ERLEADA™ for Non-Metastatic Castration-Resistant Prostate Cancer (nmCRPC)

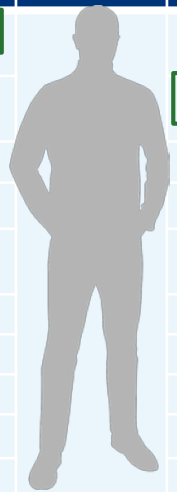
janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

This presentation discusses product information that goes beyond FDA-approved labeling and is being provided in response to an unsolicited request.

Prostate Cancer is a leading cause of cancer death in men

~1 man in 9 will be diagnosed with prostate cancer during his lifetime[1]				~1 man in 41 will die of prostate cancer[1]		
Prostate	164,690	19%		Lung and bronchus	83,550	26%
Lung and bronchus	121,680	14%		Prostate	29,430	9%
Colon and rectum	75,610	9%		Colon and rectum	27,390	8%
Urinary bladder	62,380	7%		Pancreas	23,020	7%
Melanoma of the skin	55,150	6%		Liver and intrahepatic bile duct	20,540	6%
Kidney and renal pelvis	42,680	5%		Leukemia	14,270	4%
Non-Hodgkin lymphoma	41,730	5%		Esophagus	12,850	4%
Oral cavity and pharynx	37,160	4%		Urinary bladder	12,520	4%
Leukemia	35,030	4%		Non-Hodgkin lymphoma	11,510	4%
Liver and intrahepatic bile duct	30,610	4%		Brain and other nervous system	10,010	3%
All sites	856,370	100 %		All sites	323,630	100%

