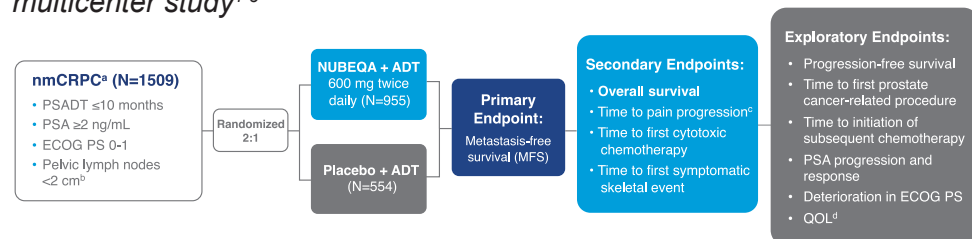


## NUBEQA is an androgen receptor inhibitor indicated for the treatment of adult patients with:

- Non-metastatic castration-resistant prostate cancer (nmCRPC)
- Metastatic castration-sensitive prostate cancer (mCSPC)
- Metastatic castration-sensitive prostate cancer (mCSPC) in combination with docetaxel

### ARAMIS Study Design<sup>1</sup>

Double-blind (DB), placebo-controlled, international, multicenter study<sup>1-3</sup>



- Treatment continued until radiographic disease progression as assessed by conventional imaging (CT, MRI, 99mTc bone scan) by blinded independent central review, discontinuation due to adverse reactions, or withdrawal of consent

“Following the primary analysis of the ARAMIS study, the trial was unblinded, enabling patients in both treatment arms to receive open-label NUBEQA. Upon study completion, patients without evidence of metastases who were experiencing clinical benefits were allowed to continue NUBEQA treatment under the ARAMIS ROS Design.<sup>2-4</sup>”

—Neal Shore, MD, FACS

### IMPORTANT SAFETY INFORMATION

#### Warnings & Precautions

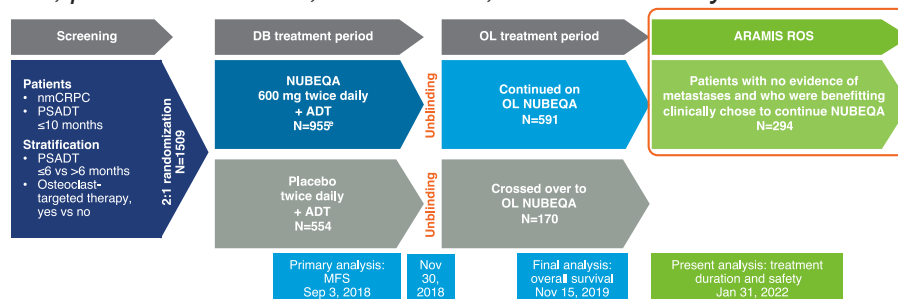
**Ischemic Heart Disease** – Ischemic heart disease, including fatal cases, occurred in patients receiving NUBEQA.

In a pooled analysis of ARAMIS and ARANOTE, ischemic heart disease occurred in 3.4% of patients receiving NUBEQA and 2.2% receiving placebo, including Grade 3-4 events in 1.4% and 0.3%, respectively. Ischemic events led to death in 0.4% of patients receiving NUBEQA and 0.4% receiving placebo.

Please see additional Important Safety Information on reverse side. For full Prescribing information, please visit [NUBEQA PI](#).

### ARAMIS Rollover Study (ROS) Design<sup>4</sup>

DB, placebo-controlled, international, multicenter study<sup>1-3</sup>



- In the ARAMIS study after the primary analysis, the study was unblinded, and patients in both treatment groups could receive open-label NUBEQA
- After study completion, patients with no evidence of metastases who were benefitting clinically could continue on NUBEQA in the ARAMIS ROS Design

<sup>a</sup>All patients received concurrent ADT (treatment with GnRH analog or previous bilateral orchiectomy).

<sup>b</sup>Lymph nodes located below the aortic bifurcation as measured by the short axis.

<sup>c</sup>Time to pain progression was defined as at least a 2-point worsening from baseline of pain score on BPI-SF (a validated health-related QOL instrument) or initiation of opioids and reported in 28% of all patients on study.

