

Johnson & Johnson announces ERLEADA® (apalutamide) treatment before and after surgery reduces risk of recurrence or death by 62% versus surgery alone in high-risk prostate cancer

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- New substudy results showed a 51% lower estimated risk of metastasis or death over time with perioperative apalutamide plus ADT compared with immediate surgery
- Twice as many patients remained free from subsequent treatment at three years with perioperative apalutamide plus ADT compared with surgery alone
- Results evaluated outcomes versus surgery alone, building on the primary results presented at ASCO 2026

NEW BRUNSWICK, N.J., Oct. 24, 2026 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) today announced new results from the Phase 3 PROTEUS substudy that directly compared the investigational use of apalutamide plus androgen deprivation therapy (ADT), given for six months before and after surgery, with radical prostatectomy alone in patients with high-risk localized or locally advanced prostate cancer. The apalutamide plus ADT regimen reduced the risk of disease recurrence or death by 62 percent compared with surgery alone. The regimen also showed a numerical improvement in metastasis-free survival (MFS), with a 51 percent lower risk of metastasis or death. Patients receiving apalutamide plus ADT also went longer before needing subsequent therapy.¹

These substudy findings build on the primary PROTEUS results **presented** during the plenary session of the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting and evaluate a remaining clinical question by directly comparing perioperative apalutamide plus ADT with surgery alone, a longstanding standard of care.^{1,2}

The new results were presented as a late-breaking abstract in a proffered paper session at the **European Society for Medical Oncology (ESMO) Congress 2026 (#LBA53)**. The accompanying manuscript has been accepted for publication by European Urology.¹

The burden of recurrence in high-risk localized prostate cancer

For patients with high-risk localized or locally advanced prostate cancer, surgery has long been a standard of care performed with curative intent. Yet nearly half of patients will see their cancer return and require additional treatment.^{3,4} Recurrence can mean facing further therapy and the continued risk that the disease will spread, underscoring the need for approaches that can improve outcomes earlier in the course of disease.⁵

Apalutamide blocks androgen hormones from binding to their receptor, which can help slow prostate cancer progression. It is currently approved for use in advanced prostate cancer, including cases where the disease has spread (metastatic castration-sensitive) or is no longer responding to certain hormone therapies (non-metastatic castration-resistant prostate cancer).⁶

Expert and company perspectives on improving outcomes earlier in high-risk prostate cancer

"Radical prostatectomy has long been a cornerstone of curative-intent treatment for high-risk localized prostate cancer, yet recurrence remains a concern for patients with aggressive disease," said Alberto Briganti, M.D.,* Professor of Urology and Urologic Surgeon at IRCCS San Raffaele Hospital, Milan. "In this substudy, median event-free survival was 19.1 months with surgery alone, highlighting the challenges these patients continue to face despite treatment intended to cure their cancer. The reduction in the risk of recurrence and metastases after radical prostatectomy seen with apalutamide plus androgen deprivation therapy suggests we may be able to build on surgery and help more patients achieve lasting disease control."

"For people with high-risk early prostate cancer, finishing surgery doesn't necessarily mean the uncertainty is over. The possibility of recurrence can weigh heavily on patients and their families, even as they try to move forward with their lives," said Courtney Bugler,[†] President and CEO of ZERO Prostate Cancer, a leading prostate cancer patient advocacy organization in the U.S. "The possibility of helping more people remain free from disease recurrence, and potentially avoid or delay additional treatment, is incredibly meaningful. More time without another treatment can mean more time focused on family, work and life, rather than what comes next for their cancer."

"The primary PROTEUS study showed the potential of treating high-risk prostate cancer earlier with apalutamide plus androgen deprivation therapy. We designed this substudy to take that evidence further by evaluating the regimen against surgery alone, a longstanding standard of care for these patients," said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Global Therapeutic Area Head, Oncology, Johnson & Johnson. "These findings provide important

additional insight into what this approach could mean for patients and reinforce why we continue to investigate ways to improve outcomes earlier in the course of disease."