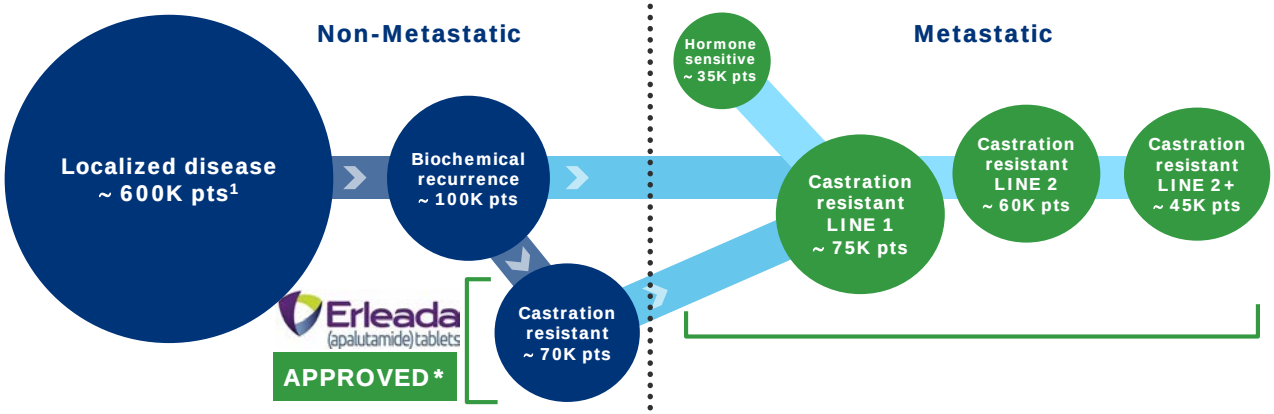
Estimated New Cases



Estimated Deaths

1. American Cancer Society. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf. Accessed February 16, 2018

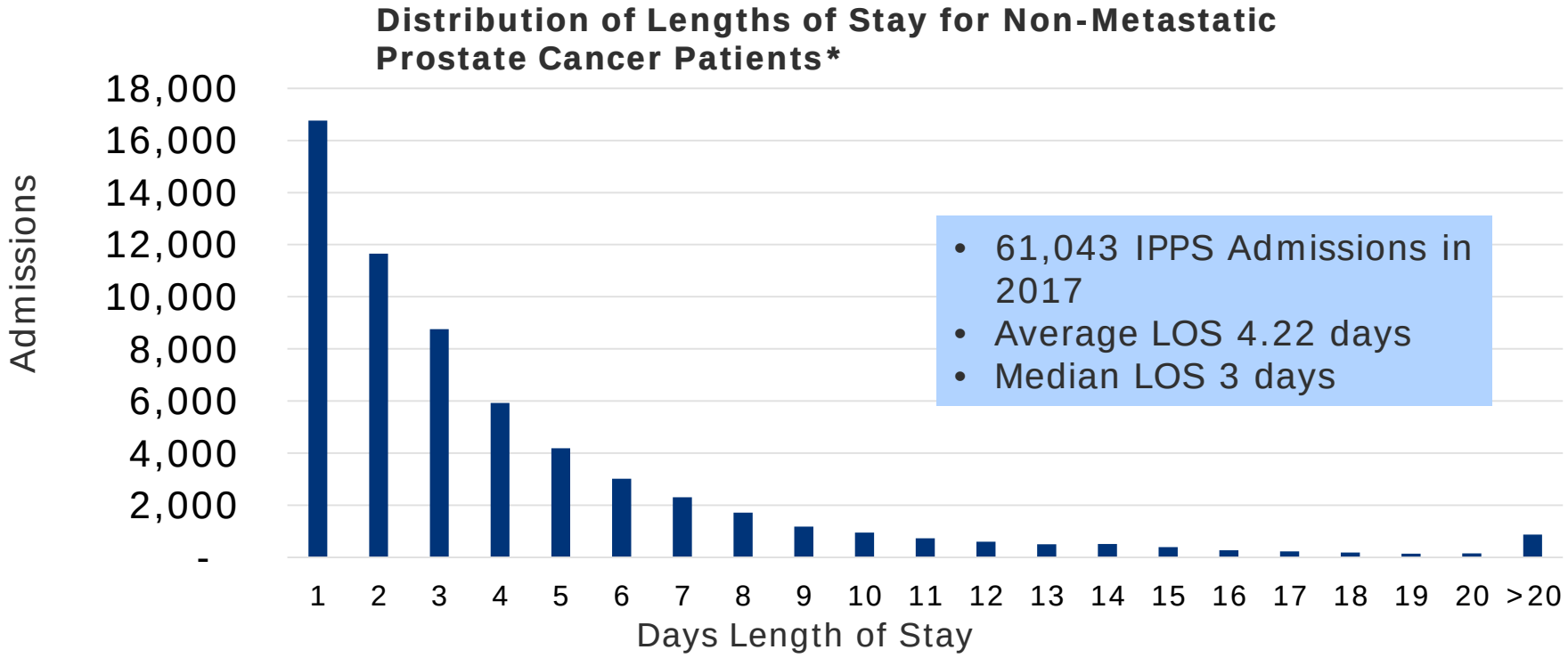
Prostate Cancer Stages of Disease



1. Decision Resources: *Prostate Cancer Landscape and Forecast*, 2016 (G7 estimates)

* FDA approved in US

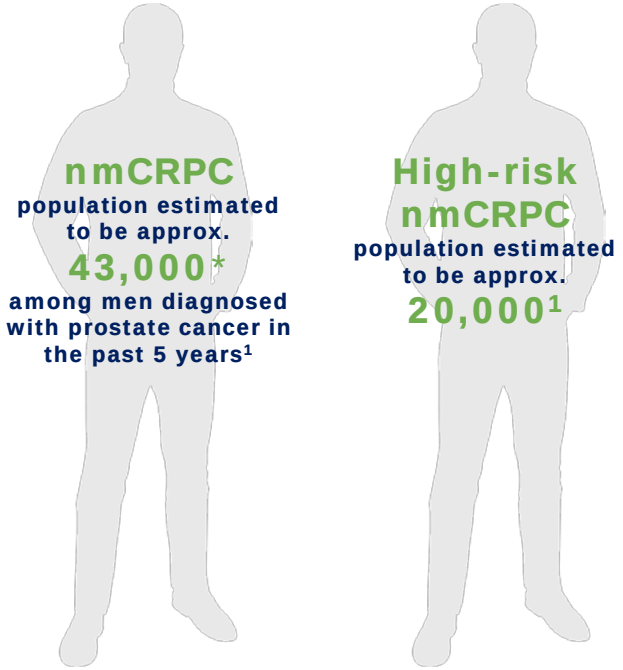
2017 MEDPAR Data Indicate About 61,000 Medicare Patients with Non-Metastatic Prostate Cancer are Hospitalized Each Year



*By presence of any diagnosis (and sometimes absence of exclusionary diagnosis) on the claim

Patients with high-risk nmCRPC represent a small, but critical to manage, proportion of the overall prostate cancer population[1]

