Johnson & Johnson Highlights Ambition to Transform the Treatment of Prostate Cancer and Bladder Cancer through Data Presentations at ASCO GU

Clinical and real-world evidence data support treatment with ERLEADA® (apalutamide) and niraparib plus abiraterone acetate given with prednisone in patients with prostate cancer

Additional updates will be presented on innovative targeted releasing systems TAR-200 and TAR-210 in bladder cancer

RARITAN, N.J., January 24, 2024 – Johnson & Johnson announced today new clinical and real-world evidence data will be featured in 18 abstracts at this year's ASCO GU Symposium (San Francisco, January 25-27), highlighting the Company's commitment to transform the science of genitourinary (GU) cancers. Key presentations will include new real-world evidence data adding to the strong and differentiated clinical profile of ERLEADA® (apalutamide) in the treatment of various stages of prostate cancer, patient-reported outcomes data from the Phase 3 MAGNITUDE study of niraparib plus abiraterone acetate given with prednisone, and updates on targeted releasing systems TAR-200 and TAR-210.

"We are applying our GU expertise to advance the science of prostate cancer and bladder cancer," said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Johnson & Johnson Innovative Medicine. "A recent FDA approval of new labelling for ERLEADA reinforces the impact of this standard-of-care treatment on reducing PSA to undetectable levels when added to androgen deprivation therapy. With the addition of new analyses presented at ASCO GU, we are progressing in our ambition to address unmet patient needs through earlier treatment intervention with the goal of improving and extending patients' lives."

"Our data across six different mechanisms of action underscore the breadth and depth of J&J's GU portfolio and our commitment to redefine treatment paradigms and pioneer new therapeutic advances for people with prostate and bladder cancers," said Luca Dezzani, M.D., U.S. Vice President, Medical Affairs, Solid Tumors, Johnson & Johnson Innovative Medicine. "In addition to traditional endpoints like overall survival, we are committed to assessing patients' well-being and investing in studies and real-world analyses based on patient populations that reflect everyday clinical practice."

Delivering patient-centric innovation in prostate cancer

With a deep legacy in the treatment of prostate cancer, J&J is committed to improve outcomes in metastatic disease, while defining new standards of care for patients at all stages of disease. New data at ASCO GU build on the strong clinical profile of ERLEADA® with real-world evidence supporting its impact on survival and PSA responses. Additional presentations highlight the company's commitment to advance equity in clinical trials.

Key presentations include:

- Real-world survival rates as presented in the ROME (Abstract #57) and ROMA (Abstract #58) studies, which reviewed patients in an oncology database with metastatic castration-sensitive prostate cancer (mCSPC) who were treated with ERLEADA® or enzalutamide (ROME) or ERLEADA® or abiraterone acetate (ROMA).
- U.S. real-world evidence comparing PSA90 response in patients with mCSPC six months after initiating ERLEADA® or enzalutamide (Abstract #51).
- A first look at the design of the LIBERTAS study, the first Phase 3 trial evaluating ERLEADA® plus intermittent vs continuous androgen deprivation therapy (ADT) in patients with mCSPC, inclusive of all gender identities (Abstract #TPS236).
- Patient-reported outcomes from the Phase 3 MAGNITUDE study evaluating niraparib with abiraterone acetate plus prednisone in patients with *BRCA*-positive metastatic castration-resistant prostate cancer (mCRPC) (Abstract #105).
- Data from the ongoing Phase 3 PRIMORDIUM study, including baseline characteristics of PSMA-PET positive and negative high-risk patients with biochemical recurrence after radical prostatectomy (Abstract #119).

Working to transform bladder cancer treatment with novel drug delivery technology and precision therapies

Data in bladder cancer underscore J&J's vision to advance the treatment paradigm and address unmet patient needs through bladder-sparing and Bacillus Calmette-Guérin (BCG)-free therapies in earlier-stage disease, and precision

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medicine for patients with specific genetic mutations. ASCO GU presentations showcase innovative targeted releasing systems TAR-200 and TAR-210, and new real-world evidence data on the proportion and prognosis of fibroblast growth factor receptors (FGFR) alterations in Japan.

