Press Release

Astellas Announces First Clinical Data from Phase I Study of Gilteritinib in Combination with Intensive Chemotherapy in Patients Newly Diagnosed with Acute Myeloid Leukemia

– Gilteritinib combined with intensive chemotherapy was well-tolerated in newly diagnosed AML patients –

TOKYO – December 11, 2017 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Yoshihiko Hatanaka, "Astellas") announced today the first reported data of the investigational agent gilteritinib from the ongoing, open-label, dose escalation/expansion Phase 1 study (NCT02236013) in newly diagnosed patients with acute myeloid leukemia (AML). The data are being presented today in an oral presentation at the 2017 American Society of Hematology (ASH) Annual Meeting.

"These initial data shed encouraging light on the safety and tolerability of gilteritinib when combined with intensive chemotherapy for newly diagnosed AML patients," said Keith W. Pratz, M.D., of John Hopkins Sidney Kimmel Comprehensive Cancer Center, who is the principal investigator for the study. "In addition, while evaluating antitumor effects is an exploratory goal, the response rates in FLT3mut+ patients are promising and warrant expanded investigation of gilteritinib in this upfront treatment setting. Continuing research to evaluate the potential role for a FLT3 inhibitor in newly diagnosed patients and other stages of AML should continue to be a priority in our collective efforts to improve outcomes for patients."

The primary objective of this Phase 1 study is to assess the safety/tolerability profile, including dose-limiting toxicities (DLTs) and maximum tolerated dose (MTD), of gilteritinib when combined with 7+3 induction (cytarabine and idarubicin) and high-dose cytarabine (HiDAC) consolidation chemotherapy, followed by single agent maintenance therapy in patients 18 years of age and older who have been newly diagnosed with AML. Assessment of antitumor effects of this combination therapy is an exploratory objective.

The two-part trial first enrolled patients to successive cohorts to determine the MTD. Successive cohorts received gilteritinib doses of 40, 80 or 120 mg/day. Dose escalation decisions were made based on DLTs that occurred following the first dose of gilteritinib during induction. Patients in the dose expansion cohort received gilteritinib at the recommended expansion dose established during dose escalation. Patients also received gilteritinib during consolidation, and then received maintenance therapy with once-daily gilteritinib over a 28-day cycle for up to 26 cycles.

"We are very encouraged by this initial data from our ongoing study of gilteritinib in combination with intensive chemotherapy in newly diagnosed AML patients, and pleased that it earned selection for oral presentation at ASH," said Steven Benner,

M.D., senior vice president and global therapeutic area head, Oncology Development, Astellas. “Mutations of FLT3 in AML are associated with a poor prognosis across the course of disease treatment and, through our comprehensive clinical development program, Astellas is committed to understanding how selective inhibition by gilteritinib might be beneficial to as many patients as possible.”

As of July 9, 2017, 50 patients (n=17, dose escalation cohort; n=33, dose expansion cohort) had been enrolled in this ongoing study and 49 had received at least one dose of gilteritinib. Of the 48 patients with documented FLT3 mutation status, 23 (47.9%) were FLT3mut+, of whom 13 (56.5%) had internal tandem duplications (ITD).

Additional key findings include:

- During dose escalation, two subjects in the 40 mg/day cohort who had received gilteritinib on days 1-14 experienced DLTs (neutropenia, thrombocytopenia and decreased ejection fraction). After gilteritinib induction schedule modification, no additional DLTs were observed.
- The maximum tolerated dose was not reached; gilteritinib 120 mg/day was chosen as the recommended expansion dose.
- Grade ≥ 3 treatment-emergent adverse events (TEAEs) occurring in ≥ 10% of subjects were febrile neutropenia (36.7%), thrombocytopenia (18.4%), neutropenia (16.3%) and decreased platelet count (12.2%).
- Serious drug-related TEAEs occurring in >1 subject were febrile neutropenia (n=8), sepsis (n=2), small intestinal obstruction (n=2), lung infection (n=2), and decreased ejection fraction (n=2).
- In FLT3mut+ and FLT3 wild type subjects, end-of-treatment CRc rates were 100% and 60.9%, respectively.

About Acute Myeloid Leukemia
Acute Myeloid Leukemia (AML) is a cancer that impacts the blood and bone marrow, and its incidence increases with age. The American Cancer Society estimates that in 2017, approximately 21,000 new patients will be diagnosed with AML in the United States and about 10,000 cases will result in death.

About Gilteritinib
Gilteritinib is an investigational compound that has demonstrated inhibitory activity against FLT3 internal tandem duplication (ITD) as well as FLT3 tyrosine kinase domain (TKD), two common types of FLT3 mutations that are seen in approximately one-third of patients with AML. Further, gilteritinib has also demonstrated inhibition of the AXL receptor in AML cell lines, which has been reported to be associated with therapeutic resistance. Astellas is currently investigating gilteritinib in various AML patient populations through several additional Phase 3 trials. Visit AstellasAMLTrials.com to learn more about ongoing gilteritinib clinical trials.

Gilteritinib was discovered through a research collaboration with Kotobuki Pharmaceutical Co., Ltd., and Astellas has exclusive global rights to develop, manufacture and potentially commercialize gilteritinib. Gilteritinib has been granted Orphan Drug designation and Fast Track designation by the U.S. FDA, and SAKIGAKE designation by the Japan Ministry of Health, Labor and Welfare.

The safety and efficacy of the agent discussed herein are under investigation and have not been established. There is no guarantee that the agent will receive regulatory approval and become commercially available for the uses being investigated. Information about pharmaceutical products (including products currently in development), which is included in this press release are not intended to constitute an advertisement or medical advice.

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. We focus on Urology, Oncology, Immunology, Nephrology and Neuroscience as prioritized therapeutic areas while advancing new therapeutic areas and discovery research leveraging new technologies/modalities. We are also creating new value by combining internal capabilities and external expertise in the medical/healthcare business. Astellas is on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at 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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