- Data has estimated that 10% to 20% of patients diagnosed with prostate cancer may develop CRPC within approximately 5 years of follow-up[2]
- Data has shown that patients with a shorter PSA doubling time (PSADT) were at higher risk of metastasis[3]

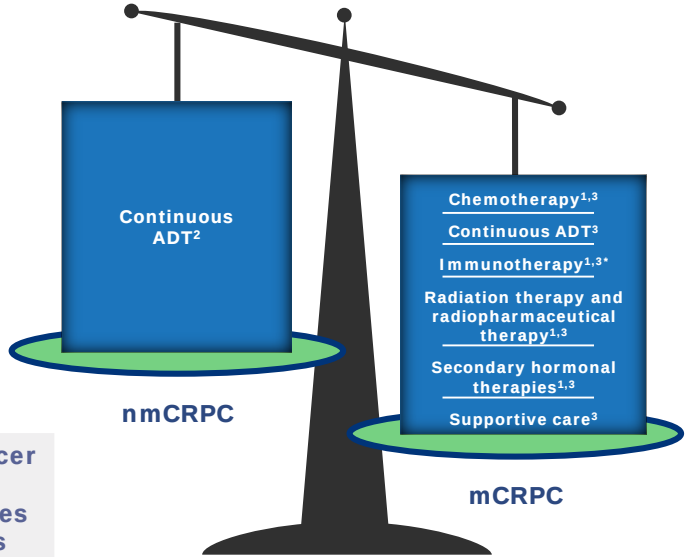


* Based on a patient-flow model that was developed to estimate 5-year limited duration prevalence of prostate cancer, including nmCRPC, using incidence and survival data from cancer registries from 19 countries. Estimates are based on a 5-year prevalence in the United States in 2013[1] and a prevalence rate of 4% within prostate cancer [4]

References: 1. Liede A et al. *Eur J Cancer.* 2013;49(suppl):S710. Abstract 2938. 2. Kirby M et al. *Int J Clin Pract.* 2011;65(11):1180-1192.
3. Howard LE et al. *BJU Int.* 2017. doi:10.1111/bju.13856. 4. Liede A et al. *J Clin Oncol.* 2013;31(15 suppl):1-2. ascopubs.org/doi/abs/10.1200/jco.2013.31.15_suppl.e16052. Accessed October 11, 2017.

Limited options existed until patients with non-metastatic CRPC developed metastatic disease[1]

- **Prior to ERLEADA™** there were no FDA-approved treatments for nmCRPC to prevent or delay the onset of mCRPC[1]



Both the National Comprehensive Cancer Network® (NCCN®) and American Urological Association (AUA) guidelines reflect the limited treatment options for nmCRPC.[2,3]

* Immunotherapy includes sipuleucel-T if asymptomatic or minimally symptomatic, no liver metastases, life expectancy >6 months, ECOG performance status 0-1.[2]

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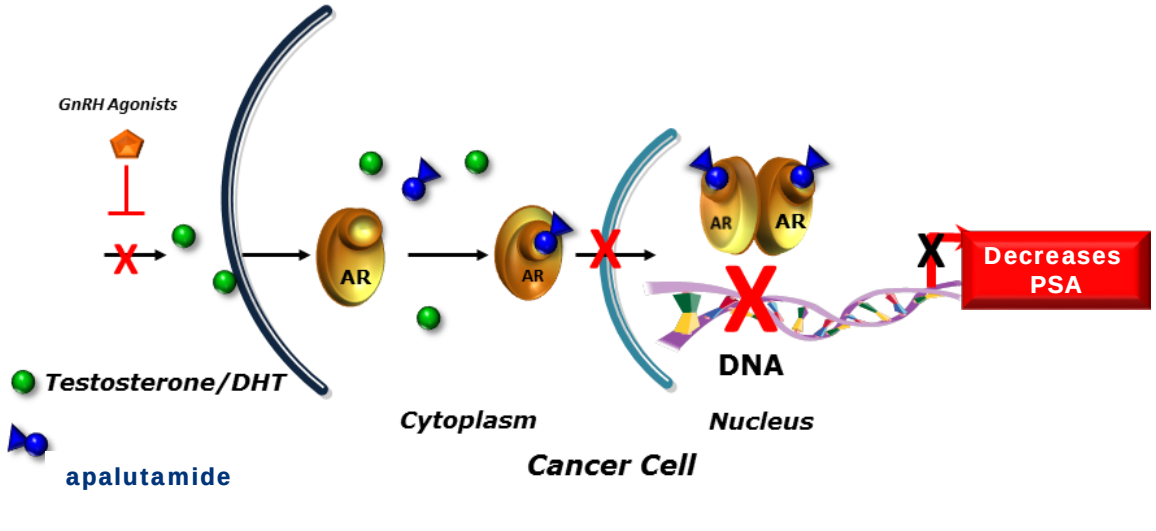
References: 1. Vaishampayan U. *Curr Opin Oncol*. 2014;26(3):265-273. 2. Lowrance WT, et al. *J Urol*. 2016;195(5):1444-1452. 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer NCCN Evidence Blocks V.2.2017. © National Comprehensive Cancer Network, Inc. 2017. All rights reserved. Accessed November 3, 2017. To view the most recent and complete version of the guideline, go online to NCCN.org.