Highlights include:

- Insights on the reasons for refusal or ineligibility for radical cystectomy from an analysis of the SunRISe-1 study evaluating TAR-200, a gemcitabine-containing targeted releasing system being studied in patients with BCG-unresponsive high-risk non-muscle-invasive bladder cancer (HR-NMIBC) (Abstract #701).
- Preliminary results evaluating a novel urine-based screening assay to detect FGFR alterations and select patients who may respond to TAR-210, an erdafitinib-containing targeted releasing system being studied in patients with NMIBC with select FGFR alterations (Abstract #676).
- Data describing the proportion and prognosis of Japanese patients with fibroblast growth factor receptor 2 or 3 (FGFR2 or 3) altered advanced or metastatic urothelial cancer (Abstract #647).

The complete list of Company-sponsored abstracts follows:

Prostate Cancer	
ERLEADA® (apalutamide)	
Poster Session	
Abstract #**51**	Real-world comparison of prostate-specific antigen (PSA) response in patients with metastatic castration-sensitive prostate cancer (mCSPC) treated with apalutamide (APA) or enzalutamide (ENZ)
Abstract #**57**	Real-world survival of men with metastatic castration-sensitive prostate cancer (mCSPC) initiated on apalutamide (APA) or enzalutamide (ENZ) in an oncology database: ROME study
Abstract #**58**	Analysis of real-world survival for patients with metastatic castration-sensitive prostate cancer (mCSPC) treated with apalutamide (APA) or abiraterone acetate (ABI) in an oncology database: ROMA study
Abstract #**65**	Treatment of metastatic castration-sensitive prostate cancer (mCSPC): Impact of starting treatment on real-world clinical outcomes
Abstract #**119**	Baseline characteristics of PSMA-PET positive and negative patients with high-risk biochemical recurrence (BCR) after radical prostatectomy (RP) in the ongoing Phase 3 PRIMORDIUM study
Abstract **#223**	Phase 3 TITAN OS Extrapolation: Estimating median overall survival of apalutamide compared to placebo in metastatic hormone-sensitive prostate cancer (mHSPC) populations: statistical extrapolations of the TITAN study
Abstract #**294**	Influential factors impacting treatment decision-making (TDM) and decision regret (DR) in patients with localized or locally advanced prostate cancer (LPC/LAPC)
Abstract #**316**	Impact of a rash management guide on incidence and severity of rash with apalutamide: experience from the APA-RP study in high-risk localized prostate cancer
Abstract #**53D**	Prostate-specific antigen (PSA) response among patients with metastatic castration-sensitive prostate cancer (mCSPC) initiated on apalutamide (APA) or abiraterone acetate (ABI) in real-world urology practices
Abstract #**TPS236**	Apalutamide (APA) plus intermittent versus continuous androgen-deprivation therapy (ADT) in participants with metastatic castration-sensitive prostate cancer (mCSPC): LIBERTAS Phase 3 study design
AKEEGA® (niraparib)	

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Poster Session	
Abstract #**52**	Real-world treatment patterns in patients with BRCA 1/2-positive (BRCA+) metastatic castration-resistant prostate cancer (mCRPC) initiating first-line (1L) therapy
Abstract #**64**	Real-world economic burden of patients with metastatic castration-sensitive prostate cancer (mCSPC)
Abstract #**105**	Patient-reported outcomes in patients with BRCA 1/2-altered metastatic castration-resistant prostate cancer (mCRPC) receiving niraparib (NIRA) with abiraterone acetate and prednisone: results from the MAGNITUDE study
Early Development	
Poster Session	
Abstract #**202**	Preclinical characterization of human kallikrein 2 as a novel target for the treatment of prostate cancer
Bladder Cancer	
BALVERSA® (erdafitinib)	
Poster Session	
Abstract #**647**	Real-world experience of FGFR gene alterations and clinical outcomes in advanced/metastatic urothelial cancer in Japan: MONSTAR-SCREEN database study
Bladder (TAR-200)	
Poster Session	
Abstract #**699**	Population based trends in intravesical gemcitabine use among patients with high-risk non-muscle-invasive bladder cancer
Abstract #**701**	Reasons for refusal of or ineligibility for radical cystectomy in patients with Bacillus Calmette-Guérin-unresponsive high-risk non-muscle-invasive bladder cancer from the SunRISe-1 study
Bladder (TAR-210)	
Poster Session	
Abstract # **676**	Urine-based testing for patient selection and genomic characterization of patients with FGFR alteration-positive non-muscle-invasive bladder cancer treated with TAR-210