Perioperative treatment demonstrates improvement in event-free survival

The PROTEUS substudy evaluated apalutamide plus ADT before and after surgery compared with radical prostatectomy alone in 408 patients with newly diagnosed, non-metastatic, high-risk localized or locally advanced prostate cancer who were fit for surgery and systemic therapy. The primary endpoint was event-free survival (EFS), defined as the time to biochemical failure, local or regional recurrence, distant metastasis or death.¹

At a median follow-up of 37.8 months, apalutamide plus ADT significantly improved EFS, reducing the risk of recurrence or death by 62 percent compared with surgery alone (hazard ratio [HR], 0.38; 95 percent confidence interval [CI], 0.26-0.55; $p < 0.0001$). Median EFS was not reached with apalutamide plus ADT, compared with 19.1 months with surgery alone. At three years, 63 percent of patients receiving apalutamide plus ADT remained event-free compared with 41.4 percent of those undergoing surgery alone.¹

Numerical improvements were also observed across secondary and exploratory endpoints. For the secondary endpoint of MFS, apalutamide plus ADT showed a 51 percent lower risk of distant metastasis or death (HR, 0.49; 95 percent CI, 0.26-0.90; nominal $p = 0.0193$). For the exploratory endpoint of time to first subsequent therapy, the regimen showed a 71 percent lower risk of needing subsequent treatment (HR, 0.29; 95 percent CI, 0.20-0.43; nominal $p < 0.0001$). At three years, 64.6 percent of patients receiving apalutamide plus ADT remained free from subsequent therapy compared with 32 percent undergoing surgery alone. Additional follow-up is underway to evaluate overall survival.¹

The safety profile was consistent with the primary PROTEUS study results. Grade 3 or 4 treatment-emergent adverse events occurred in 31 percent of patients receiving apalutamide plus ADT and 22 percent receiving surgery alone. No treatment-emergent adverse events leading to death were reported in either arm. The most common adverse events with apalutamide included hot flush (64 percent) and urinary incontinence (63 percent).¹

Apalutamide plus ADT has not been approved by regulatory authorities for the treatment of high-risk localized or locally advanced prostate cancer. These findings add to the growing body of evidence evaluating the potential of treating selected patients with high-risk prostate cancer earlier in the course of disease.

About the PROTEUS substudy

The **PROTEUS substudy** is a randomized, open-label study evaluating perioperative apalutamide plus androgen deprivation therapy (ADT) compared with radical prostatectomy alone in patients with high-risk localized or locally

advanced prostate cancer who are candidates for radical prostatectomy. The substudy was designed to further evaluate the efficacy and safety of adding apalutamide plus ADT before and after surgery compared with surgery alone.⁷

A total of 408 patients were randomized to one of two treatment groups, with 102 receiving apalutamide plus ADT and 306 undergoing radical prostatectomy alone. Patients receiving apalutamide plus ADT were treated for six 28-day cycles before radical prostatectomy with pelvic lymph node dissection and for six cycles after surgery, with apalutamide paused two weeks before and resumed four weeks after radical prostatectomy with pelvic lymph node dissection. Apalutamide was administered orally at 240 mg once daily. Patients in the comparator arm underwent radical prostatectomy with pelvic lymph node dissection followed by standard institutional practice or observation.⁷

The primary endpoint is event-free survival (EFS), defined as the time to biochemical failure, local or regional recurrence, distant metastasis or death. Secondary endpoints include prostate-specific antigen (PSA)-free survival and metastasis-free survival (MFS), with exploratory endpoints including time to first subsequent systemic therapy and overall survival.⁷

About high-risk localized or locally advanced prostate cancer

Approximately 330,000 people are diagnosed with prostate cancer each year in the U.S.⁸ Up to 40 percent of patients will be classified as high-risk.⁹ Despite advancements in treatment, disease recurrence remains common in patients with high-risk localized or locally advanced prostate cancer. Real-world data show that approximately half of patients undergoing prostatectomy experience recurrence, metastasis or death within five years. Patients with high-risk disease also face increased risk of requiring additional therapy, metastatic progression and death from prostate cancer.⁴ It's estimated that more than 36,000 patients will succumb to prostate cancer in 2026, which reinforces the importance of choosing the best possible therapy early for patients with advanced prostate cancer.^{9,10}

About ERLEADA

ERLEADA (apalutamide) is an androgen receptor 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. Food and Drug Administration (FDA) approval for nmCRPC in February 2018 and **received** U.S. FDA approval for mCSPC in September 2019. ERLEADA is the first and only next-generation androgen receptor inhibitor offering a once-daily, single-tablet treatment option for patients. To date, more than 380,000 patients worldwide have been treated with ERLEADA. Additional studies are ongoing to evaluate ERLEADA in earlier stages of prostate cancer, including high-risk localized and locally advanced disease.

The legal manufacturer for ERLEADA is Janssen Biotech, Inc. For more information, visit <https://www.jnj.com/>.

ERLEADA INDICATIONS AND IMPORTANT SAFETY INFORMATION⁶

INDICATIONS

ERLEADA[®] (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with:

- Metastatic castration-sensitive prostate cancer (mCSPC)
- Non-metastatic castration-resistant prostate cancer (nmCRPC)

WARNINGS AND PRECAUTIONS

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.