Apalutamide Antagonizes and Blocks the Androgen Receptor, DNA Binding and Inhibits Tumor Growth

- Apalutamide competitively inhibits AR-androgen binding, with a higher affinity than bicalutamide
- AR antagonism impairs AR activation and subsequent AR signaling
- Apalutamide inhibits AR-mediated nuclear localization as well as DNA binding and transcription



For patients with non-metastatic* CRPC

FEBRUARY 8 2018

Phase 3 data on apalutamide published
in the
New England Journal of Medicine[1]

FEBRUARY 14 2018

US FDA Approves ERLEADA™ (apalutamide)
for the treatment of patients with non-metastatic, castration-resistant prostate cancer[2,3]

MARCH 8 2018

Apalutamide was included in the NCCN Guidelines for Prostate Cancer as a **category 1 treatment** recommendation for non-metastatic (M0) CRPC[4†]

MAY 17 2018

AUA Guideline
Apalutamide (ERLEADA™) is included as an option
for patients with asymptomatic nmCRPC (Index 1)[Ω]
(Standard*; Evidence Level Grade A¶)[5]

†Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

AUA = American Urological Association; FDA = Food and Drug Administration. *Standard: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade A or B evidence. ¶Evidence Level Grade A: The quality of the evidence is high. ‡Especially if PSA doubling time is ≤10 months. Ω Apalutamide should be offered with continued ADT as a treatment option to patients with non-metatastatic CRPC at high risk for developing metastatic disease.

1. Smith MR, et al. N Engl J Med. 2018;378:1408-1418. **2.** ERLEADA™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.
3. FDA news release. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm596768.htm. Accessed March 2, 2018. 4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.2.2018. © National Comprehensive Cancer Network, Inc. 2018. All rights reserved. Accessed March 8, 2018. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.
5. American Urological Association. https://www.auanet.org/guidelines/castration-resistant-prostate-cancer-(2013-amended-2018). Accessed May 23, 2018.

SPARTAN: Study Design

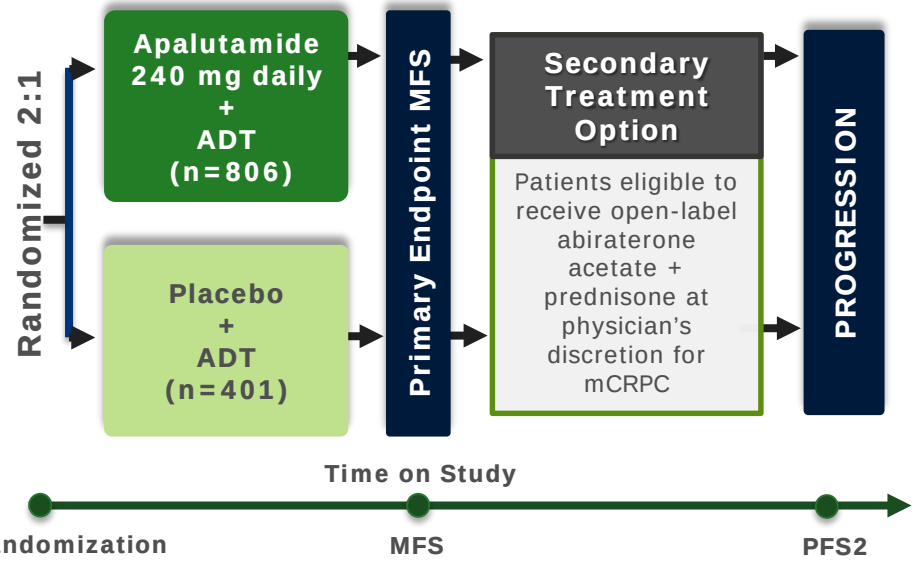
Phase 3 Placebo-Controlled, Randomized International Study