About ERLEADA®

ERLEADA® (apalutamide) is an androgen receptor signaling inhibitor indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC) and for the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC). ERLEADA® received U.S. FDA approval for nmCRPC in February 2018, and received U.S. FDA approval for mCSPC in September 2019. To date, more than 150,000 patients worldwide have been treated with ERLEADA®. Additional ongoing Phase 3 studies include ATLAS, evaluating ERLEADA® for patients with localized prostate cancer with radiation therapy, and PROTEUS, evaluating ERLEADA® for patients with localized prostate cancer treatment after radical prostatectomy.

For more information, visit www.ERLEADA.com.

About AKEEGA®

AKEEGA® is a combination, in the form of a dual-action tablet (DAT), of niraparib, a highly selective poly (ADP-ribose) polymerase (PARP) inhibitor, and abiraterone acetate, a CYP17 inhibitor. AKEEGA® together with prednisone or prednisolone was approved in April 2023 by the European Medicines Agency, and in August 2023 by the U.S. FDA, for the treatment of patients with BRCA-mutated metastatic castration-resistant prostate cancer (mCRPC). Additional marketing authorization applications are under review across a number of countries globally.

Additional ongoing studies include the Phase 3 AMPLITUDE study, evaluating AKEEGA® with prednisone or prednisolone in a biomarker-selected patient population with metastatic castration-sensitive prostate cancer (mCSPC).

For more information, visit www.AKEEGA.com.

About BALVERSA®

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BALVERSA® (erdafitinib) is a once-daily, oral FGFR kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) with susceptible fibroblast growth factor receptor 3 (FGFR3) genetic alterations whose disease progressed on or after at least one line of prior systemic therapy. BALVERSA® is not recommended for the treatment of patients who are eligible for and have not received prior PD-1 or PD-(L)1 inhibitor therapy.[1] Patients are selected for therapy based on an FDA-approved companion diagnostic for BALVERSA®. Information on FDA-approved tests for the detection of FGFR genetic alterations in urothelial cancer is available at: http://www.fda.gov/CompanionDiagnostics.

BALVERSA® received Breakthrough Therapy Designation from the U.S. FDA in 2018 and received accelerated approval in 2019 for the treatment of adults with locally advanced or mUC which has susceptible FGFR3 or FGFR2 genetic alterations and who have progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.[2]

The Company submitted a marketing authorization application to the European Medicines Agency in September 2023 for BALVERSA® as a treatment for adult patients with FGFR3-altered, locally advanced unresectable or metastatic urothelial carcinoma that has progressed following therapy with a PD-(L)1 inhibitor.

In 2008, Janssen Pharmaceuticals entered into an exclusive worldwide license and collaboration agreement with Astex Pharmaceuticals to develop and commercialize BALVERSA®.

For more information, visit www.BALVERSA.com.

About TAR-200

TAR-200 is an investigational targeted releasing system designed to provide controlled release of gemcitabine into the bladder, sustaining local drug exposure for weeks at a time. The safety and efficacy of TAR-200 are being evaluated in Phase 2 and Phase 3 studies in patients with muscle-invasive bladder cancer (MIBC) in SunRISe-2 and SunRISe-4 and non-muscle-invasive bladder cancer (NMIBC) in SunRISe-1 and SunRISe-3.

About TAR-210

TAR-210 is an investigational targeted releasing system designed to provide controlled release of erdafitinib into the bladder. The safety and efficacy of TAR-210 is being evaluated in a Phase 1 study in patients with MIBC and NMIBC (NCT05316155).

About Cetrelimab

Cetrelimab is an investigational anti-programmed cell death receptor-1 (PD-1) monoclonal antibody being studied to treat bladder cancer, prostate cancer, melanoma, and multiple myeloma as part of a combination treatment. Cetrelimab is also being evaluated in multiple other combination regimens across the Johnson & Johnson portfolio.

AKEEGA® IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

The safety population described in the WARNINGS and PRECAUTIONS reflect exposure to AKEEGA® in combination with prednisone in *BRCA*m patients in Cohort 1 (N=113) of MAGNITUDE.

Myelodysplastic Syndrome/Acute Myeloid Leukemia
AKEEGA® may cause myelodysplastic syndrome/acute myeloid leukemia (MDS/AML).

