MEDIA RELEASE

THE THERAPEUTIC GOODS ADMINISTRATION (TGA) OF AUSTRALIA APPROVES XTANDI® (enzalutamide) FOR THE TREATMENT OF METASTATIC HORMONE-SENSITIVE PROSTATE CANCER

April 13 2021, SYDNEY: Astellas Pharma Australia Pty. Ltd. (Astellas) is pleased to announce the Therapeutic Goods Administration (TGA) has approved XTANDI® (enzalutamide) as an oral once-daily therapy for patients with metastatic hormone-sensitive prostate cancer (mHSPC) in Australia.

The Australian Institute of Health and Welfare estimates that in 2020 16,741 men were diagnosed with prostate cancer.[1] It is estimated that up to one third of patients with prostate cancer will develop metastases at some point over their disease course.[2]

Prostate cancer is considered metastatic once the cancer has spread beyond the prostate. The disease is considered hormone-sensitive if it still responds to androgen deprivation therapy (ADT) or surgical treatment to lower testosterone levels.[2]

Men diagnosed with metastatic hormone-sensitive prostate cancer tend to have a poor prognosis, with a median survival of approximately 3–4 years. This underscores the need for new treatment options.[3]

Associate Professor Arun Azad, a medical oncologist from Peter MacCallum Cancer Centre, an investigator on the ARCHES clinical trial and a member of Australian New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) says, “new treatment options are very welcome for this group of patients.”

“For many decades we had limited treatment options for men who have a cancer that has spread beyond the prostate but is still sensitive to hormone therapy. Androgen deprivation therapy was the mainstay, but the development of treatment resistance is inevitable and, in some cases, very quick. Now we are seeing additional effective oral medications being approved for these patients and that really is excellent news.”

“It’s especially pleasing to see that the approval was in part based on new research from the phase 3 ENZAMET clinical trial, sponsored by ANZUP and led by Professor Ian Davis and Professor Chris Sweeney. The ENZAMET and ARCHES trials both demonstrated the effectiveness of enzalutamide in men with metastatic hormone-sensitive prostate cancer and provide evidence of the benefit of adding enzalutamide to androgen deprivation therapy in these patients,” said Associate Professor Azad.

Prostate Cancer Foundation of Australia CEO, Professor Jeff Dunn AO, welcomed the TGA’s approval stating, “This is a great step forward for Australian men and families impacted by prostate cancer and we commend Astellas and the TGA for responding to the evidence.”

“We are excited to be adding another indication for enzalutamide and hope that this will make a meaningful difference to Australian men with metastatic hormone-sensitive prostate cancer,” said Lizzie Marett, Managing Director of Astellas.

XTANDI is not currently reimbursed under the Pharmaceutical Benefits Scheme (PBS) for mHSPC. In support of patient access and associated out-of-pocket costs, Astellas will make XTANDI available for this indication via a patient access program for patients that qualify for the program.

About XTANDI® XTANDI (enzalutamide) belongs to a class of drugs known as anti-androgens. It works by blocking the effects of testosterone to slow the growth and spread of prostate cancer. XTANDI is the only oral treatment approved by the TGA to treat the following three distinct types of advanced prostate cancer (PC): non-metastatic castration-resistant PC (nmCRPC), metastatic castration-resistant PC (mCRPC) and metastatic hormone-sensitive PC (mHSPC).[4] The approval for the new indication, mHSPC, was based on data from the Phase 3 clinical trials, ARCHES and ENZAMET, investigating enzalutamide in men with mHSPC.[5] The Pharmaceutical Benefits Scheme (PBS) listing for XTANDI is authority required for metastatic castrate resistant prostate cancer (mCRPC). XTANDI is not listed on the PBS for the treatment of metastatic hormone-sensitive (mHSPC) or non-metastatic castrate resistant prostate cancer (nmCRPC).

