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News Release

Not intended for U.S. and UK Media

CHMP recommends third indication for Bayer's Nubeqa™ (darolutamide) for patients with advanced prostate cancer

- CHMP adopts positive opinion for the marketing authorization of darolutamide in combination with androgen deprivation therapy (ADT) for patients with metastatic hormone-sensitive prostate cancer (mHSPC) in the European Union
- Positive opinion is based on results from the pivotal Phase III ARANOTE trial and reinforces darolutamide's established safety and tolerability profile for prostate cancer patients across all approved indications
- Pending approval, this broadened indication would give physicians the option to use darolutamide plus ADT, with or without chemotherapy, offering greater flexibility to tailor treatment plans to meet mHSPC patients' needs

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Berlin, June 20, 2025 – The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency has recommended darolutamide, an oral androgen receptor inhibitor (ARi), plus androgen deprivation therapy (ADT) for marketing authorization in the European Union (EU), for the treatment of patients with metastatic hormone-sensitive prostate cancer (mHSPC). CHMP recommendation is based on positive results from the pivotal Phase III ARANOTE trial which showed that darolutamide plus ADT significantly reduced the risk of radiological progression or death by 46% compared to placebo plus ADT (HR 0.54; 95% CI 0.41–0.71; P<0.0001) in patients with mHSPC.

"This positive CHMP opinion reinforces darolutamide's potential to become a leading therapy across various stages of prostate cancer and underscores our commitment to advancing innovative solutions for men living with this disease," said Christine Roth, Executive Vice President, Global Product Strategy and Commercialization and Member of the Pharmaceuticals Leadership Team at Bayer. "European regulatory approval will mean that darolutamide plus ADT can be used with or without chemotherapy, expanding

treatment options that would enable physicians to better meet the individual needs of patients living with mHSPC."

"Results from the ARANOTE trial show darolutamide plus ADT significantly reduces the risk of radiological progression or death. As the first androgen receptor inhibitor with clinically meaningful health-related quality of life benefits, this new treatment option could further empower physicians to better personalize care and improve outcomes for their patients," said Fred Saad, M.D., Professor and Chairman of Surgery and Director of Genitourinary Oncology at the University of Montreal Hospital Center (CHUM), and Principal Investigator of the ARANOTE trial.

A final decision on marketing authorization from the European Commission is anticipated in the coming months. The U.S. Food and Drug Administration (FDA) recently approved darolutamide in combination with ADT for mHSPC in June 2025, making it the first in the US approved ARi for the treatment of patients with mHSPC, in combination with ADT, with or without chemotherapy. Darolutamide, under the brand name Nubeqa™, is approved in over 85 countries for use with ADT and docetaxel in mHSPC, and with ADT alone in non-metastatic castration-resistant prostate cancer (nmCRPC) in patients who are at high risk of developing metastatic disease.

Prostate cancer is the second most common cancer and the fifth most common cause of cancer death in men worldwide. In 2022, an estimated 1.5 million men were diagnosed with prostate cancer, and about 397,000 died from the disease worldwide. In Europe, there were almost 474,000 estimated new cases of prostate cancer in 2022 with approximately 115,000 deaths. Prostate cancer diagnoses are projected to increase to 2.9 million by 2040.

Darolutamide is developed jointly by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company.

About the ARANOTE Trial

The ARANOTE trial is a randomized, double-blind, placebo-controlled Phase III study designed to assess the efficacy and safety of darolutamide plus ADT in patients with mHSPC. 669 patients were randomized 2:1 to receive 600 mg of darolutamide twice daily or matching placebo in addition to ADT.

The primary endpoint is radiological progression free survival (rPFS), measured as time from randomization to date of first documented radiological progressive disease or death due to any cause, whichever occurs first. Secondary endpoints include overall survival (time to death from any cause), time to first castration resistant event, time to initiation of subsequent anti-cancer therapy, time to prostate-specific antigen (PSA) progression, PSA undetectable rates, time to pain progression, and safety assessments.

Results from the Phase III ARANOTE trial presented at ESMO 2024 and published in *The Journal of Clinical Oncology* showed that darolutamide plus ADT significantly reduced the risk of radiological progression or death by 46% compared to placebo plus ADT (HR 0.54; 95% CI 0.41–0.71; P<0.0001), in patients with mHSPC. Consistent benefits in rPFS were observed across prespecified subgroups, including patients with high-volume (HR 0.60, 95% CI: 0.44-0.80) and low-volume (HR 0.30, 95% CI: 0.15-0.60) mHSPC. The incidence of all adverse events (AE), including the incidence of serious and grade 3 and grade 4 AE, in the treatment group with darolutamide plus ADT in the ARANOTE study was comparable to placebo plus ADT. Darolutamide plus ADT was generally well tolerated and showed lower discontinuation rates due to adverse events compared to placebo plus ADT.

About darolutamide (Nubeqa™)
Darolutamide is an oral ARi with a unique chemical structure that binds with high affinity to the androgen receptor and exhibits a strong antagonistic effect against the androgen receptor inhibiting the receptor function and growth of prostate cancer cells. Additionally, preclinical models and neuroimaging data in healthy humans, support darolutamide's low potential for blood-brain barrier penetration.

Darolutamide (plus ADT or plus ADT and docetaxel) demonstrated a side effect profile, in both mHSPC registrational studies where the incidences of adverse events were similar to the respective comparator arm. With this tolerability profile and limited risk of interactions with other medications, Nubeqa offers an advancement in treatment management for physicians and patients.

A robust clinical development program is underway investigating darolutamide across various stages of prostate cancer. The program includes the Phase III ARASTEP trial evaluating darolutamide plus ADT compared to ADT alone in hormone-sensitive high-risk biochemical recurrence (BCR) prostate cancer, who have no evidence of metastatic

disease by conventional imaging and a positive PSMA PET/CT at baseline. Furthermore, darolutamide is also being investigated in the collaborative Phase III DASL-HiCaP (ANZUP1801) trial led by the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP). The study evaluates darolutamide as a treatment for localized prostate cancer in combination with radiotherapy.

About Metastatic Hormone-Sensitive Prostate Cancer

At the time of diagnosis, most men have localized prostate cancer, meaning their cancer is confined to the prostate gland and can be treated with curative surgery or radiotherapy. mHSPC is a stage in the disease where the cancer has spread outside of the prostate to other parts of the body. Up to 10% of men will present with mHSPC when first diagnosed. For patients with mHSPC, ADT is the cornerstone of treatment, in combination with chemotherapy docetaxel and/or an ARi.

Despite treatment, most men with mHSPC will eventually progress to castration-resistant prostate cancer, a condition with limited survival.

About Prostate Cancer at Bayer

Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The company has the passion and determination to develop new medicines that help improve and extend the lives of people living with cancer. Prostate cancer is the second most commonly diagnosed cancer in men and a key area of focus for Bayer. The company’s franchise includes two products on the market (Nubeqa™ and Xofigo™) and several compounds in development. Bayer is focused on addressing the unique needs of patients with prostate cancer, providing treatments that extend their lives throughout the different stages of the disease and allowing them to continue with their everyday activities, so that patients can live longer, better lives.

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. In line with its mission, “Health for all, Hunger for none,” the company’s products and services are designed to help people and the planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to driving sustainable development and generating a positive impact with its businesses. At the same time, the Group aims to increase its earning power and create value through innovation and growth. The Bayer brand stands

for trust, reliability and quality throughout the world. In fiscal 2024, the Group employed around 93,000 people and had sales of 46.6 billion euros. R&D expenses amounted to 6.2 billion euros. For more information, go to www.bayer.com.

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