Press Release

Astellas Receives Positive CHMP Opinion for XTANDI™ in Additional Recurrent Early Prostate Cancer Treatment Setting

- If approved, XTANDI would become the first and only NHT treatment available for metastatic and high risk biochemical recurrent non-metastatic hormone sensitive prostate cancer patient populations in the European Union (EU)

- A decision on the EU marketing authorisation is expected by June 2024-

TOKYO, March 22, 2024 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending approval of XTANDI™ (enzalutamide) as monotherapy or in combination with androgen deprivation therapy for the treatment of adult men with high risk biochemical recurrent (BCR) non-metastatic hormone sensitive prostate cancer (nmHSPC) who are unsuitable for salvage radiotherapy.[1]

Ahsan Arozullah, MD, MPH, Senior Vice President and Head of Oncology Development, Astellas
"Men with nmHSPC with high-risk biochemical recurrence are very likely to experience disease progression. With approximately 9 out of 10 of these men developing metastatic disease, the need for new and effective treatment options is critical. Today's positive opinion from the Committee is an important step forward for providing an additional treatment option for these patients and complements the existing efficacy and safety data supporting the use of XTANDI across the prostate cancer disease continuum. We look forward to XTANDI being potentially the first and only androgen receptor signaling inhibitor approved for this patient population in the European Union."

The positive CHMP opinion is based on the results from the Phase 3 EMBARK trial, which were presented as a plenary session during the 2023 American Urological Association Annual Meeting and subsequently published in the *New England Journal of Medicine*.

The positive opinion will now be reviewed by the European Commission (EC), which has the authority to approve medicines in all 27 European Union (EU) member states as well as Iceland, Liechtenstein and Norway.[2]

XTANDI was approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with non-metastatic castration-sensitive prostate cancer

(nmCSPC; also known as nmHSPC) with BCR at high risk for metastasis in November 2023. Astellas is also discussing the EMBARK data with other regulatory authorities to support additional license applications for XTANDI in this indication in 2024 and beyond.

Astellas has already reflected the impact from this result in its financial forecast for the current fiscal year ending March 31, 2024.

For more information, please see the press release "European Medicines Agency Validates Type II Variation for Astellas' XTANDI® (enzalutamide) for Treatment of Non-Metastatic Hormone-Sensitive Prostate Cancer with High-Risk Biochemical Recurrence" issued on September 12, 2023.

About EMBARK
The Astellas- and Pfizer-led Phase 3, randomized, double-blind, placebo-controlled, multi-national trial enrolled 1,068 patients with nonmetastatic hormone- (or castration-) sensitive prostate cancer (nmHSPC or nmCSPC) with high-risk BCR at sites in the U.S., Canada, Europe, South America, and the Asia-Pacific region. Patients who were considered to experience high-risk BCR had a prostate-specific antigen doubling time (PSA-DT) ≤ 9 months; serum testosterone ≥ 150 ng/dL (5.2 nmol/L); and screening PSA by the central laboratory ≥ 1 ng/mL if they had a radical prostatectomy (with or without radiotherapy) as primary treatment for prostate cancer, or at least 2 ng/mL above the nadir if they had radiotherapy only as primary treatment for prostate cancer. Patients in the EMBARK trial were randomized to receive enzalutamide 160 mg daily plus leuprolide (n=355), enzalutamide 160 mg as a single agent (n=355), or placebo plus leuprolide (n=358). Leuprolide 22.5 mg was administered every 12 weeks.

EMBARK met its primary endpoint of metastasis-free survival (MFS) for the XTANDI plus leuprolide arm, demonstrating a statistically significant reduction in the risk of metastasis or death over placebo plus leuprolide. MFS is defined as the duration of time in months between randomization and the earliest objective evidence of radiographic progression by central imaging or death due to any cause, whichever occurred first.

The study also met a key secondary endpoint, by demonstrating that patients treated with XTANDI (single agent) had a statistically significant reduction in the risk of metastasis or death versus placebo plus leuprolide, meeting its MFS endpoint.

In EMBARK, Grade 3 or higher adverse events (AEs) were reported in 46% of XTANDI plus leuprolide patients, 50% of patients treated with XTANDI (single agent), and 43% of patients receiving placebo plus leuprolide. Permanent discontinuation due to AEs as the primary reason was reported in 21% of XTANDI plus leuprolide patients, 18% in XTANDI (single agent) patients, and 10% in placebo plus leuprolide patients.

For more information on the EMBARK trial (NCT02319837) go to www.clinicaltrials.gov.

About High Risk Biochemical Recurrent Non-Metastatic Hormone Sensitive Prostate Cancer
In non-metastatic hormone (or castration-) sensitive prostate cancer (nmHSPC or nmCSPC), no evidence of the cancer spreading to distant parts of the body (metastases) is detectable with conventional radiological methods (CT/MRI), and the cancer still responds to medical or surgical treatment designed to lower testosterone levels.[3,4] Of men who have undergone definitive prostate cancer treatment, including radical prostatectomy, radiotherapy, or both, an estimated 20-40% will experience a BCR within 10 years.[5] About 9 out of 10 men with high-risk BCR will develop metastatic disease, and 1 in 3 will die as a result of their metastatic prostate cancer.[3] The EMBARK trial focused on men with high-risk BCR. Per the EMBARK protocol, patients with nmHSPC and high-risk BCR are those initially treated by radical prostatectomy or radiotherapy, or both, with a PSA-DT ≤ 9 months. High-risk BCR patients with a PSA-DT of ≤ 9 months have a higher risk of metastases and death.[6]

About XTANDI™ (enzalutamide)
XTANDI™ (enzalutamide) is an androgen receptor signaling inhibitor. XTANDI is a standard of care and has received regulatory approvals in one or more countries around the world for use in men with metastatic

hormone-sensitive prostate cancer (mHSPC), metastatic castration-resistant prostate cancer (mCRPC), non-metastatic castration-resistant prostate cancer (nmCRPC) and non-metastatic hormone-sensitive prostate cancer (nmHSPC) with high-risk biochemical recurrence (BCR). XTANDI is currently approved for one or more of these indications in more than 90 countries, including in the United States, European Union and Japan. Over one million patients have been treated with XTANDI globally.[7]

About XTANDI™ (enzalutamide) in the E.U.
Enzalutamide is an androgen receptor signaling inhibitor indicated in the E.U. for the treatment of adult men with:

- Metastatic hormone-sensitive prostate cancer (mHSPC, also known as metastatic castration-sensitive prostate cancer or mCSPC) in combination with androgen deprivation therapy (ADT).
- High-risk non-metastatic castration-resistant prostate cancer (CRPC).
- Metastatic CRPC who are asymptomatic or mildly symptomatic after failure of ADT in whom chemotherapy is not yet clinically indicated. It is also indicated in adult men with metastatic CRPC whose disease has progressed on or after docetaxel therapy.

Important Safety Information
For important Safety Information for enzalutamide please see the full Summary of Product Characteristics at: https://www.ema.europa.eu/en/documents/product-information/xtandi-epar-product-information_en.pdf.

Important Safety Information
For Important Safety Information for enzalutamide please see the Package Insert.

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.

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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