

Safety and Efficacy of JNJ-6143, a First-in-Class Oral AR-Targeted Regulated Induced Proximity Targeting Chimera Molecule in Patients With mCRPC/mAPMR, Including High-Risk Molecular Features

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AR, androgen receptor; mAPMR, metastatic androgen pathway modulation-resistant prostate cancer; mCRPC, metastatic castration-resistant prostate cancer.

<https://www.congresshub.com/Oncology/ESMO2026/ProstateEarlyAssets/Garnezy>

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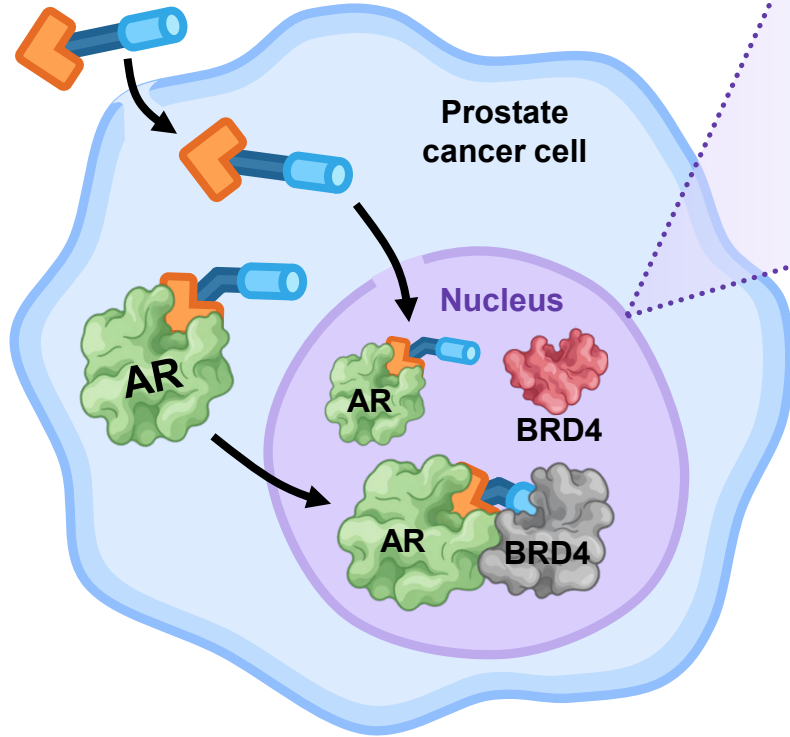
Disclosures

- Received consulting or advisory fees from AbbVie, Adaptimmune, Adicet Therapeutics, AIQ Global, Amgen, Arcus Biosciences, Arvinas, AstraZeneca, AVEO, Bayer, Bicycle Therapeutics, Bristol Myers Squibb, Eisai, EMD Serono, Exelixis, Genentech/Roche, Janssen, Merck, Monte Rosa Therapeutics, Novartis, Pfizer, Rondo Therapeutics, Seagen, Specialty Networks, Takeda, and Xencor
- Received institutional research funding from AbbVie, Accutar Biotech, Adcentrx Therapeutics, Adicet Therapeutics, Amgen, Arcus Biosciences, Arvinas, AstraZeneca, Avenzo Therapeutics, AVEO, Bicycle Therapeutics, CRISPR Therapeutics, Eikon Therapeutics, Envision Pharma Group, Exelixis, Flare Therapeutics, Halda Therapeutics, Harbour Biomed, HiberCell, IDEAYA Biosciences, Janssen Oncology, Janux Therapeutics, Jubilant Therapeutics, Kineta, Kinnate Biopharma, Loxo, Merck, MiNK Therapeutics, Novartis, Nuvation Bio, Pfizer, ProfoundBio, Roche/Genentech, Takeda, Teon Therapeutics, Tmunity Therapeutics, Inc, Xencor, and Zenshine

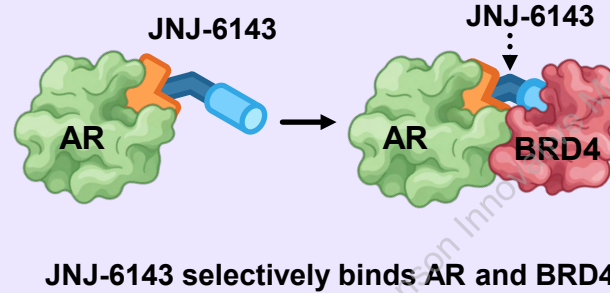


JNJ-6143,^a First-in-Class RIPTAC™ Therapeutic: Targeted Dual-Protein Lock in an Oral Small Molecule

