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News Release

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Data from Phase III ARASENS trial presented at 2022 ASCO GU Cancers Symposium:

Darolutamide plus androgen deprivation therapy and docetaxel significantly increases overall survival in patients with metastatic hormone-sensitive prostate cancer

- Results from the Phase III ARASENS trial evaluating darolutamide plus androgen deprivation therapy (ADT) and docetaxel showed a statistically significant increase in overall survival with a reduction in the risk of death by 32.5% compared to ADT plus docetaxel (HR=0.68, 95% CI 0.57-0.80; P<0.001) in patients with metastatic hormone-sensitive prostate cancer (mHSPC)
 - Consistent benefits were also seen across secondary endpoints, which are of key relevance to patients, such as delaying the time to castration-resistant prostate cancer (CRPC), time to pain progression, time to first symptomatic skeletal event (SSE) and time to initiation of subsequent systemic antineoplastic therapy
 - Overall incidence of treatment-emergent adverse events (TEAEs) was similar between treatment arms
 - First results from the pivotal Phase III ARASENS trial presented as an oral presentation at the 2022 ASCO GU Cancers Symposium and simultaneously published in *The New England Journal of Medicine*
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Abstract: 13

Berlin, February 17, 2022 – Results from the Phase III ARASENS trial have shown that the use of the oral androgen receptor inhibitor (ARi) darolutamide plus androgen deprivation therapy (ADT) and docetaxel significantly increased overall survival (OS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC) compared to ADT plus docetaxel. Darolutamide plus ADT and docetaxel significantly reduced the risk of death by 32.5% compared to ADT plus docetaxel (HR=0.68, 95% CI 0.57-0.80; P<0.001). At the data cutoff date for the primary analysis (October 25, 2021), the median treatment

duration was longer for darolutamide plus ADT and docetaxel (41.0 months) versus ADT plus docetaxel (16.7 months). Darolutamide plus ADT and docetaxel also showed consistent benefits for secondary endpoints and pre-specified subgroups. Adverse event (AE) rates were not increased by the addition of darolutamide. These results were presented at the [2022 ASCO GU Cancers Symposium](#) and simultaneously published in *The New England Journal of Medicine*.

“Metastatic prostate cancer is a uniformly fatal disease and despite progress in recent years, only 30% of these men will survive beyond five years. ARASENS demonstrated that the addition of darolutamide, an androgen receptor inhibitor, significantly increased overall survival for patients receiving standard androgen deprivation therapy and docetaxel as initial treatment for metastatic hormone-sensitive prostate cancer. Darolutamide also improved time to castration-resistant prostate cancer and other key secondary endpoints,” said Matthew Smith, M.D., Ph.D., Director of the Genitourinary Malignancies Program, Massachusetts General Hospital Cancer Center. “These results are an important step forward for the treatment of patients with metastatic hormone-sensitive prostate cancer.”

“With the ARASENS results in mHSPC adding to the existing Phase III ARAMIS data in non-metastatic castration-resistant prostate cancer (nmCRPC), darolutamide has now shown positive data in two pivotal clinical trials for patients across these key disease stages in prostate cancer,” said Robert LaCaze, Member of the Executive Committee of Bayer’s Pharmaceutical Division and Head of the Oncology SBU at Bayer. “We believe darolutamide has the potential to become a foundational drug for appropriate prostate cancer patients. We are committed to making this potential new treatment option in mHSPC available to patients and their treating physicians, and therefore are pursuing the fastest possible regulatory timelines.”

ARASENS is the only randomized, double-blind pivotal study 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.

Darolutamide is 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 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. 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).

Detailed results from ARASENS

The significant improvement in OS was observed despite substantially higher use of subsequent systemic antineoplastic therapies (such as abiraterone, enzalutamide, cabazitaxel, docetaxel, radium-223 dichloride, sipuleucel-T, lutetium-177 PSMA, or apalutamide) among patients receiving ADT plus docetaxel who entered follow-up (75.6%) compared with the group who received darolutamide plus ADT and docetaxel (56.8%). The ARASENS data also showed consistent improvements in key secondary endpoints including delaying the time to CRPC compared to the placebo arm (HR=0.36, 95% CI 0.30-0.42; P<0.001). Darolutamide plus ADT and docetaxel also significantly delayed time to pain progression versus ADT plus docetaxel (HR=0.79, 95% CI 0.66-0.95; P=0.01), time to first symptomatic skeletal event (SSE) (HR=0.71, 95% CI 0.54-0.94; P=0.02) and time to initiation of subsequent systemic antineoplastic therapy (HR=0.39, 95% CI 0.33-0.46; P<0.001).

Treatment-emergent adverse events (TEAEs) were similar between treatment arms. The most common TEAEs (≥10%) were highest during the overlapping docetaxel treatment period for both arms and decreased progressively thereafter. The most frequently reported AEs in the treatment arms (darolutamide plus ADT and docetaxel versus ADT plus docetaxel) were alopecia (40.5% and 40.6%, respectively), neutropenia (39.3% and 38.8, respectively), fatigue (33.1% and 32.9%, respectively) and anemia (27.8% and 25.1%, respectively). Grade 3 or 4 AEs reported in 66.1% versus 63.5% of patients were mainly due to neutropenia (33.7% versus 34.2%, respectively), which is a well-known effect of docetaxel treatment. Serious AEs occurred in 44.8% versus 42.3% of patients, and TEAEs leading to treatment discontinuation occurred in 13.5% versus 10.6% of patients.

AEs of special interest in patients treated with AR pathway inhibitors for prostate cancer such as fatigue, falls, fractures, mental impairment, and cardiovascular events were similar between study arms.

About the ARASENS Trial

The ARASENS trial is a randomized, Phase III, multi-center, double-blind, placebo-controlled trial which was prospectively designed to investigate the efficacy and safety of oral darolutamide, an androgen receptor inhibitor (ARi), plus androgen deprivation therapy (ADT) and the chemotherapy docetaxel in patients with 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, 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, most 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 2020, the Group employed

around 100,000 people and had sales of 41.4 billion euros. R&D expenses before special items amounted to 4.9 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.