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.

Fractures occurred in patients receiving ERLEADA. 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.

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.

Falls occurred in patients receiving ERLEADA with increased frequency in the elderly. Evaluate patients for fall risk.

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.

Seizure occurred in patients receiving ERLEADA. 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.

In two randomized studies (SPARTAN and TITAN), five patients (0.4%) treated with ERLEADA and one patient treated with placebo (0.1%) experienced a seizure. Seizure occurred from 159 to 650 days after initiation of ERLEADA. Patients with a history of seizure or, predisposing factors for seizure, or receiving drugs known to decrease the seizure threshold or to induce seizure were excluded. There is no clinical experience in re-administering ERLEADA to patients who experienced a seizure.

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)].

Interstitial Lung Disease (ILD)/Pneumonitis — Fatal and life-threatening interstitial lung disease (ILD) or pneumonitis can occur in patients treated with ERLEADA.

Post-marketing cases of ILD/pneumonitis, including fatal cases, occurred in patients treated with ERLEADA. Across clinical trials (TITAN and SPARTAN, n=1327), 0.8% of patients treated with ERLEADA experienced ILD/pneumonitis, including 0.2% who experienced Grade 3 events [see Adverse Reactions (6.1, 6.2)].

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever).

Immediately withhold ERLEADA if ILD/pneumonitis is suspected. Permanently discontinue ERLEADA in patients with severe ILD/pneumonitis or if no other potential causes of ILD/pneumonitis are identified [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)].

Interference with Immunoassay Measurement of Digoxin

ERLEADA can interfere with certain digoxin immunoassays (e.g., Chemiluminescent Microparticle Immunoassays), resulting in falsely elevated digoxin plasma concentration results. Notify the laboratory conducting the digoxin plasma concentration assay to use an appropriate method in patients receiving ERLEADA and digoxin [see Drug Interactions (7.3)].

ADVERSE REACTIONS

The most common adverse reactions ($\geq 10\%$) that occurred more frequently in the ERLEADA-treated patients ($\geq 2\%$ 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 and 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

ERLEADA Strong CYP2C8 or CYP3A4 Inhibitors

Reduce the ERLEADA dose as recommended for adverse reactions [see Dosage and Administration (2.2)]. Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties (sum of unbound apalutamide plus the potency-adjusted unbound N-desmethyl-apalutamide).

Effect of ERLEADA on Other Drugs

Substrates of CYP3A4, CYP2C9, CYP2C19, P-gp, BCRP, or OATP1B1

Refer to the Prescribing Information for these substrates. Consider alternative agents when possible or evaluate for loss of activity of the substrate if concomitant use cannot be avoided.

Apalutamide is a strong inducer of CYP3A4 and CYP2C19, a weak inducer of CYP2C9, and an inducer of P-gp, BCRP, and OATP1B1. Apalutamide decreases exposure of substrates of CYP3A4, CYP2C19, CYP2C9, P-gp, BCRP, or OATP1B1, which may decrease the effectiveness of these substrates.

USE IN SPECIFIC POPULATIONS

The recommended ERLEADA dosage in patients with severe hepatic impairment (Child-Pugh C) is lower than the recommended dosage in patients with normal hepatic function. No dosage modification is recommended for

patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment.

Please see full **Prescribing Information** for ERLEADA.

cp-50507v11

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.innovativemedicine.jnj.com. Follow us at @JNJInnovMed.

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 ERLEADA (apalutamide). 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 of 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 most recent Annual Report on Form 10-K, 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, www.investor.jnj.com or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

* Alberto Briganti, M.D., has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

† Courtney Bugler has provided consulting, advisory, and speaking services to Johnson & Johnson; she has not been paid for any media work.

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- [†] Briganti, A. et al. A PROTEUS substudy of perioperative apalutamide (APA) plus androgen deprivation therapy (ADT) with radical prostatectomy plus pelvic lymph node dissection (RP + PLND) vs RP + PLND alone in patients (pts) with high-risk localized or locally advanced prostate cancer (HR LPC/LAPC). Presented at: European Society for Medical Oncology (ESMO) 2026 Congress; October 24, 2026; Madrid.
- ² Taplin, M. et al. Perioperative (neoadjuvant and adjuvant) apalutamide (APA) + androgen deprivation therapy (ADT) vs placebo (PBO) + ADT with radical prostatectomy (RP) in high-risk localized or locally advanced prostate cancer (HR LPC/LAPC): Final analysis of the PROTEUS phase 3 study. Presented at: 2026 American Society of Clinical Oncology (ASCO); May 31, 2026; Chicago.
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