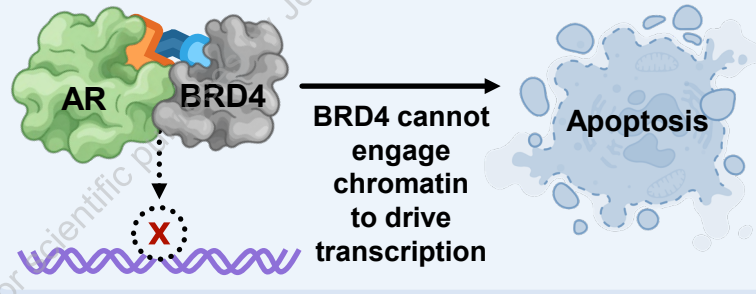
JNJ-6143: A Regulated Induced Proximity Targeting Chimera (RIPTAC™) molecule



Ternary Complex Formation: AR-JNJ-6143-BRD4



Ternary complex sequesters and functionally inactivates BRD4



- Selectively binds AR and BRD4, resulting in BRD4 loss of function and death in PC cells¹⁻³
- Induces tumor regression across preclinical *in vivo* CRPC models with AR and non-AR alterations^{2,3}
- Preliminary phase 1 data suggest a favorable safety profile with evidence of tumor shrinkage and PSA decline in patients with mCRPC³

We report updated phase 1 data evaluating JNJ-6143 in mCRPC

^aFormerly HLD-0915.

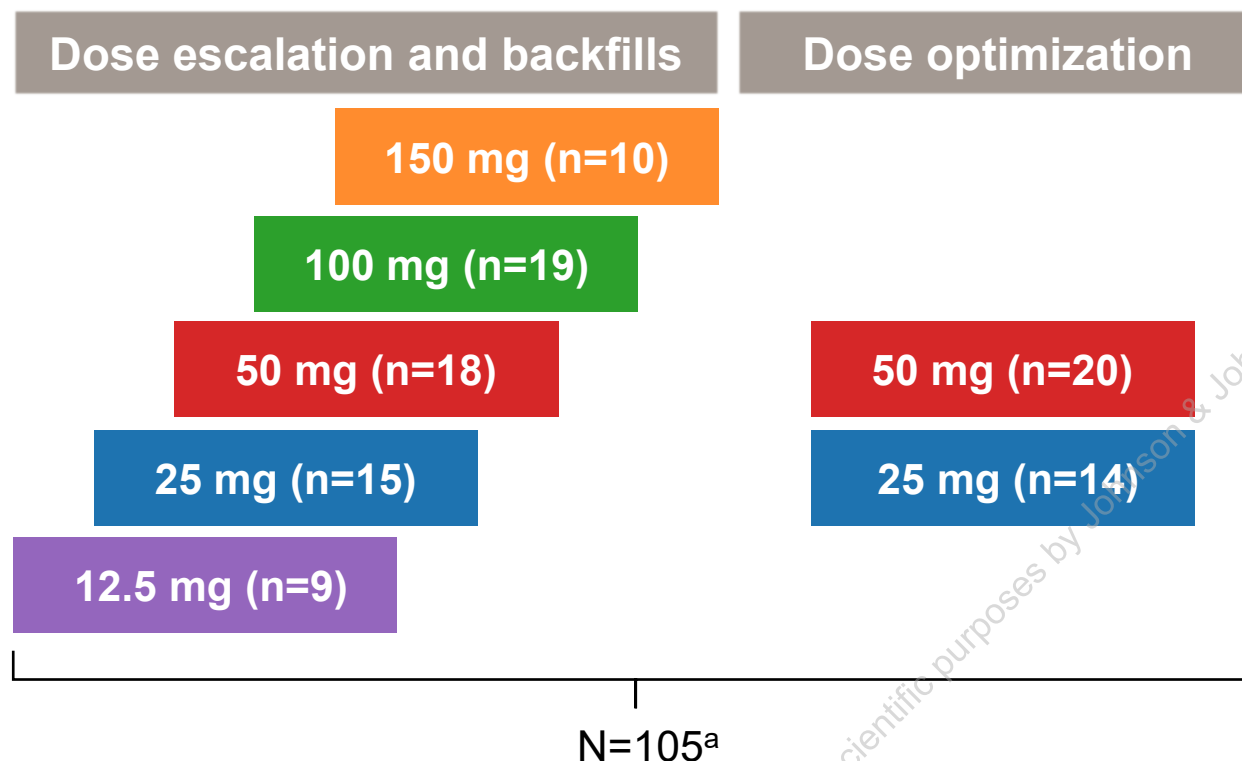
BRD4, bromodomain-containing protein 4; CRPC, castration-resistant prostate cancer; PC, prostate cancer; PSA, prostate-specific antigen; RIPTAC™, Regulated Induced Proximity Targeting Chimera.