<sup>d</sup>Tools used to prespecify QOL exploratory endpoints are the EQ-5D-3L, a preference-based instrument, and the FACT-P, BPI-SF, and EORTC-QLQ-PR25 prostate-specific questionnaires.

<sup>e</sup>One patient initially randomized to receive NUBEQA did not receive treatment and is not included in the analyses presented here.

ADT; androgen deprivation therapy; BPI-SF, Brief Pain Inventory Short Form; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC-QLQ-PR25, European Organization for Research and Treatment of Cancer quality of life questionnaire, a 25-item questionnaire; EQ-5D-3L, EuroQoL Group 5-dimension 3-level; FACT-P, Functional Assessment of Cancer Therapy-Prostate; GnRH, gonadotropin-releasing hormone; MRI, magnetic resonance imaging; OL, open label; PSA, prostate-specific antigen; PSADT, prostate-specific antigen doubling time; QOL, quality of life; rPFS, radiographic progression-free survival.

In ARASENS, ischemic heart disease occurred in 3.2% of patients receiving NUBEQA with docetaxel and 2% receiving placebo with docetaxel, including Grade 3-4 events in 1.3% and 1.1%, respectively. Ischemic events led to death in 0.3% of patients receiving NUBEQA with docetaxel and 0% receiving placebo with docetaxel.

Monitor for signs and symptoms of ischemic heart disease. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue NUBEQA for Grade 3-4 ischemic heart disease.

# Additional IMPORTANT SAFETY INFORMATION



## Warnings & Precautions (cont.)

**Seizure** – Seizure occurred in patients receiving NUBEQA.

In a pooled analysis of ARAMIS and ARANOTE, Grade 1-3 seizure occurred in 0.2% of patients receiving NUBEQA. Seizure occurred from 261 to 665 days after initiation of NUBEQA.

In ARASENS, seizure occurred in 0.8% of patients receiving NUBEQA with docetaxel, including two Grade 3 events. Seizure occurred from 38 to 1754 days after initiation of NUBEQA.

It is unknown whether anti-epileptic medications will prevent seizures with NUBEQA. Advise patients of the risk of developing a seizure while receiving NUBEQA and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others. Consider discontinuation of NUBEQA in patients who develop a seizure during treatment.

**Embryo-Fetal Toxicity** – The safety and efficacy of NUBEQA have not been established in females. NUBEQA can cause fetal harm and loss of pregnancy. Advise males with female partners of reproductive potential to use effective contraception during treatment with NUBEQA and for 1 week after the last dose.

## Adverse Reactions

In ARAMIS, serious adverse reactions occurred in 25% of patients receiving NUBEQA and in 20% of patients receiving placebo. Serious adverse reactions in  $\geq 1\%$  of patients who received NUBEQA included urinary retention, pneumonia, and hematuria. Fatal adverse reactions occurred in 3.9% of patients receiving NUBEQA and 3.2% of patients receiving placebo. Fatal adverse reactions that occurred in  $\geq 2$  patients who received NUBEQA included death (0.4%), cardiac failure (0.3%), cardiac arrest (0.2%), general physical health deterioration (0.2%), and pulmonary embolism (0.2%). The most common ( $>2\%$  with a  $\geq 2\%$  increase compared to placebo) adverse reactions, including laboratory test abnormalities, were increased AST (23%), decreased neutrophil count (20%), fatigue (16%), increased bilirubin (16%), pain in extremity (6%), and rash (4%). Clinically relevant adverse reactions occurring in 2% or more of patients treated with NUBEQA included ischemic heart disease (4%) and heart failure (2.1%).

In ARANOTE, serious adverse reactions occurred in 24% of patients receiving NUBEQA. Serious adverse reactions in  $\geq 1\%$  of patients who received NUBEQA included pneumonia (2%), urinary tract infection (1.8%), musculoskeletal pain (1.6%), hemorrhage (1.6%), arrhythmias (1.3%), and spinal cord compression (1.1%). Fatal adverse reactions occurred in 4.7% of patients receiving NUBEQA and those that occurred in  $\geq 2$  patients included sepsis (1.1%), craniocerebral injury (0.4%), and myocardial infarction (0.4%). The most common ( $\geq 10\%$  with a  $\geq 2\%$  increase compared to placebo) adverse reaction is urinary tract infection (12%). The most common laboratory test abnormalities ( $\geq 15\%$  with a  $\geq 5\%$  increase over placebo) are increased AST (32%), increased ALT (28%), increased bilirubin (17%), and decreased neutrophil count (16%). Clinically relevant adverse reactions in  $<10\%$  of patients who received NUBEQA included arrhythmia (8.8%), pneumonia (3.6%), and myocardial infarction (0.7%).

