan Arozullah, M.D., M.P.H., Senior Vice President and Head of Development Therapeutic Areas, Astellas. "We will be conducting a thorough review of the full data set and plan to share detailed results in the future."

"Though the Phase 3 MORPHO clinical trial did not meet its primary endpoint, we are proud of the fact that we were able to garner international cooperation to address this important question in a rare disease," said Mary M. Horowitz, M.D., Principal Investigator of the BMT CTN Data and Coordination Center. "In collaboration with Astellas, we will continue the evaluation of the study results, which included multiple clinically meaningful secondary endpoints, and assess their impact on AML patient care."

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.

This result will have no impact on the financial forecasts of the current fiscal year ending March 31, 2023.

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

What is XOSPATA?
XOSPATA is a prescription medicine used to treat adults with acute myeloid leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation when the disease has come back or has not improved after previous treatment(s). Your healthcare provider will perform a test to make sure XOSPATA is right for you. It is not known if XOSPATA is safe and effective in children.

Important Safety Information

What is the most important information I should know about XOSPATA?
XOSPATA may cause serious side effects including Differentiation Syndrome. Differentiation Syndrome is a condition that affects your blood cells and may be life-threatening or lead to death if not treated. Differentiation Syndrome can happen as early as 1 day after starting XOSPATA and during the first 3 months of treatment. Call your healthcare provider or go to the nearest hospital emergency room right away if you develop any of the following symptoms of differentiation syndrome while taking XOSPATA: fever, cough, dizziness or lightheadedness, rapid weight gain, trouble breathing, swelling of your arms or legs, rash, decreased urination. If you develop any of these symptoms of differentiation syndrome, your healthcare provider may treat you with a corticosteroid medicine and may monitor you in the hospital.

Who should not take XOSPATA?
Do not take XOSPATA if you are allergic to gilteritinib or any of the ingredients in XOSPATA.

What are the possible side effects of XOSPATA?
XOSPATA may cause serious side effects including:

- See "What is the most important information I should know about XOSPATA?" above.
- Posterior Reversible Encephalopathy Syndrome (PRES). If you take XOSPATA, you may be at risk of developing a condition involving the brain called PRES. Tell your healthcare provider right away if you have a seizure or quickly worsening symptoms such as headache, decreased alertness, confusion, reduced eyesight, blurred vision, or other visual problems. Your healthcare provider will do a test to check for PRES. Your healthcare provider will stop XOSPATA if you develop PRES.
- Changes in the electrical activity of your heart called QTc prolongation. QTc prolongation can cause irregular heartbeats that can be life-threatening. Your healthcare provider will check the electrical activity of your heart with a test called an electrocardiogram (ECG) before you start taking XOSPATA and during your treatment with XOSPATA. Tell your healthcare provider right away if you feel dizzy, lightheaded, or faint. The risk of QT prolongation is higher in people with low blood magnesium or low blood potassium levels. Your healthcare provider will do blood tests to check your potassium and magnesium levels before and during your treatment with XOSPATA.
- Inflammation of the pancreas (pancreatitis). Tell your healthcare provider right away if you have severe stomach (abdomen) pain that does not go away. This pain may happen with or without nausea and vomiting.

The most common side effects of XOSPATA include:

- Changes in liver function tests
- Joint or muscle pain
- Tiredness
- Fever
- Pain or sores in mouth or throat
- Swelling of arms or legs
- Rash
- Diarrhea
- Shortness of breath
- Nausea
- Cough
- Constipation
- Eye problems

- Headache
- Dizziness
- Low blood pressure
- Vomiting
- Decreased urination

Your healthcare provider may tell you to decrease your dose, temporarily stop, or completely stop taking XOSPATA if you develop certain side effects during treatment with XOSPATA.

These are not all of the possible side effects of XOSPATA. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

What should I tell my doctor before taking XOSPATA?
Tell your doctor:

- About all of your medical conditions.
- If you have heart problems, including a condition called long QT syndrome.
- If you have problems with abnormal electrolytes such as sodium, potassium, or magnesium levels.
- If you are pregnant or plan to become pregnant. XOSPATA can cause harm to your unborn baby. Tell your healthcare provider right away if you become pregnant during treatment with XOSPATA or think you may be pregnant.
    - If you are able to become pregnant, your healthcare provider may perform a pregnancy test 7 days before you start treatment with XOSPATA.
    - Females who are able to become pregnant should use effective birth control (contraception) during treatment with XOSPATA and for 6 months after the last dose of XOSPATA.
    - Males who have female partners that are able to become pregnant should use effective birth control (contraception) during treatment with XOSPATA and for 4 months after the last dose of XOSPATA.
- If you are breastfeeding or plan to breastfeed. It is not known if XOSPATA passes into your breast milk. Do not breastfeed during treatment with XOSPATA and for 2 months after the last dose of XOSPATA.
- About all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. XOSPATA may affect the way other medicines work and other medicines may affect how XOSPATA works.

How should I take XOSPATA?

- Take XOSPATA exactly as your healthcare provider tells you.
- Do not change your dose or stop taking XOSPATA unless your healthcare provider tells you to.
- Take XOSPATA 1 time a day at about the same time each day.
- Swallow XOSPATA tablets whole.
- XOSPATA can be taken with or without food.
- Do not break, crush or chew XOSPATA tablets.
- If you miss a dose of XOSPATA, take your dose as soon as possible on the same day at least 12 hours before your next scheduled dose. Return to your normal schedule the following day. Do not take 2 doses within 12 hours.

Please see Full Prescribing Information, including BOXED WARNING, and Medication Guide.

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 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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