Patients (N=1207)

Eligibility:
- nmCRPC
  - Negative ^{99m}Tc bone scan
  - Negative CT of pelvis abdomen, chest and brain
  - Pelvic nodes <2 cm below aortic bifurcation (N1) allowed
- PSADT ≤10 months

On-Study Requirement:
- Continuous ADT

Stratification Factors:
- PSADT >6 mo or ≤6 mo
- Bone-sparing agents (yes vs no)
- Locoregional disease (N0 vs N1)



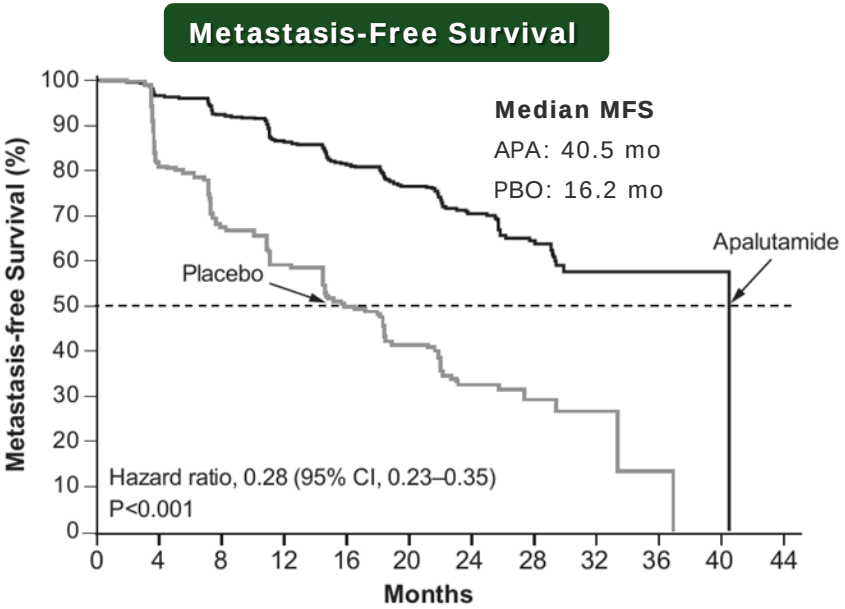
Secondary Endpoints:
- Time to metastasis, PFS, time to symptomatic progression, OS, and time to initiation of cytotoxic chemotherapy

Exploratory Endpoints:
- PSA progression, PSA response rate, patient reported outcomes, and PFS2

ADT, androgen deprivation therapy; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; MFS, metastasis-free survival; OS, overall survival; PFS, progression-free survival; PFS2, 2nd progression-free survival; PSA, prostate-specific antigen; PSADT, prostate-specific antigen doubling time.

Smith MR, et al. *N Engl J Med*. 2018;378:1408-1418.

Primary Endpoint: Metastasis-Free Survival



No. at Risk												
Apalutamide	806	713	652	514	398	282	180	96	36	16	3	0
Placebo	401	291	220	153	91	58	34	13	5	1	0	0

The final analysis for MFS was performed after distant metastasis or death was observed in 378 patients, in 23% and 48% of patients in the APA and PBO groups, respectively

Among patients who developed metastases, 60.5% in the APA group and 54.4% in the PBO group had bone metastases

DEFINITION	
Metastasis-Free Survival	Time from randomization to first evidence of BICR-confirmed radiographically detectable **distant metastasis** (bone or soft tissue) or **death** whichever comes first

BICR, blinded independent central review; MFS, metastasis-free survival.

Smith MR, et al. *N Engl J Med*. 2018;378:1408-1418.

Summary

- ERLEADA™ is the first FDA-approved therapy to treat patients with non-metastatic castration-resistant prostate cancer
- Apalutamide (ERLEADA™) has a category 1 recommendation from NCCN*
- ERLEADA™ decreased the risk of metastasis or death by 72%
- ERLEADA™prolonged the median MFS by more than 2 years in men with high-risk nmCRPC

MFS, metastasis-free survival

Thank You!