In ARASENS, serious adverse reactions occurred in 45% of patients receiving NUBEQA with docetaxel. Serious adverse reactions in  $\geq 2\%$  of patients who received NUBEQA with docetaxel included febrile neutropenia (6%), neutrophil count decreased (2.8%), musculoskeletal pain (2.6%) and pneumonia (2.6%). Fatal adverse reactions occurred in 4% of patients receiving NUBEQA with docetaxel. Fatal adverse reactions in  $\geq 2$  patients who received NUBEQA included COVID-19/COVID-19 pneumonia (0.8%), myocardial infarction (0.3%), and sudden death (0.3%). The most common ( $\geq 10\%$  with a  $\geq 2\%$  increase over placebo with docetaxel) adverse reactions are constipation (23%), rash (20%), decreased appetite (19%), hemorrhage (18%), increased weight (18%), and hypertension (14%). The most common laboratory test abnormalities ( $\geq 30\%$ ) are anemia (72%), hyperglycemia (57%), decreased lymphocyte count (52%), decreased neutrophil count (49%), increased AST (40%), increased ALT (37%), and hypocalcemia (31%). Clinically relevant adverse reactions in  $<10\%$  of patients who received NUBEQA with docetaxel included fractures (8%), ischemic heart disease (3.2%), seizures (0.6%), and drug-induced liver injury (0.3%).

## Drug Interactions

**Effect of Other Drugs on NUBEQA** – Concomitant use of NUBEQA with a combined P-gp and strong or moderate CYP3A4 inducer decreases darolutamide exposure which may decrease NUBEQA activity. Avoid concomitant use of NUBEQA with combined P-gp and strong or moderate CYP3A4 inducers.

Concomitant use of NUBEQA with a combined P-gp and strong CYP3A4 inhibitor increases darolutamide exposure which may increase the risk of NUBEQA adverse reactions. Monitor patients more frequently for NUBEQA adverse reactions and modify NUBEQA dosage as needed.

**Effects of NUBEQA on Other Drugs** – NUBEQA is an inhibitor of BCRP transporter. Concomitant use of NUBEQA increases the AUC and  $C_{max}$  of BCRP substrates, which may increase the risk of BCRP substrate-related toxicities. Avoid concomitant use with drugs that are BCRP substrates where possible. If used together, monitor patients more frequently for adverse reactions, and consider dose reduction of the BCRP substrate drug.

NUBEQA is an inhibitor of OATP1B1 and OATP1B3 transporters. Concomitant use of NUBEQA may increase the plasma concentrations of OATP1B1 or OATP1B3 substrates. Monitor patients more frequently for adverse reactions of these drugs and consider dose reduction while patients are taking NUBEQA.

Review the Prescribing Information of drugs that are BCRP, OATP1B1, and OATP1B3 substrates when used concomitantly with NUBEQA.

You are encouraged to report side effects or quality complaints of products to the FDA by visiting [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or calling 1-800-FDA-1088.

**References:** 1. NUBEQA® (darolutamide) [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; June 2025. 2. Fizazi K et al. *N Engl J Med*. 2019;380(13):1235-1246. 3. Fizazi K et al. *N Engl J Med*. 2020;383(11):1040-1049. 4. Shore ND et al. Treatment duration and long-term safety and tolerability of darolutamide in nonmetastatic castration-resistant prostate cancer (nmCRPC): ARAMIS Rollover Study. Poster presented at: AUA Annual Meeting; April 28-May 1, 2023; Chicago, IL.



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PP-NUB-US-4439-1 06/25

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For full Prescribing information, please visit [NUBEQA PI](#).

  
**NUBEQA®**  
(darolutamide) 300 mg tablets