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News Release

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Bayer's darolutamide plus androgen deprivation therapy (ADT) significantly extends metastasis-free survival with a favorable safety profile compared to placebo plus ADT in non-metastatic castration-resistant prostate cancer

- Statistically significant improvement in metastasis-free survival (MFS), with a median MFS of 40.4 months with darolutamide plus androgen deprivation therapy (ADT) versus placebo plus ADT (18.4 months)
- Positive trend in overall survival with a 29% reduction in risk of death at interim analysis (P=0.045)
- Incidence of treatment-emergent adverse events was similar for darolutamide plus ADT and placebo plus ADT
- Health-related quality of life was maintained
- First results from the Phase III ARAMIS trial with the androgen receptor antagonist darolutamide were presented in an oral presentation at American Society of Clinical Oncology Genitourinary Cancers Symposium and simultaneously published in *The New England Journal of Medicine*

Abstract: *140*

Berlin, February 14, 2019 – Results from the pivotal Phase III ARAMIS trial in patients with non-metastatic castration-resistant prostate cancer (nmCRPC) showed a statistically significant improvement in metastasis-free survival (MFS) with darolutamide plus androgen deprivation therapy (ADT) compared to placebo plus ADT (HR=0.41, 95% CI 0.34-0.50; P<0.001). This translates to a 59 percent reduction in the risk of metastasis or

death. The median MFS was 40.4 months in the darolutamide arm compared with 18.4 months for the placebo arm – an overall improvement in median MFS of 22 months.

A positive trend in overall survival (OS) was also observed (HR=0.71, 95% CI 0.50-0.99; P=0.045), and all other secondary endpoints demonstrated a benefit in favor of darolutamide. Importantly, the incidence of treatment-emergent adverse events (AEs) with greater than or equal to 5 percent frequency or of grade 3–5 was comparable between darolutamide and placebo arms; only fatigue occurred in more than 10 percent of patients (darolutamide plus ADT resulted in 12.1 percent versus 8.7 percent in patients with placebo plus ADT). Quality of life outcomes were similar between the treatment groups.

These data were presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) in San Francisco and published simultaneously in *The New England Journal of Medicine.*

“In addition to a benefit in MFS, a favorable safety profile is critical for these largely asymptomatic nmCRPC patients because treatment decisions can impact their overall well-being, prognosis and compliance with the treatment as well as other medications that are typical for this patient population. These data are exciting for the prostate cancer community; they not only show darolutamide’s significant efficacy in preventing the spread of prostate cancer, but also its favorable tolerability profile that, once approved, may allow patients to continue their day-to-day life without adding any burden,” said Karim Fizazi, M.D., Ph.D., Professor of Medicine at the Institut Gustave Roussy, University of Paris Sud, France.

“While many new treatment options in the field of prostate cancer have been developed in recent years, gaps persist, particularly in providing patients with treatments that are both effective and have a safety profile that does not constitute an additional toxicity burden in their lives,” said Scott Z. Fields, M.D., senior vice president and head of Oncology Development at Bayer's Pharmaceutical Division. “Bayer is working diligently to bring innovative, efficacious and tolerable treatments to patients in need. With the positive results of the ARAMIS trial, we are one step closer to our goal of bringing darolutamide to patients and physicians.”

Bayer plans to discuss the data from the ARAMIS trial with health authorities regarding the submission of new drug applications. Bayer has been granted Fast Track designation

by the U.S. Food and Drug Administration (FDA) for darolutamide in men with nmCRPC. Darolutamide is being developed jointly by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company.

Detailed study results

The MFS benefit observed with darolutamide was consistent across all subgroups of patients. In an interim analysis of OS, darolutamide showed a positive trend, with a 29 percent reduction in the risk of death (HR=0.71, 95% CI 0.50-0.99; P=0.045, median not reached).

In addition, darolutamide plus ADT demonstrated a significant benefit over placebo plus ADT for time to pain progression (40.3 months compared to 25.4 months; HR=0.65, 95% CI 0.53-0.79; P<0.001) and time to cytotoxic chemotherapy (median not reached compared to 38.2; HR=0.43, 95% CI 0.31-0.60; P<0.001). Another secondary endpoint, time to first symptomatic skeletal event (SSE), also demonstrated a benefit in favor of darolutamide (median not reached). Darolutamide extended progression-free survival (PFS) (36.8 months compared to 14.8 months; HR=0.38, 95% CI 0.32-0.45; P<0.001), with a 62 percent risk reduction of local progression, distant metastases or death.

