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News Release

Not intended for U.S. and UK Media

U.S. FDA accepts supplemental new drug application (sNDA) and grants priority review for darolutamide in combination with docetaxel for metastatic hormone-sensitive prostate cancer (mHSPC)

Application is being reviewed concurrently among participating international health authorities under the FDA Oncology Center of Excellence's (OCE) Project Orbis initiative

Berlin, May 3, 2022 – Bayer today announced the U.S. Food and Drug Administration (FDA) has accepted a supplemental New Drug Application (sNDA) and granted Priority Review for the oral androgen receptor inhibitor (ARi) darolutamide in combination with docetaxel for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC).

The application is being conducted under the FDA Oncology Center of Excellence's (OCE) Project Orbis initiative, which provides a framework for concurrent submission and review of cancer treatments among participating international health authorities.

"Bayer remains dedicated to addressing unmet needs in prostate cancer treatment for various stages of the disease," said Christine Roth, Member of the Executive Committee of Bayer's Pharmaceutical Division and Head of the Oncology SBU at Bayer. "Today's sNDA acceptance, confirmation of Priority Review and participation in Project Orbis, bring us closer to adding a new indication for darolutamide in combination with docetaxel to benefit men with mHSPC."

The sNDA is based on positive results from the pivotal Phase III ARASENS trial demonstrating a statistically significant improvement in overall survival (OS) for darolutamide plus androgen deprivation therapy (ADT) and docetaxel in men with mHSPC compared to ADT plus docetaxel, which were published in *The New England*

Journal of Medicine. Darolutamide is already approved in more than 60 markets around the world, including the U.S., the European Union (EU), Japan and China, under the brand name Nubeqa™, for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC), who are at high risk of developing metastatic disease.

Darolutamide is developed jointly by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company. Bayer recently submitted applications to the European Medicine Agency (EMA), the Ministry of Health, Labor and Welfare (MHLW) in Japan, and China's Center of Drug Evaluation (CDE). Additional submissions in mHSPC are planned globally.

About the ARASENS Trial

The ARASENS trial is the only randomized, Phase III, multi-center, double-blind trial which was prospectively designed to compare the use of a second-generation oral androgen receptor inhibitor (ARi) plus androgen deprivation therapy (ADT) and docetaxel to ADT plus docetaxel (a guideline recommended standard-of-care) in metastatic hormone-sensitive prostate cancer (mHSPC). A total of 1,306 newly diagnosed patients were randomized in a 1:1 ratio to receive 600 mg of darolutamide twice a day or matching placebo, plus ADT and docetaxel.

The primary endpoint of this trial was overall survival (OS). Secondary endpoints included time to castration-resistant prostate cancer (CRPC), time to pain progression, time to first symptomatic skeletal event (SSE), time to initiation of subsequent anticancer therapy, all measured at 12-week intervals, as well as adverse events (AEs) as a measure of safety and tolerability.

About Metastatic Hormone-Sensitive Prostate Cancer

Prostate cancer is the second most commonly diagnosed malignancy in men worldwide. In 2020, an estimated 1.4 million men were diagnosed with prostate cancer, and about 375,000 died from the disease worldwide.[1]

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. Upon relapse, when the disease will metastasize or spread, the disease is hormone-sensitive and androgen deprivation therapy (ADT) is the cornerstone of treatment. Current

treatment options for men with metastatic hormone-sensitive prostate cancer (mHSPC) include hormone therapy, such as ADT, androgen receptor pathway inhibitors plus ADT or a combination of docetaxel chemotherapy and ADT. Despite these treatments, a large proportion of men with mHSPC will eventually experience progression to metastatic castration-resistant prostate cancer (mCRPC), a condition with high morbidity and limited survival.

About Nubeqa™ (darolutamide)

Darolutamide is an oral androgen receptor inhibitor (ARi) with a distinct chemical structure that binds to the receptor with high affinity and exhibits strong antagonistic activity, thereby inhibiting the receptor function and the growth of prostate cancer cells. The low potential for blood-brain barrier penetration for darolutamide is supported by preclinical models and neuroimaging data in healthy humans. A low blood-brain barrier penetration would explain 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 improved verbal learning and memory observed in the darolutamide arm of the Phase II ODENZA trial.

The product is approved under the brand name Nubeqa™ in more than 60 markets around the world, including the U.S., EU, Japan, China, for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC), who are at high risk of developing metastatic disease. The compound is also being investigated in further studies across various stages of prostate cancer, including in the ARANOTE Phase III trial evaluating darolutamide plus androgen deprivation therapy (ADT) versus ADT alone for metastatic hormone-sensitive prostate cancer (mHSPC), as well as in the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) led international Phase III co-operative group DASL-HiCaP (ANZUP1801) trial evaluating darolutamide as an adjuvant treatment for localized prostate cancer with very high risk of recurrence. Information about these trials can be found at www.clinicaltrials.gov.

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, including a unique approach of advancing targeted alpha therapies. Bayer is focused on addressing the unique needs of prostate cancer patients, providing treatments that extend their lives throughout the different stages of the disease and allowing them to continue their everyday activities, so that they 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. Its products and services are designed to help people and planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to drive sustainable development and generate 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 2021, the Group employed around 100,000 people and had sales of 44.1 billion euros. R&D expenses before special items amounted to 5.3 billion euros. For more information, go to www.bayer.com.

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Forward-Looking Statements
This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

Reference

1. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: *A Cancer Journal for Clinicians*. https://acsjournals.onlinelibrary.wiley.com/doi/epdf/10.3322/caac.21660. Accessed March 2022.