Investor News

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2019 American Society of Clinical Oncology (ASCO) Annual Meeting

Bayer's darolutamide plus androgen deprivation therapy (ADT) delays worsening of disease-related symptoms and maintains quality of life beyond end of study treatment compared to placebo plus ADT in men with non-metastatic castration-resistant prostate cancer

- Results of a new post-hoc analysis showed that treatment with darolutamide plus androgen deprivation therapy (ADT) delayed worsening of urinary and bowel symptoms versus placebo plus ADT
- Exposure-adjusted incidences of treatment-emergent adverse events (TEAEs), including notably TEAEs associated with androgen receptor (AR) antagonists, were generally similar for darolutamide plus ADT compared to placebo plus ADT
- Darolutamide plus ADT maintained quality of life in men with non-metastatic castration-resistant prostate cancer (nmCRPC) beyond end of study treatment with scores similar to placebo plus ADT
- Analysis on quality of life related endpoints from pivotal Phase III ARAMIS trial presented at the American Society of Clinical Oncology (ASCO) Annual Meeting as an oral presentation on May 31, 2019
- Darolutamide is under Priority Review in the U.S., and has been filed in Europe, Japan and additional countries

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Abstract: *5000*

Leverkusen, Germany, May 31, 2019 – Darolutamide plus androgen deprivation therapy (ADT) delays worsening of disease-related symptoms in men with non-metastatic castration-resistant prostate cancer (nmCRPC) compared with placebo plus ADT, according to exploratory data from the pivotal Phase III ARAMIS trial presented in an oral presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting in

Chicago. Exposure-adjusted incidences of TEAEs including notably TEAEs associated with androgen receptor (AR) antagonists, were generally similar with darolutamide plus ADT versus placebo plus ADT. Data also indicate that darolutamide plus ADT maintained quality of life, compared to placebo plus ADT even beyond the end of study treatment. Primary results of this study have been previously published in the *New England Journal of Medicine*. Based on the study results, the U.S. Food and Drug Administration (FDA) granted Priority Review for the New Drug Application (NDA) for darolutamide in April 2019, and Bayer has filed for approval in the European Union (EU), Japan, as well as other health authorities. Darolutamide is being developed jointly by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company.

“At this stage of prostate cancer when men typically feel well and generally do not have symptoms, it is important that we have potential treatment options that will prevent the spread of prostate cancer for as long as possible, while limiting burdensome side effects of therapy, which allows patients to continue their day-to-day lives,” said Karim Fizazi, M.D., Ph.D., Professor of Medicine at the Institut Gustave Roussy, University of Paris Sud, France. “These new data demonstrate darolutamide’s ability to maintain patients’ quality of life while receiving treatment. When you add these findings to previously reported data, the product has the potential to become an important treatment option for men with nmCRPC.”

“These additional analyses from the pivotal phase III ARAMIS trial are encouraging for the prostate cancer community who is in need for new therapeutic options that are effective and do not add additional toxicity burden to the patients. The data reaffirm the potential benefit that darolutamide can provide to men with nmCRPC. We continue to focus our efforts on bringing this new treatment to nmCRPC patients as soon as possible,” said Scott Z. Fields, M.D., Senior Vice President and Head of Oncology Development at Bayer's Pharmaceutical Division.

Darolutamide data presented at ASCO

In an analysis focusing on patient-relevant endpoints, data on the secondary endpoint of time to pain progression, assessed by the BPI-SF (Brief Pain Inventory – Short Form) patient questionnaire, show that darolutamide plus ADT delayed worsening of pain in men with nmCRPC versus placebo plus ADT (40.3 versus 25.4 months; HR 0.65; 95% CI 0.53–0.79; P<0.0001). At this interim analysis, the results are not statistically significant.

In a pre-planned analysis on the FACT-P PCS (Functional Assessment of Cancer Therapy – Prostate, Prostate Cancer Subscale) questionnaire, quality of life was maintained in men receiving treatment with darolutamide plus ADT, as demonstrated by mean scores from the FACT-P PCS. FACT-P PCS assesses both impact of disease- and treatment related symptoms on men's quality of life, and was assessed every 16 weeks until the end of study treatment, and at every visit thereafter until end of study or death. Mean scores were maintained and similar in both treatment arms throughout the study. At the end of treatment, the mean change from baseline of -8.55 with darolutamide plus ADT was similar to placebo plus ADT. The quality of life scores were maintained beyond the end of study treatment.

A new post-hoc analysis of the ARAMIS data shows that treatment with darolutamide plus ADT delays the onset of urinary and bowel symptoms in men with nmCRPC compared to placebo plus ADT (urinary symptoms: 25.8 versus 14.8 months; HR=0.64; 95% CI 0.54–0.76; P<0.01; bowel symptoms: 18.4 versus 11.5 months; HR=0.78; 95% CI 0.66-0.92; P<0.01), as shown by time to deterioration of symptoms in the European Organisation for Research and Treatment of Cancer QoL Prostate Cancer module (EORTC-QLQ-PR25). Statistical significance cannot be reported as these are exploratory endpoint data.

Exposure-adjusted incidences of treatment emergent adverse events (TEAEs), including notably TEAEs associated with AR antagonists, were generally similar with darolutamide plus ADT versus placebo plus ADT and included fatigue/asthenic conditions (11.3% versus 11.1%), hypertension (4.7% versus 5.1%), falls (3.0% versus 4.6%), cognitive disorder (0.3% versus 0.2%), and memory impairment (0.4% versus 1.2%).

About the ARAMIS trial

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 androgen deprivation therapy (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.

About darolutamide

Darolutamide is a non-steroidal androgen receptor (AR) 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 preclinical studies, darolutamide demonstrated lower blood-brain barrier penetration compared to other currently available AR antagonists.

In addition to the Phase III ARAMIS trial 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 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 rapid PSA doubling time has been consistently associated with reduced time to first metastasis and death.

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 nutrition. Its products and services are designed to benefit people by supporting efforts to overcome the major challenges presented by a growing and aging global population. At the same time, the Group aims to increase its earning power and create value through innovation and growth. Bayer is committed to the principles of sustainable development, and the Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2018, the Group employed around 117,000 people and had sales of 39.6 billion euros. Capital expenditures amounted to 2.6 billion euros, R&D expenses to 5.2 billion euros. For more information, go to www.bayer.com.

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