Incidence of treatment-emergent AEs was similar between darolutamide and placebo; most AEs were grade 1 and 2 (55 percent with darolutamide plus ADT and 54 percent with placebo plus ADT). Compared to placebo plus ADT, darolutamide plus ADT did not increase rates of critical AEs including, but not limited to, seizures, falls, fractures, rash, cognitive disorder, mental impairment or hypertension. Patients with a history of seizure were not excluded from the study.

The results of Patient Reported Outcomes (PRO)-based endpoints (based on the Functional Assessment of Cancer Therapy-Prostate; FACT-P, European Organisation for Research and Treatment of Cancer quality of life; EORTC-QLQ-PR25, and EQ-5D-3L questionnaires) demonstrated maintenance of health-related quality of life (HRQoL) with a positive trend favoring darolutamide over placebo.

About the ARAMIS trial design

The ARAMIS trial is a randomized, Phase III, multi-center, double-blind, placebo-controlled trial evaluating the safety and efficacy of oral darolutamide in patients with

nmCRPC who are currently being treated with ADT as standard of care and are at high risk for developing metastatic disease. 1,509 patients were randomized in a 2:1 ratio to receive 600 mg of darolutamide twice a day or placebo along with ADT.

The primary endpoint of this trial is MFS defined as time between randomization and evidence of metastasis or death. The secondary endpoints of this trial are OS, time to pain progression, time to initiation of first cytotoxic chemotherapy, time to first SSE, and characterization of the safety and tolerability of darolutamide.

About castration-resistant prostate cancer (CRPC)

Prostate cancer is the second most commonly diagnosed malignancy in men worldwide. In 2018, an estimated 1.2 million men were diagnosed with prostate cancer, and about 358,000 died from the disease worldwide. Prostate cancer is the fifth leading cause of death from cancer in men. Prostate cancer results from the abnormal proliferation of cells within the prostate gland, which is part of a man´s reproductive system. It mainly affects men over the age of 50, and the risk increases with age. Treatment options range from surgery to radiation treatment to therapy using hormone-receptor antagonists, i.e. substances that stop the formation of testosterone or prevent its effect at the target location. However, in nearly all cases, the cancer eventually becomes resistant to conventional hormone therapy.

CRPC is an advanced form of the disease where the cancer keeps progressing even when the amount of testosterone is reduced to very low levels in the body. The field of treatment options for castration-resistant patients is evolving rapidly, but until recently, there have been no effective treatment options for CRPC patients who have rising prostate-specific antigen (PSA) levels while on ADT and no detectable metastases. In men with progressive nmCRPC, a short PSA doubling time has been consistently associated with reduced time to first metastasis and death.

About darolutamide

Darolutamide is a non-steroidal androgen receptor antagonist 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. In addition to the Phase III trial ARAMIS in men with nmCRPC, darolutamide is also being investigated in a Phase III study in metastatic hormone-sensitive prostate cancer

(ARASENS). Information about these trials can be found at www.clinicaltrials.gov.

Darolutamide is not approved by the U.S. FDA, the European Medicines Agency or any other health authority.

About Oncology at Bayer
Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The oncology franchise at Bayer includes five marketed products and several other assets in various stages of clinical development. Together, these products reflect the company's approach to research, which prioritizes targets and pathways with the potential to impact the way that cancer is treated.

About Bayer
Bayer is a global enterprise with core competencies in the Life Science fields of health care and agriculture. Its products and services are designed to benefit people and improve their quality of life. At the same time, the Group aims to create value through innovation, growth and high earning power. Bayer is committed to the principles of sustainable development and to its social and ethical responsibilities as a corporate citizen. In fiscal 2017, the Group employed around 99,800 people and had sales of EUR 35.0 billion. Capital expenditures amounted to EUR 2.4 billion, R&D expenses to EUR 4.5 billion. For more information, go to www.bayer.com.

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Forward-Looking Statements
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