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News Release

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Nubeqa™ approved for additional indication in Japan

- Darolutamide approved for metastatic prostate cancer as well as non-metastatic castration-resistant prostate cancer
- New approval based on data from the pivotal Phase III ARASENS trial

Berlin, February 27, 2023 – The Ministry of Health, Labor and Welfare (MHLW) in Japan has approved the oral androgen receptor inhibitor (ARi) darolutamide plus ADT in combination with docetaxel in the indication of metastatic prostate cancer. The MHLW approval is based on the positive results from the Phase III ARASENS trial, which demonstrated that darolutamide plus androgen deprivation therapy (ADT) in combination with docetaxel significantly reduced the risk of death by 32.5% compared to ADT with docetaxel, in patients with metastatic hormone-sensitive prostate cancer (mHSPC). Additionally, the darolutamide combination showed consistent benefits across clinically relevant secondary endpoints, with the overall incidence of treatment-emergent adverse events being similar between treatment arms. These results were published in *The New England Journal of Medicine*.[1]

Darolutamide is already approved in Japan for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC) under the brand name Nubeqa™.

“The number of prostate cancer patients in Japan has increased rapidly in recent years, almost doubling in the past decade. As many patients with metastatic prostate cancer still lead active lifestyles, we are delighted to provide patients in Japan with a new treatment option that extends survival and delays disease progression whilst maintaining quality of life,” said Christine Roth, Member of the Executive Committee of Bayer’s Pharmaceuticals Division and Head of the Oncology SBU at Bayer. “At Bayer, we continue in our mission

to redefine what it means to live with prostate cancer, so that those living with the disease can have more quality moments with their loved ones."

Darolutamide plus ADT in combination with docetaxel was recently recommended for EU marketing authorization for the treatment of mHSPC by the European Medicine Agency's Committee for Medicinal Products for Human Use (CHMP), with a final decision expected in the coming months. The compound is already approved in its second indication, mHSPC, in a number of markets including the U.S. under the brand name Nubeqa. Filings in other regions are underway or planned.

Darolutamide is being investigated in a broad development program with three additional ongoing or planned large clinical studies, to evaluate its potential across prostate cancer patients from the early- to the late-stage of this disease. This includes the ARANOTE Phase III trial evaluating darolutamide plus androgen deprivation therapy (ADT) versus ADT alone for mHSPC.

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

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), darolutamide, plus ADT in combination with 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 in combination with 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 evaluated at 12-week intervals, as well as adverse events (AEs) as a measure of safety and tolerability. Results from this trial were published in the *New England Journal of Medicine*.[1] A plain language summary publication of these data was published in *Future Oncology*.[2] The ARASENS trial demonstrated that darolutamide plus ADT in combination with docetaxel significantly reduced the risk of death by 32.5% compared to ADT with

docetaxel alone.[1] Improvements in the secondary endpoints supported the benefit observed in the primary endpoint, overall survival.[1]

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.[3]

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, or if the disease is newly diagnosed, but has already 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 the 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. This is 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[4] and the improved verbal learning and memory observed in the darolutamide arm of the Phase II ODENZA trial.[5]

The product is approved under the brand name Nubeqa™ in more than 80 countries around the world, including the U.S., EU, Japan and China, for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC), who are at high risk of developing metastatic disease. It is also approved for the treatment of patients with metastatic hormone-sensitive prostate cancer (mHSPC) in a number of markets including the U.S. Filings in other regions are underway or planned. Bayer expects the peak sales potential for Nubeqa to exceed €3 billion. 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 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. In addition, a study to explore the potential of darolutamide in the early setting for patients who have experienced a rise in their prostate specific antigen (PSA) levels following surgery or radiation, is also planned.

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[3] 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 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 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

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Reference

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