Press release

Astellas Announces the Approval of XTANDI® (enzalutamide) by the China National Medical Products Administration (NMPA)

Approval based on Asian PREVAIL study of men with metastatic castration-resistant prostate cancer

TOKYO, November 26, 2019 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced that the China National Medical Products Administration (NMPA) approved a new drug application (NDA) for XTANDI® (enzalutamide) on November 18 for the treatment of adult men with metastatic castration-resistant prostate cancer (CRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy (ADT) in whom chemotherapy is not yet clinically indicated.

The approval by the NMPA was based on the results of an Asian multinational Phase 3, randomized, double-blind, placebo controlled efficacy and safety study of enzalutamide in asymptomatic or mildly symptomatic patients with progressive metastatic prostate cancer who had disease progression despite ADT and a single-dose pharmacokinetic study in healthy Chinese volunteers (Protocol 9785-CL-0013).[1]

The study, Asian PREVAIL (also known as 9785-CL-0232), evaluated oral enzalutamide (160 mg/day) versus placebo plus gonadotropin-releasing hormone (GnRH) therapy or after bilateral orchiectomy. The study, involving Asian patients including approximately 200 Chinese patients, showed consistent results with those in the global pivotal Phase 3 PREVAIL study in the same target population.[2]

"Currently the treatment options are limited in China for men with metastatic castration-resistant prostate cancer," said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Global Therapeutic Area Head, Oncology Development, Astellas. "The approval of enzalutamide in China brings us one step closer to offering physicians a meaningful treatment option in an area where there is a high medical need."

Patients treated with enzalutamide demonstrated a statistically significant reduction in the risk of Prostate Specific Antigen (PSA) progression (Hazard Ratio of 0.38 [95% confidence interval: 0.27, 0.52], P < 0.0001). The median time to PSA progression was 8.31 months in the enzalutamide group versus 2.86 months in the placebo group. Treatment with enzalutamide also resulted in a statistically significant reduction in risk of radiographic disease progression or death compared with treatment with placebo with a Hazard Ratio (HR) of 0.31 (95% confidence interval: 0.20, 0.46; P<0.0001). Additionally, treatment with enzalutamide showed a statistically significant improvement in overall survival compared to treatment with placebo, with a 67% decrease in the risk of death (HR 0.33, [95% CI: 0.16, 0.67]; P=0.0015).

The safety profile observed in the Asian PREVAIL study was generally consistent with previous clinical studies in patients with metastatic CRPC.[2] The most common adverse reactions (≥10%) that occurred more frequently (≥2% over placebo) in the enzalutamide-treated patients from the randomized placebo-controlled clinical trials were asthenia/fatigue, decreased appetite, hot flush, arthralgia, dizziness/vertigo, hypertension, headache, and decreased weight.

In addition to the Asian PREVAIL data involving a Chinese sub-population, the approval was supported by results from the global Phase 3 PREVAIL trial, which were published in the *New England Journal of Medicine* in 2014. The Phase 3 PREVAIL trial was a randomized, 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.[2]

Enzalutamide is a standard of care for men with metastatic CRPC in countries where it is available. Since 2012, it has been prescribed to more than 420,000 patients worldwide.[3] Prostate cancer is the second most common cancer in men worldwide[4] and in China it has become the most common tumor in male urinary malignancies.[5]

“The approval of enzalutamide is an important milestone. Tens of thousands of Chinese patients with metastatic castration-resistant prostate cancer could potentially benefit from the reduced risk of disease progression and death found in the Asian PREVAIL study,” said Hiroshi Hamaguchi, President, Astellas Greater China Commercial. “The approval also demonstrates a significant step forward for Astellas, with enzalutamide being the first Astellas oncology treatment approved in China.”

About Asian PREVAIL (9785-CL-0232)
The Asian PREVAIL study involving a Chinese sub-population was a multinational Phase 3, randomized, double-blind, placebo-controlled efficacy and safety study of oral enzalutamide (formerly MDV3100) in asymptomatic or mildly symptomatic participants with progressive metastatic prostate cancer who have disease progression despite ADT. The study enrolled 388 participants who were not previously treated with cytotoxic chemotherapy. The trial was designed to evaluate enzalutamide at a dose of 160 mg taken orally once daily on time to PSA progression as compared to placebo in chemotherapy-naïve participants with progressive metastatic prostate cancer who had failed ADT. The study completed its double-blind period and is now in the open-label period.

About metastatic Castration-Resistant Prostate Cancer
Prostate cancer is considered metastatic once the cancer has spread outside of the prostate gland to other parts of the body.[6] Metastatic CRPC is fatal, with a median survival of approximately 3-4 years for men starting treatment with ADT.[7]

About Enzalutamide[8]
Enzalutamide is an oral, once-daily androgen receptor signaling inhibitor. Enzalutamide directly targets the androgen receptors (AR) and exerts its effects on three steps of the AR signaling pathway:

- Inhibits androgen binding: Androgen binding induces a conformational change that triggers activation of the receptor
- Prevents nuclear translocation: Translocation of the AR to the nucleus is an essential step in AR-mediated gene regulation
- Impairs DNA binding: Binding of the AR to the DNA is essential for modulation of gene expression

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. For more information, please visit our website at https://www.astellas.com/en.

About the Pfizer/Astellas Collaboration
In October 2009, Medivation, Inc., which is now part of Pfizer (NYSE: PFE), and Astellas (TSE: 4503) entered into a global agreement to jointly develop and commercialize enzalutamide. The companies jointly commercialize enzalutamide in the United States and Astellas has responsibility for manufacturing and all additional regulatory filings globally, as well as commercializing enzalutamide outside the United States.

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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