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News Release

Not intended for U.S. and UK Media

Bayer submits application for additional indication of Nubeqa™ (darolutamide) in Japan

- Submission to the Ministry of Health, Labor and Welfare (MHLW) in Japan for an additional indication of darolutamide in prostate cancer with distant metastases
- Application is based on data from the pivotal Phase III ARASENS trial, in which the use of darolutamide plus ADT and docetaxel showed a statistically significant improvement in overall survival as well as consistent benefits in secondary endpoints in patients with metastatic hormone-sensitive prostate cancer (mHSPC), with the overall incidence of treatment-emergent adverse events being similar between treatment arms
- Additional submissions in other regions planned or underway
- Broad development program underway with three additional ongoing or planned large clinical studies for darolutamide across a broad spectrum of prostate cancer

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Berlin, March 11, 2022 – Bayer today announced the submission to the Ministry of Health, Labor and Welfare (MHLW) in Japan for an additional indication for the oral androgen receptor inhibitor (ARi) darolutamide. The application seeks marketing authorization for darolutamide in combination with docetaxel and androgen deprivation therapy (ADT) for the treatment of patients with prostate cancer with distant metastasis. Darolutamide is already marketed 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.

The MHLW submission is based on positive results from the pivotal Phase III ARASENS trial recently presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) and published in *The New England Journal of Medicine*. Results demonstrated a statistically significant improvement in overall survival for

darolutamide plus ADT and docetaxel compared to ADT plus docetaxel in men with metastatic hormone-sensitive prostate cancer (mHSPC).

“Prostate cancer is the most common new cancer diagnosis in Japanese men annually. Despite treatment advancements, for a large proportion of patients living with mHSPC, their disease will progress within 2-3 years. This highlights the unmet medical need for new and differentiated therapeutic options earlier in the patient’s treatment journey,” said Christine Roth, Member of the Executive Committee of Bayer’s Pharmaceutical Division and Head of the Oncology Strategic Business Unit at Bayer. “The submission to the MHLW for darolutamide in this new indication is an important next step in Bayer’s commitment to bring forward a potential new therapy for eligible patients with mHSPC to extend lives and delay disease progression, while providing a promising safety profile.”

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

Additional filings for the indication of mHSPC have been made in the US and in the EU, and filings in additional regions are underway or planned. The compound is also being investigated in further studies across various stages of prostate cancer, including another Phase III trial in mHSPC (ARANOTE) as well as an ANZUP-led international co-operative group Phase III trial, evaluating darolutamide as an adjuvant treatment for localized prostate cancer with very high risk of recurrence (DASL-HiCaP, ANZUP1801).

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 ARi plus ADT and docetaxel to ADT plus docetaxel (a guideline recommended standard-of-care) in 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, androgen deprivation therapy (ADT) is the cornerstone of treatment for this hormone-sensitive disease. Approximately 5% of men will already suffer from prostate cancer with distant metastases when first diagnosed. 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 chemotherapy docetaxel and ADT. Despite these treatments, a large proportion of men with mHSPC will eventually progress to metastatic castration-resistant prostate cancer (mCRPC), a condition with 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 another Phase III trial in mHSPC (ARANOTE) as well as an ANZUP-led international co-operative group Phase III trial, evaluating darolutamide as an adjuvant treatment for localized prostate cancer with very high risk of recurrence (DASL-HiCaP, ANZUP1801). 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 men1 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
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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 February 2022.