Important Safety Information
For important safety information for XTANDI please see the full Product Information at:
http://www.guildlink.com.au/gc/ws/ax/rss.cfm?product=axpxtand10919

About ENZAMET
ENZAMET (ANZUP 1304) is a global investigator-initiated trial led by ANZUP and sponsored by the University of Sydney in collaboration with the Canadian Cancer Trials Group, Dana-Farber Cancer Institute and Cancer Trials Ireland (enrolling patients from Ireland and the United Kingdom). Astellas provided drug and financial support but was not involved in study conduct or data analysis. The trial evaluated the potential of enzalutamide plus androgen deprivation therapy (ADT) versus a conventional non-steroidal anti androgen (NSAA) plus ADT in 1,125 men with mHSPC. The primary endpoint for the trial is overall survival (OS; 3-years). [5] ENZAMET's first interim analysis was presented at the Plenary Session at ASCO in 2019 with simultaneous New England Journal of Medicine (NEJM) publication. Additional details about ENZAMET (NCT02446405) are available on www.clinicaltrials.gov.

About ARCHES
Astellas sponsored, Phase 3, randomised, double-blind, placebo-controlled, multinational ARCHES trial (NCT02677896) enrolled 1,150 patients with mHSPC at sites in the U.S., Canada, Europe, South America, and the Asia-Pacific region. Patients in the trial were randomised to receive enzalutamide 160 mg daily or placebo and continued on a luteinizing hormone-releasing hormone (LHRH) agonist or antagonist or had a history of bilateral orchiectomy. The primary endpoint of the trial was radiographic progression-free survival (rPFS) assessed by blinded independent central review. rPFS was defined as the time from randomisation to radiographic disease progression at any time or death within 24 weeks after study drug discontinuation. Radiographic disease progression was defined by identification of two or more new bone lesions on a bone scan with confirmation (Prostate Cancer Working Group 2 criteria) and/or progression in soft tissue disease. Patients were stratified by volume of disease (low vs high) and prior docetaxel therapy for prostate cancer (no prior docetaxel, 1-5 cycles, or 6 prior cycles).[6]

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/au

MINIMUM PRODUCT INFORMATION: Xtandi® (enzalutamide) 40 mg soft capsules. **Indications:** Treatment of patients with metastatic hormone-sensitive prostate cancer. Treatment of patients with non- metastatic castration-resistant prostate cancer (CRPC). Treatment of patients with metastatic CRPC following failure of androgen deprivation therapy in whom chemotherapy is not yet indicated. Treatment of patients with metastatic CRPC who have previously received docetaxel. **Contraindications**: Hypersensitivity to enzalutamide or any of the excipients. Women who are, or may become, pregnant (Category X). **Precautions:** Risk of seizure, posterior reversible encephalopathy syndrome, drug interactions. Refer to full PI for additional precautions. **Interactions:** Strong inhibitors of CYP2C8, paracetamol, midazolam, warfarin and coumarin-like anticoagulants, omeprazole, colchicine, dabigatran etexilate, digoxin. For a list of medicinal products that may be affected, refer to full PI. **Adverse effects:** Very common (≥10%): fatigue, nausea, hot flush, diarrhoea, hypertension, asthenia and falls. Common (≥1% and <10%): cognitive disorders, dry skin, gynaecomastia, headache, ischaemic heart disease, pruritus, restless legs syndrome, fracture, anxiety. **Dosage:** 160 mg (four 40 mg capsules) as a single oral daily dose. Swallow capsules whole with water. Do not chew, dissolve, or open the capsules. If a patient experiences a ≥ Grade 3 toxicity or an intolerable adverse reaction, withhold dosing for one week or until symptoms improve to ≤ Grade 2, then resume at the same or a reduced dose (120 mg or 80 mg) if warranted. The concomitant use of strong CYP2C8 inhibitors should be avoided if possible, but if co-administered, reduce dose to 80 mg once daily. Based on Product Information dated 30 March 2021.

Associate Professor Azad, Prostate Cancer Foundation of Australia and ANZUP did not receive compensation for their contribution to this media release. Associate Professor Arun Azad has worked with Astellas as a paid consultant on other projects.
The information about pharmaceutical products included in this press release is not intended to constitute an advertisement or medical advice.

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5. Davis I, et al. Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer. NEJM. 2019; 381:121-131 DOI: 10.1056/NEJMoa1903835.
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