Astellas Contacts:
Mindy Dooa
Astellas Pharma EMEA
+44 (0) 7826 912339

Marie Turner
Red Door Communications
+44 (0) 2083 928056

XTANDI™ (ENZALUTAMIDE) CAPSULES RECEIVE POSITIVE CHMP OPINION FOR THE TREATMENT OF MEN WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER WHO ARE CHEMOTHERAPY-NAÏVE

- For chemotherapy-naïve patients, enzalutamide demonstrated a significant impact on overall survival compared to placebo
- Enzalutamide reduced the risk of death by 29% versus placebo
- Enzalutamide significantly reduced the risk of radiographic progression or death by 81% compared with placebo
- Patients experienced delayed time to initiation of chemotherapy with enzalutamide compared with those taking placebo

Chertsey, England – 24th October 2014 – Astellas Pharma Europe Ltd. today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency has adopted a positive opinion recommending a variation to amend the Marketing Authorisation for enzalutamide (trade name XTANDI™). The positive opinion relates to the use of enzalutamide for the treatment of adult men with metastatic castrate-resistant prostate cancer (mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen-deprivation therapy in whom chemotherapy is not yet clinically indicated.[1]

“For us urologists treating patients with mCRPC, this positive opinion from the CHMP is an important milestone towards making enzalutamide available across Europe. Enzalutamide marks a significant step for many patients who live with mCRPC as encouraging, it demonstrates benefits in overall survival, has a positive impact on quality of life and has been shown to be well tolerated”, said Professor Bertrand Tombal, MD, PhD, Chairman of the Division of the Urology and Professor of Physiology, Université Catholique de Louvain (UCL)

and European Principal Investigator for PREVAIL. “As well as clear efficacy and safety benefits over placebo, enzalutamide has the additional advantage of not requiring steroids to be taken concomitantly and requires only basic monitoring, making it a simple option for both healthcare professionals and patients. It is my hope that the European Commission follows this opinion, providing us with a viable new treatment option for those patients not suitable for chemotherapy.”

The positive CHMP opinion is based on results from the phase III PREVAIL study which showed that men treated with enzalutamide demonstrated a statistically significant reduction both in the risk of death and a delay in cancer progression and the time to initiation of chemotherapy as compared to those treated with placebo.[2]

Enzalutamide reduced the risk of death by 29% (HR=0.71; p<0.001), compared with placebo. In addition, treatment with enzalutamide significantly reduced the risk of radiographic progression or death by 81% compared with placebo treatment (HR=0.19; p<0.001). Men taking enzalutamide experienced a 17-month delay in the time to initiation of chemotherapy compared with men taking placebo (28.0 months versus 10.8 months; HR=0.35; p<0.0001).2

The most common clinically relevant adverse events among the enzalutamide population as compared with placebo-treated patients in the PREVAIL trial included fatigue, hot flush and hypertension. Hypertension was observed in 13% of enzalutamide versus 4% of placebo-treated patients. Grade 3 or higher cardiac adverse events were reported in 3% of enzalutamide versus 2% of placebo-treated patients. One patient (0.1%) out of the 871 patients treated with enzalutamide, and one patient (0.1%) receiving placebo experienced a seizure.2

In the EU, the European Commission generally follows the recommendations of the CHMP opinion and delivers its final decision around two months after the CHMP recommendation.

XTANDI is currently licensed in Europe for the treatment of adult men with mCRPC whose disease has progressed on or after docetaxel therapy.[3] Marketing authorisation was granted by the European Commission in June 2013.

- Ends -

Notes to editors

About the PREVAIL Trial
The Phase III PREVAIL trial is a randomised, double-blind, placebo-controlled, multi-national trial that enrolled more than 1,700 patients at sites in the United States, Canada, Europe, Australia, Russia, Israel and Asia including Japan. The trial enrolled patients with chemotherapy-naïve metastatic prostate cancer whose disease progressed on a luteinizing hormone-releasing hormone analogue or after bilateral orchiectomy. The co-primary endpoints of the trial were overall survival and radiographic progression-free survival. The trial was designed to evaluate enzalutamide at a dose of 160 mg taken orally once daily versus placebo.[2]

About XTANDI™
XTANDI is a novel, oral, once-daily androgen receptor signalling inhibitor. XTANDI directly targets the androgen receptors (AR) and exerts its effects on all three steps of AR signalling pathway:

- Blocks androgen binding[4]
  - Androgen binding induces a conformational change that triggers activation of the receptor[5]
- Prevents nuclear translocation[4]
  - Transit of the AR to the nucleus is an essential step in AR-mediated gene regulation[5]
- Impairs DNA binding[4]
  - Binding of the AR to the DNA is essential for modulation of gene expression[5]

XTANDI is currently licensed in Europe for the treatment of adult men with mCRPC whose disease has progressed on or after docetaxel therapy.[3] Marketing authorisation was granted by the European Commission on June 21, 2013.

Important Safety Information for XTANDI™
For important Safety Information for XTANDI please see the full Summary of Product Characteristics at:
http://www.medicines.org.uk/emc/medicine/27912/SPC/Xtandi+40mg+soft+capsules/.

About Astellas
Astellas Pharma Europe Ltd. operates in 40 countries across Europe, the Middle East and Africa, and is the regional business of Tokyo-based Astellas Pharma Inc. Astellas is a pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceuticals. The organisation's focus is to deliver outstanding R&D and marketing to continue growing in the world pharmaceutical market. Astellas' presence in Europe also includes an R&D site and three manufacturing plants. The company employs approximately 4,350 staff across these countries. For more information about Astellas Pharma Europe Ltd., please visit www.astellas.eu.

About the Astellas/Medivation Collaboration
In October 2009, Medivation Inc. (Nasdaq: MDVN) and Astellas entered into a global agreement to jointly develop and commercialise enzalutamide. The companies are collaborating on a comprehensive development program that includes studies to develop enzalutamide across the full spectrum of advanced prostate cancer as well as advanced breast cancer. The companies jointly commercialise XTANDI in the United States and Astellas has responsibility for

manufacturing and all additional regulatory filings globally, as well as commercialising XTANDI outside the United States.

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[1] Committee for Medicinal Products for Human Use (CHMP). Summary of opinion - XTANDI
[2] Beer TM, et al. Enzalutamide in Metastatic Prostate Cancer before Chemotherapy. *N Engl J Med* 2014; DOI: 10.1056/NEJMoa1405095
[3] European Medicines Agency. XTANDI (enzalutamide) Summary of Product Characteristics, 2013
[4] Tran C, et al. Development of a second-generation antiandrogen for treatment of advanced prostate cancer. *Science* 2009; 324:787-790
[5] Hu R, Denmeade SR and Luo J. Molecular processes leading to aberrant androgen receptor signaling and castration resistance in prostate cancer. *Expert Rev Endocrinol Metab* 2010; 5 (5): 753–764