MDS/AML, including cases with fatal outcome, has been observed in patients treated with niraparib, a component of AKEEGA®.

All patients treated with niraparib who developed secondary MDS/cancer-therapy-related AML had received previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

For suspected MDS/AML or prolonged hematological toxicities, refer the patient to a hematologist for further evaluation. Discontinue AKEEGA® if MDS/AML is confirmed.

Myelosuppression

AKEEGA® may cause myelosuppression (anemia, thrombocytopenia, or neutropenia).

In MAGNITUDE Cohort 1, Grade 3-4 anemia, thrombocytopenia, and neutropenia were reported, respectively in 28%, 8%, and 7% of patients receiving AKEEGA®. Overall, 27% of patients required a red blood cell transfusion, including 11% who required multiple transfusions. Discontinuation due to anemia occurred in 3% of patients.

Monitor complete blood counts weekly during the first month of AKEEGA® treatment, every two weeks for the next two months, monthly for the remainder of the first year and then every other month, and as clinically indicated. Do not start AKEEGA® until patients have adequately recovered from hematologic toxicity caused by previous therapy. If hematologic toxicities do not resolve within 28 days following interruption, discontinue AKEEGA® and refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics.

Hypokalemia, Fluid Retention, and Cardiovascular Adverse Reactions

AKEEGA® may cause hypokalemia and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. In post-marketing experience, QT prolongation and Torsades de Pointes have been observed in patients who develop hypokalemia while taking abiraterone acetate, a component of AKEEGA®. Hypertension and hypertensive crisis have also been reported in patients treated with niraparib, a component of AKEEGA®.

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In MAGNITUDE Cohort 1, which used prednisone 10 mg daily in combination with AKEEGA®, Grades 3-4 hypokalemia was detected in 2.7% of patients on the AKEEGA® arm and Grades 3-4 hypertension were observed in 14% of patients on the AKEEGA® arm.

The safety of AKEEGA® in patients with New York Heart Association (NYHA) Class II to IV heart failure has not been established because these patients were excluded from MAGNITUDE.

Monitor patients for hypertension, hypokalemia, and fluid retention at least weekly for the first two months, then once a month. Closely monitor patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia, or fluid retention, such as those with heart failure, recent myocardial infarction, cardiovascular disease, or ventricular arrhythmia. Control hypertension and correct hypokalemia before and during treatment with AKEEGA®.

Discontinue AKEEGA® in patients who develop hypertensive crisis or other severe cardiovascular adverse reactions.

Hepatotoxicity

AKEEGA® may cause hepatotoxicity.

Hepatotoxicity in patients receiving abiraterone acetate, a component of AKEEGA®, has been reported in clinical trials. In post-marketing experience, there have been abiraterone acetate-associated severe hepatic toxicity, including fulminant hepatitis, acute liver failure, and deaths.

In MAGNITUDE Cohort 1, Grade 3-4 ALT or AST increases (at least 5 x ULN) were reported in 1.8% of patients. The safety of AKEEGA® in patients with moderate or severe hepatic impairment has not been established as these patients were excluded from MAGNITUDE.

Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with AKEEGA®, every two weeks for the first three months of treatment and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring and may require dosage modifications.

Permanently discontinue AKEEGA® for patients who develop a concurrent elevation of ALT greater than 3 x ULN and total bilirubin greater than 2 x ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation, or in patients who develop ALT or AST ≥20 x ULN at any time after receiving AKEEGA®.

Adrenocortical Insufficiency

AKEEGA® may cause adrenal insufficiency.

Adrenocortical insufficiency has been reported in clinical trials in patients receiving abiraterone acetate, a component of AKEEGA®, in combination with prednisone, following interruption of daily steroids and/or with concurrent infection or stress. Monitor patients for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress. Symptoms and signs of adrenocortical insufficiency may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with abiraterone acetate. If clinically indicated, perform appropriate tests to confirm the diagnosis of adrenocortical insufficiency. Increased doses of corticosteroids may be indicated before, during, and after stressful situations.

Hypoglycemia

AKEEGA® may cause hypoglycemia in patients being treated with other medications for diabetes.

Severe hypoglycemia has been reported when abiraterone acetate, a component of AKEEGA®, was administered to patients receiving medications containing thiazolidinediones (including pioglitazone) or repaglinide.

