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News Release

Not intended for U.S. and UK Media

Bayer submits application to U.S. FDA for third indication of darolutamide

- Submission is based on positive results from the pivotal Phase III ARANOTE trial which showed that darolutamide plus androgen deprivation therapy (ADT) significantly reduced the risk of radiological progression or death by 46% compared to placebo plus ADT in patients with metastatic hormone-sensitive prostate cancer (mHSPC)
- Darolutamide plus ADT now has positive data both with and without docetaxel based on two pivotal Phase III studies in patients with mHSPC
- If regulatory approval is granted in this additional indication in the U.S., physicians could have greater flexibility to tailor treatment to individual patient needs

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Berlin, September 26, 2024 – Bayer today announced the submission of a supplemental new drug application (sNDA) to the U.S. Food and Drug Administration (FDA) for the oral androgen receptor inhibitor (ARi) darolutamide. Bayer is seeking approval for the use of darolutamide in combination with androgen deprivation therapy (ADT) in patients with metastatic hormone-sensitive prostate cancer (mHSPC). The compound is already approved in mHSPC, under the brand name Nubeqa™, in combination with ADT and docetaxel in over 80 markets around the world. The compound is also approved in combination with ADT for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease in more than 85 countries around the world. In September 2024, sales of Nubeqa exceeded sales of one billion euros year-to-date.

“Our ambition is to redefine what it means to live with prostate cancer at different stages of the disease, extending survival and delaying disease progression, while maintaining daily living,” said Christine Roth, Executive Vice President, Global Product Strategy and Commercialization and Member of the Pharmaceuticals Leadership Team at Bayer. “This supplemental new drug application is important to us because we want to offer physicians

suitable options to tailor treatment plans for prostate cancer based on a patient's individual need."

Results from the Phase III ARANOTE trial 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 radiological progression-free survival (rPFS) were observed across prespecified subgroups, including patients with high- and low-volume mHSPC. Treatment-emergent adverse events (TEAEs) were low and similar between treatment groups and the safety analysis reconfirmed the established tolerability profile of darolutamide as observed in the ARAMIS and ARASENS trials. The ARANOTE results were simultaneously presented at the 2024 ESMO Congress and published in *The Journal of Clinical Oncology*.

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 to receive 600 mg of darolutamide twice daily or matching placebo in addition to ADT.

The primary endpoint of this study is 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.

About darolutamide (Nubeqa™)
Darolutamide is an oral ARi with a distinct chemical structure that binds to the androgen receptor with high affinity and exhibits strong antagonistic activity, thereby inhibiting the receptor function and the growth of prostate cancer cells while minimizing side effects. Darolutamide also reduces the risk of interactions with other medications. The low potential for blood-brain barrier penetration for darolutamide is supported by preclinical

models and neuroimaging data in healthy humans. This is also supported by the overall low incidence of central nervous system (CNS)-related adverse events (AEs) compared to placebo as seen in the ARAMIS Phase III trial and the maintained verbal learning and memory observed in the darolutamide arm of the Phase II ODENZA trial.

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 an adjuvant treatment for localized prostate cancer with very high risk of recurrence.

About Metastatic Hormone-Sensitive Prostate Cancer

Prostate cancer is the second most common cancer in men and the fifth most common cause of cancer death in men worldwide.[1] In 2022, an estimated 1.5 million men were diagnosed with prostate cancer, and about 397,000 died from the disease worldwide.[1] Prostate cancer diagnoses are projected to increase to 2.9 million by 2040.[2]

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.[3,4,5] For patients with mHSPC, ADT is the cornerstone of treatment, often in combination with chemotherapy docetaxel and/or an androgen receptor inhibitor (ARi). Despite treatment, most men with mHSPC will eventually progress to castration-resistant prostate cancer (CRPC), 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[1] 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 2023, the Group employed around 100,000 people and had sales of 47.6 billion euros. R&D expenses before special items amounted to 5.8 billion euros. For more information, go to www.bayer.com.

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