Astellas reports positive topline phase 3 results for antifungal isavuconazole

- Isavuconazole phase 3 invasive aspergillosis study (SECURE) meets primary endpoint -

Tokyo, September 30, 2013 – Astellas Pharma Inc. (Tokyo:4503) announced today positive topline data from the isavuconazole phase 3 invasive aspergillosis study (SECURE). The antifungal agent isavuconazole is being co-developed with Basilea Pharmaceutica Ltd.

The randomized, double-blind isavuconazole study (SECURE) achieved its primary objective in demonstrating non-inferiority versus voriconazole for the primary treatment of invasive fungal disease caused by *Aspergillus* species or certain other filamentous fungi. Isavuconazole was effective as determined by the primary endpoint of all-cause mortality through day 42 in the intent-to-treat population (N=516). The all-cause-mortality was 18.6% in the isavuconazole treatment group and 20.2% in the voriconazole group. The 95% confidence interval of the treatment difference between isavuconazole and voriconazole was within the pre-specified non-inferiority margin of 10%.

In addition, the key secondary endpoint of overall success rate (composite of clinical, mycological, radiological responses) at the end-of-therapy in patients with proven/probable disease was similar between isavuconazole and voriconazole (35.0% and 36.4%, respectively). This outcome was based on a blinded assessment by the Independent Data Review Committee.

Overall, drug- and non-drug-related adverse events were reported in 96.1% and 98.5% of patients in the isavuconazole and voriconazole treatment groups, respectively. The most frequent adverse events reported were nausea, vomiting, pyrexia (fever), diarrhea, and hypokalaemia (deficiency of potassium in the blood), which were reported at similar rates in both treatment groups. Study drug-related adverse events were reported in 42.4% and 59.8% of patients in the isavuconazole and voriconazole treatment groups, respectively.

“We are pleased to report these topline results from the isavuconazole SECURE study, the largest interventional study conducted in patients with invasive aspergillosis. These data provide important information on patients with this life-threatening disease as we evaluate isavuconazole as a potential therapeutic agent,” said Bernie Zeiher, Senior Vice President and Global Therapeutic Area

Head of Immunology and Infectious Diseases at Astellas Pharma Global Development, Inc.

Update on Other Ongoing Phase 3 Isavuconazole Studies (VITAL and ACTIVE)
Enrollment in the open-label phase 3 isavuconazole study (VITAL) including patients with invasive fungal disease caused by mucormycetes and other emerging fungal pathogens and patients with aspergillosis and pre-existing renal impairment has been completed (N=150). Based on the investigator reported data, approximately 45 patients were enrolled with mucormycosis and a similar number of patients were enrolled with pre-existing renal impairment. Review of diagnosis and outcomes by an Independent Data Review Committee is ongoing.

Enrollment in the randomized, double-blind phase 3 isavuconazole study (ACTIVE), evaluating the use of isavuconazole i.v. and oral versus caspofungin i.v. followed by oral voriconazole for the treatment of invasive *Candida* infections, is continuing.

About isavuconazole
Isavuconazole is an investigational once daily intravenous and oral broad-spectrum antifungal for the potential treatment of severe invasive and life-threatening fungal infections. It is currently in phase 3 of clinical development. Isavuconazole demonstrated *in-vitro* and *in-vivo* coverage of a broad range of yeasts (such as *Candida* species) and molds (such as *Aspergillus* species) as well as *in-vitro* activity against emerging and often fatal molds including those that cause mucormycosis. Isavuconazole received U.S. FDA fast-track and U.S. orphan drug designation for invasive aspergillosis. Isavuconazole is being co-developed with Basilea Pharmaceutica Ltd.

About the isavuconazole phase 3 program
The phase 3 program with isavuconazole includes three studies, SECURE, VITAL and ACTIVE. The SECURE study is a global double-blind randomized phase 3 study, designed to evaluate the safety and efficacy of once-daily isavuconazole versus twice-daily voriconazole in the primary treatment of invasive fungal disease caused by *Aspergillus* species or other filamentous fungi. The VITAL study is an open-label phase 3 study of isavuconazole in the treatment of aspergillosis patients with pre-existing renal impairment or patients with invasive fungal disease caused by emerging and often fatal molds, yeasts or dimorphic fungi. The ACTIVE phase 3 study is evaluating the safety and efficacy of intravenously (i.v.) and orally administered isavuconazole versus i.v. caspofungin followed by oral voriconazole in the treatment of invasive *Candida* infections.

About invasive aspergillosis infections
Invasive aspergillosis is estimated to occur in 5-13% of recipients of bone marrow transplants, 5-25% of patients who have received heart or lung transplants, and 10-20% of patients who are receiving intensive chemotherapy for leukemia.[1] Mortality rates for transplant patients with invasive aspergillosis have been reported to be between 34% and 58%.[2] Around 47% of solid organ transplant recipients who developed invasive aspergillosis had renal insufficiency and acute renal failure was reported for 43% of intensive care unit (ICU) patients with invasive aspergillosis,

compared to 20.5% in the general ICU population.[2, 3]

About Astellas

Astellas Pharma Inc., located in Tokyo, Japan, is a pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceuticals. The organization is committed to becoming a global category leader in Urology, Immunology (including Transplantation) and Infectious Diseases, Oncology, Neuroscience and DM Complications and Kidney Diseases. For more information on Astellas Pharma Inc., please visit the company website at www.astellas.com/en.

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2 Baddley JW et al. Factors associated with mortality in transplant patients with invasive aspergillosis. Clinical Infectious Disease 2010 (50), 1559-1567

3 Vandewoude KH et al. Invasive aspergillosis in critically ill patients: attributable mortality and excesses in length of ICU stay and ventilator dependence. Journal of Hospital Infection 2004 (56), 269-276

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