Monitor blood glucose in patients with diabetes during and after discontinuation of treatment with AKEEGA®. Assess if antidiabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

Increased Fractures and Mortality in Combination with Radium 223 Dichloride

AKEEGA® with prednisone is not recommended for use in combination with Ra-223 dichloride outside of clinical trials.

The clinical efficacy and safety of concurrent initiation of abiraterone acetate plus prednisone/prednisolone and radium Ra 223 dichloride was assessed in a randomized, placebo-controlled multicenter study (ERA-223 trial) in 806 patients with asymptomatic or mildly symptomatic castration-resistant prostate cancer with bone metastases. The study was unblinded early based on an Independent Data Monitoring Committee recommendation.

At the primary analysis, increased incidences of fractures (29% vs 11%) and deaths (39% vs 36%) have been observed in patients who received abiraterone acetate plus prednisone/prednisolone in combination with radium Ra 223 dichloride compared to patients who received placebo in combination with abiraterone acetate plus prednisone.

It is recommended that subsequent treatment with Ra-223 not be initiated for at least five days after the last administration of AKEEGA®, in combination with prednisone.

Posterior Reversible Encephalopathy Syndrome

AKEEGA® may cause Posterior Reversible Encephalopathy Syndrome (PRES).

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PRES has been observed in patients treated with niraparib as a single agent at higher than the recommended dose of niraparib included in AKEEGA®.

Monitor all patients treated with AKEEGA® for signs and symptoms of PRES. If PRES is suspected, promptly discontinue AKEEGA® and administer appropriate treatment. The safety of reinitiating AKEEGA® in patients previously experiencing PRES is not known.

Embryo-Fetal Toxicity

The safety and efficacy of AKEEGA® have not been established in females. Based on animal reproductive studies and mechanism of action, AKEEGA® can cause fetal harm and loss of pregnancy when administered to a pregnant female.

Niraparib has the potential to cause teratogenicity and/or embryo-fetal death since niraparib is genotoxic and targets actively dividing cells in animals and patients (e.g., bone marrow).

In animal reproduction studies, oral administration of abiraterone acetate to pregnant rats during organogenesis caused adverse developmental effects at maternal exposures approximately ≥0.03 times the human exposure (AUC) at the recommended dose.

Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of AKEEGA®. Females who are or may become pregnant should handle AKEEGA® with protection, e.g., gloves.

Based on animal studies, AKEEGA® may impair fertility in males of reproductive potential.

ADVERSE REACTIONS

The safety of AKEEGA® in patients with *BRCA*m mCRPC was evaluated in Cohort 1 of MAGNITUDE.

The most common adverse reactions (≥10%), including laboratory abnormalities, are decreased hemoglobin, decreased lymphocytes, decreased white blood cells, musculoskeletal pain, fatigue, decreased platelets, increased alkaline phosphatase, constipation, hypertension, nausea, decreased neutrophils, increased creatinine, increased potassium, decreased potassium, increased AST, increased ALT, edema, dyspnea, decreased appetite, vomiting, dizziness, COVID-19, headache, abdominal pain, hemorrhage, urinary tract infection, cough, insomnia, increased bilirubin, weight decreased, arrhythmia, fall, and pyrexia.

Serious adverse reactions reported in >2% of patients included COVID-19 (7%), anemia (4.4%), pneumonia (3.5%), and hemorrhage (3.5%). Fatal adverse reactions occurred in 9% of patients who received AKEEGA®, including COVID-19 (5%), cardiopulmonary arrest (1%), dyspnea (1%), pneumonia (1%), and septic shock (1%).

DRUG INTERACTIONS

Effect of Other Drugs on AKEEGA®

Avoid coadministration with strong CYP3A4 inducers.

Abiraterone is a substrate of CYP3A4. Strong CYP3A4 inducers may decrease abiraterone concentrations, which may reduce the effectiveness of abiraterone.

Effects of AKEEGA® on Other Drugs

Avoid coadministration unless otherwise recommended in the Prescribing Information for CYP2D6 substrates for which minimal changes in concentration may lead to serious toxicities. If alternative treatments cannot be used, consider a dose reduction of the concomitant CYP2D6 substrate drug.