1. Raina K, et al. *Cell Chem Biol.* 2024;31(8):1490-1502. 2. Raina K, et al. *J Clin Oncol.* 2023;41(suppl 6):184. 3. Hahn A, et al. Presented at: AACR-NCI-EORTC Molecular Targets and Cancer

Therapeutics Symposium; October 22-26, 2025; Boston, MA, USA.



JNJ-6143: First-in-Human, Multicenter, Phase 1 Dose-Escalation Study



JNJ-6143 administered **orally once daily** in 21-day cycles

50 mg once daily was selected as the RP2D based on safety, efficacy, and PK

Study design

- Phase 1 dose escalation with backfill and dose optimization in patients with mCRPC

Key eligibility criteria

- Progressive mCRPC with rising PSA (≥ 2 ng/mL for dose escalation; ≥ 20 ng/mL for dose optimization)
- Prior treatment with ≥ 1 ARPI and may have had ≤ 2 prior taxanes and ≤ 1 RLT
- ECOG PS score of 0 or 1

Objectives

- Safety and tolerability
- PK/PD and efficacy (ie, PSA, ORR, ctDNA)
- Determine recommended doses for expansion

ClinicalTrials.gov identifier: NCT06800313.

^aPatients dosed as of September 21, 2026.

ARPI, androgen receptor pathway inhibitor; ctDNA, circulating tumor DNA; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, objective response rate; PD, pharmacodynamics; PK, pharmacokinetics; RLT, radioligand therapy.



JNJ-6143: Phase 1 Study Enrolled a Heavily Pretreated Population with Advanced mCRPC

Characteristic	50 mg (n=38)	All doses ^a (N=105)
Age, years, median (range)	73 (56, 90)	72 (51, 90)
PSA, µg/L, median (range)	122.2 (17.3, 2235)	90.0 (3.6, 5000)
Lines of prior systemic therapy, ^b median (range)	4 (1, 9)	4 (1, 10)
Prior systemic therapy, ^c n (%)		
RLT	17 (46)	45 (44)
Taxane	20 (54)	68 (66)
Taxane + RLT	12 (32)	36 (35)
PARP inhibitor	2 (5)	10 (10)
Visceral disease, ^d n (%)		
Liver	4 (11)	5 (5)
Lung	3 (8)	12 (13)
Other	5 (16)	10 (10)

Data cutoff date: September 21, 2026.

^aDoses ranged from 12.5 to 150 mg.

^bLines of prior systemic therapy counting only those used in the metastatic setting.

^cn=97 in all doses.

^dn=96 in all doses.

PARP, poly (ADP-ribose) polymerase.



JNJ-6143: At RP2D, TRAEs Were Mostly Low Grade With Low Rates of Treatment Discontinuations due to TRAEs (3%)

n (%)	50 mg (n=38)		All doses ^a (N=105)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any TRAE	22 (58)	2 (5)*	71 (68)	18 (17)
Most common TRAE^b				
Hypertriglyceridemia	6 (16)	1 (3)*	29 (28)	5 (5)
Nausea	6 (16)	0	20 (19)	0
Decreased appetite	4 (11)	0	19 (18)	1 (1)
Fatigue	5 (13)	0	19 (18)	0
Hypercholesterolemia	7 (18)	0	18 (17)	3 (3)
Anemia	5 (13)	1 (3)*	17 (16)	7 (7)
Increased AST	3 (8)	0	10 (10)	1 (1)
Acute kidney injury	0	0	2 (2)	2 (2)
Syncope	0	0	2 (2)	2 (2)
TRAEs leading to dose interruption	4 (11)		17 (16)	
TRAEs leading to dose reduction	1 (3)		4 (4)	
TRAEs leading to discontinuation	1 (3)		5 (5)	
DLTs	0		1 (1) ^c	
Serious TRAEs	0		3 (3)	
TRAEs leading to death	0		1 (1) ^d	

*Both Grade ≥3 TRAEs were reclassified after data cutoff as not related to study drug

Data cutoff date: September 21, 2026.