Abiraterone is a CYP2D6 moderate inhibitor. AKEEGA® increases the concentration of CYP2D6 substrates, which may increase the risk of adverse reactions related to these substrates.

Monitor patients for signs of toxicity related to a CYP2C8 substrate for which a minimal change in plasma concentration may lead to serious or life-threatening adverse reactions. Abiraterone is a CYP2C8 inhibitor. AKEEGA® increases the concentration of CYP2C8 substrates, which may increase the risk of adverse reactions related to these substrates.

Please see the full Prescribing Information for AKEEGA®.

ERLEADA® IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Cerebrovascular and Ischemic Cardiovascular Events — In a randomized study (SPARTAN) of patients with nmCRPC, ischemic cardiovascular events occurred in 3.7% of patients treated with ERLEADA® and 2% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4.4% of patients treated with ERLEADA® and 1.5% of patients treated with placebo. Across the SPARTAN and TITAN studies, 4 patients (0.3%) treated with ERLEADA® and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. Patients with history of unstable angina, myocardial infarction, congestive heart failure, stroke, or transient ischemic attack within 6 months of randomization were excluded from the SPARTAN and TITAN studies.

In the SPARTAN study, cerebrovascular events occurred in 2.5% of patients treated with ERLEADA® and 1% of patients treated with placebo. In the TITAN study, cerebrovascular events occurred in 1.9% of patients treated with ERLEADA® and 2.1% of patients treated with placebo. Across the

SPARTAN and TITAN studies, 3 patients (0.2%) treated with ERLEADA®, and 2 patients (0.2%) treated with placebo died from a cerebrovascular event.

Cerebrovascular and ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA®. Monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA® for Grade 3 and 4 events.

Fractures — In a randomized study (SPARTAN) of patients with nmCRPC, fractures occurred in 12% of patients treated with ERLEADA® and in 7% of patients treated with placebo. In a randomized study (TITAN) of patients with mCSPC, fractures occurred in 9% of patients treated with ERLEADA® and in 6% of patients treated with placebo. Evaluate patients for fracture risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

Falls — In a randomized study (SPARTAN), falls occurred in 16% of patients treated with ERLEADA® compared with 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Falls occurred in patients receiving ERLEADA® with increased frequency in the elderly. Evaluate patients for fall risk.

Seizure — In two randomized studies (SPARTAN and TITAN), 5 patients (0.4%) treated with ERLEADA® and 1 patient treated with placebo (0.1%) experienced a seizure. Permanently discontinue ERLEADA® in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA®. Advise patients of the risk of developing a seizure while receiving ERLEADA® and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

Severe Cutaneous Adverse Reactions — Fatal and life-threatening cases of severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) occurred in patients receiving ERLEADA®.

Monitor patients for the development of SCARs. Advise patients of the signs and symptoms of SCARs (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy). If a SCAR is suspected, interrupt ERLEADA® until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended. If a SCAR is confirmed, or for other Grade 4 skin reactions, permanently discontinue ERLEADA® *[see Dosage and Administration (2.2)].*

Embryo-Fetal Toxicity — The safety and efficacy of ERLEADA® have not been established in females. Based on findings from animals and its mechanism of action, ERLEADA® can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA® *[see Use in Specific Populations (8.1, 8.3)]*.

ADVERSE REACTIONS
The most common adverse reactions (≥10%) that occurred more frequently in the ERLEADA®-treated patients (≥2% over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

Laboratory Abnormalities — All Grades (Grade 3-4)

- **Hematology** — In the TITAN study: white blood cell decreased ERLEADA® 27% (0.4%), placebo 19% (0.6%). In the SPARTAN study: anemia ERLEADA® 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA® 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA® 41% (1.8%), placebo 21% (1.6%)
- **Chemistry** — In the TITAN study: hypertriglyceridemia ERLEADA® 17% (2.5%), placebo 12% (2.3%). In the SPARTAN study: hypercholesterolemia ERLEADA® 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA® 70% (2%), placebo 59% (1.0%); hypertriglyceridemia ERLEADA® 67% (1.6%), placebo 49% (0.8%); hyperkalemia ERLEADA® 32% (1.9%), placebo 22% (0.5%)

Rash — In 2 randomized studies (SPARTAN and TITAN), rash was most commonly described as macular or maculopapular. Adverse reactions of rash were 26% with ERLEADA® vs 8% with placebo. Grade 3 rashes (defined as covering >30% body surface area [BSA]) were reported with ERLEADA® treatment (6%) vs placebo (0.5%).

The onset of rash occurred at a median of 83 days. Rash resolved in 78% of patients within a median of 78 days from onset of rash. Rash was commonly managed with oral antihistamines, topical corticosteroids, and 19% of patients received systemic corticosteroids. Dose reduction or dose interruption occurred in 14% and 28% of patients, respectively. Of the patients who had dose interruption, 59% experienced recurrence of rash upon reintroduction of ERLEADA®.

Hypothyroidism — In 2 randomized studies (SPARTAN and TITAN), hypothyroidism was reported for 8% of patients treated with ERLEADA® and 1.5% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with ERLEADA® and 7% of patients treated with placebo. The median onset was at the first scheduled assessment. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy, when clinically indicated, should be initiated or dose adjusted.

DRUG INTERACTIONS

Effect of Other Drugs on ERLEADA® — Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties. No initial dose adjustment is necessary; however, reduce the ERLEADA® dose based on tolerability *[see Dosage and Administration (2.2)].*

Effect of ERLEADA® on Other Drugs
CYP3A4, CYP2C9, CYP2C19, and UGT Substrates — ERLEADA® is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA® with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication is

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continued. Concomitant administration of ERLEADA® with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA® and evaluate for loss of activity.

P-gp, BCRP, or OATP1B1 Substrates — Apalutamide is a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. Concomitant use of ERLEADA® with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP, or OATP1B1 must be co-administered with ERLEADA® and evaluate for loss of activity if medication is continued.

Please see the full Prescribing Information for ERLEADA®.

BALVERSA® IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

The safety population described in the Warnings and Precautions reflect a pooled safety population of 479 patients with advanced urothelial cancer and *FGFR* alterations who received BALVERSA®.

Ocular Disorders – BALVERSA® can cause ocular disorders, including central serous retinopathy/retinal pigment epithelial detachment (CSR/RPED) resulting in visual field defect.

CSR/RPED occurred in 22% of patients treated with BALVERSA®, with a median time to first onset of 46 days. In 104 patients with CSR, 40% required dose interruptions and 56% required dose reductions; 2.9% of BALVERSA®-treated patients required permanent discontinuation for CSR. Of the 24 patients who restarted BALVERSA® after dose interruption with or without dose reduction, 67% had recurrence and/or worsening of CSR after restarting. CSR was ongoing in 41% of the 104 patients at the time of last evaluation.

Dry eye symptoms occurred in 26% of BALVERSA®-treated patients. All patients should receive dry eye prophylaxis with ocular demulcents as needed.

Perform monthly ophthalmological examinations during the first 4 months of treatment and every 3 months afterwards, and urgently at any time for visual symptoms. Ophthalmological examination should include assessment of visual acuity, slit lamp examination, fundoscopy, and optical coherence tomography. Withhold or permanently discontinue BALVERSA® based on severity and/or ophthalmology exam findings.

Hyperphosphatemia and Soft Tissue Mineralization – BALVERSA® can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis and vascular calcification. Increases in phosphate levels are a pharmacodynamic effect of BALVERSA®. Increased phosphate occurred in 73% of BALVERSA®-treated patients. The median onset time of increased phosphate was 16 days (range: 8–421) after initiating BALVERSA®. Twenty-four percent of patients received phosphate binders during treatment with BALVERSA®. Vascular calcification was observed in 0.2% of patients treated with BALVERSA®.

Monitor for hyperphosphatemia throughout treatment. In all patients, restrict phosphate intake to 600-800 mg daily and avoid concomitant use of agents that may increase serum phosphate levels. If serum phosphate is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to <7.0 mg/dL. Withhold, dose reduce, or permanently discontinue BALVERSA® based on duration and severity of hyperphosphatemia.

Embryo-Fetal Toxicity – Based on the mechanism of action and findings in animal reproduction studies, BALVERSA® can cause fetal harm when administered to a pregnant female. In a rat embryo-fetal toxicity study, erdafitinib caused malformations and embryo-fetal death at maternal exposures that were less than the human exposures at the maximum human recommended dose based on AUC. Advise pregnant patients of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment with BALVERSA® and for one month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with BALVERSA® and for one month after the last dose.

ADVERSE REACTIONS

In the pooled safety population described in Warnings and Precautions, the median duration of treatment was 4.8 months (range: 0.1 to 43 months). The most common (≥20%) adverse reactions were: increased phosphate, nail disorders, stomatitis, diarrhea, increased creatinine, increased alkaline phosphatase, increased alanine aminotransferase, decreased hemoglobin, decreased sodium, increased aspartate aminotransferase, fatigue, dry mouth, dry skin, decreased phosphate, decreased appetite, dysgeusia, constipation, increased calcium, dry eye, palmar-plantar erythrodysesthesia syndrome, increased potassium, alopecia, and central serous retinopathy.

In Cohort 1 of the BLC3001 study:

- Serious adverse reactions occurred in 41% of patients who received BALVERSA®. Serious reactions in >2% of patients included urinary tract infection (4.4%), hematuria (3.7%), hyponatremia (2.2%), and acute kidney injury (2.2%). Fatal adverse reactions occurred in 4.4% of patients who received BALVERSA®, including sudden death (1.5%), pneumonia (1.5%), renal failure (0.7%), and cardiorespiratory arrest (0.7%).
- Permanent discontinuation of BALVERSA® due to an adverse reaction occurred in 14% of patients. Adverse reactions which resulted in permanent discontinuation of BALVERSA® in >2% of patients included nail disorders (3%) and eye disorders (2.2%).
- Dosage interruptions of BALVERSA® due to an adverse reaction occurred in 72% of patients. Adverse reactions which required dosage interruption in >4% of patients included nail disorders (22%), stomatitis (19%), eye disorders (16%), palmar-plantar erythrodysesthesia syndrome (15%), diarrhea (10%), hyperphosphatemia (7%), increased aspartate aminotransferase (6%), and increased alanine aminotransferase (5%).
- Dose reductions of BALVERSA® due to an adverse reaction occurred in 69% of patients. Adverse reactions which required dose reductions in >4% of patients included nail disorders (27%), stomatitis (19%), eye disorders (17%), palmar-plantar erythrodysesthesia syndrome (12%), diarrhea (7%), dry mouth (4.4%), and hyperphosphatemia (4.4%).
- Clinically relevant adverse reactions in <15% of patients who received BALVERSA® included nausea (15%), pyrexia (15%), epistaxis (13%), vomiting (10%), and arthralgia (10%).

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DRUG INTERACTIONS

Effects of Other Drugs on BALVERSA®

- Moderate CYP2C9 or Strong CYP3A4 Inhibitors: Consider alternative agents; however, if co-administration is unavoidable monitor closely for adverse reactions.
- Strong CYP3A4 Inducers: Avoid co-administration with BALVERSA®.
- Moderate CYP3A4 inducers: If co-administration is required at the start of BALVERSA® treatment, administer BALVERSA® at a dose of 9 mg daily.
- Serum phosphate level-altering agents: Avoid co-administration use with agents that can alter serum phosphate levels before the initial dose increase period based on serum phosphate levels.

Effect of BALVERSA® on Other Drugs

- P-gp substrates: If co-administration is unavoidable, separate BALVERSA® administration by at least 6 hours before or after administration of P-gp substrates with narrow therapeutic indices.

Please click here to see full BALVERSA® Prescribing Information.

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at https://www.jnj.com/ or at www.janssen.com/johnson-johnson-innovative-medicine. Follow us at @JanssenUS and @JNJInnovMed. Janssen Research & Development, LLC, Janssen Biotech, Inc., and Janssen Scientific Affairs, LLC are Johnson & Johnson companies.

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of AKEEGA® (niraparib and abiraterone acetate), ERLEADA® (apalutamide), BALVERSA® (erdafitinib), TAR-200, TAR-210, and cetrelimab. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen Scientific Affairs, LLC, and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen Scientific Affairs, LLC, nor Johnson & Johnson undertake to update any forward-looking statement as a result of new information or future events or developments.

[1] BALVERSA Prescribing Information.
[2] Clinicaltrials.gov. A Study of Erdafitinib in Participants With Advanced Solid Tumors and Fibroblast Growth Factor Receptor (FGFR) Gene Alterations. https://www.clinicaltrials.gov/ct2/show/NCT04083976. Accessed May 2023.