^aDoses ranged from 12.5 to 150 mg.

^bThe most common TRAEs of any grade that occurred in ≥10% of patients or the most common grade ≥3 TRAEs that occurred in ≥2% of patients in all doses.

^cHepatotoxicity in setting of extrinsic bile duct compression.

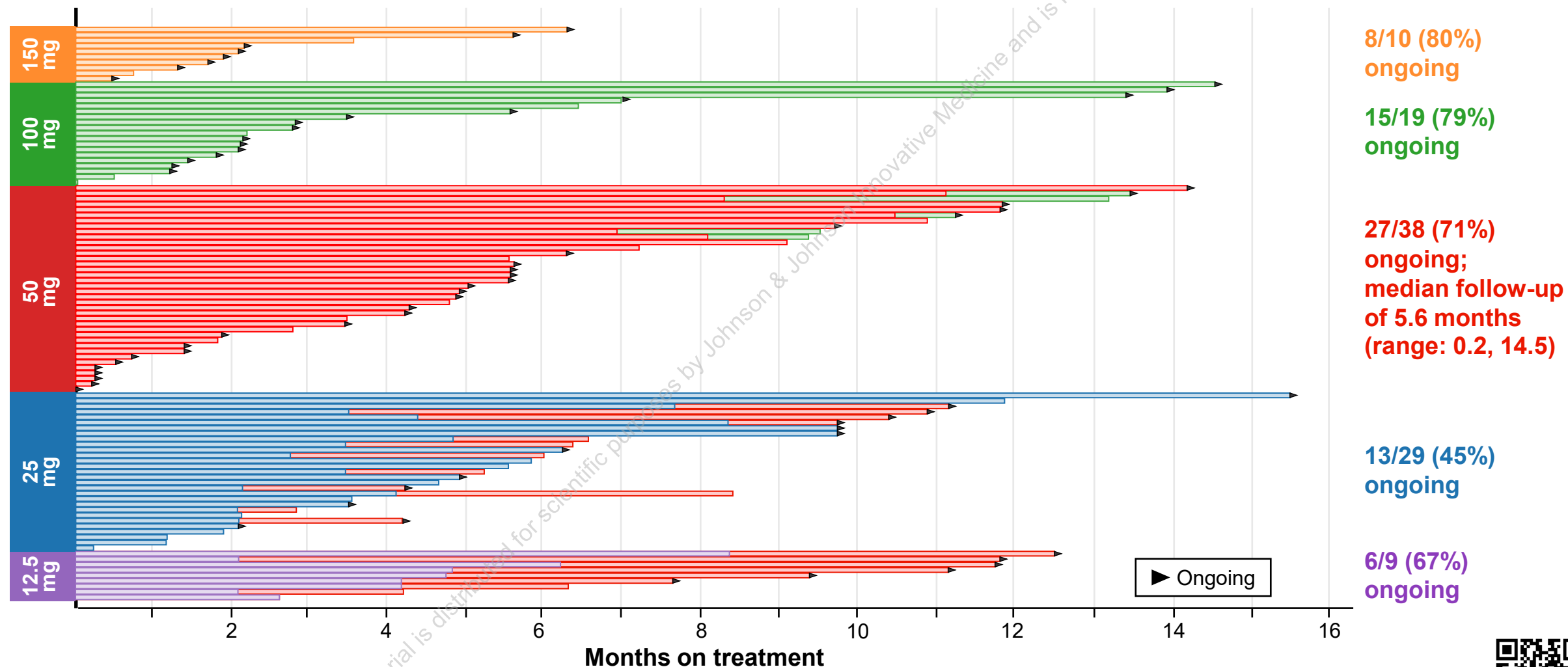
^dGrade 5 acute kidney injury: patient died after acute hemodynamic event while undergoing hemodialysis.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DLT, dose-limiting toxicity; TRAE, treatment-related adverse event.

Presented by B Garnezy at the European Society for Medical Oncology (ESMO) Annual Congress; October 23–27, 2026; Madrid, Spain



JNJ-6143: Most Patients (69/105 [66%]) Remain on Treatment

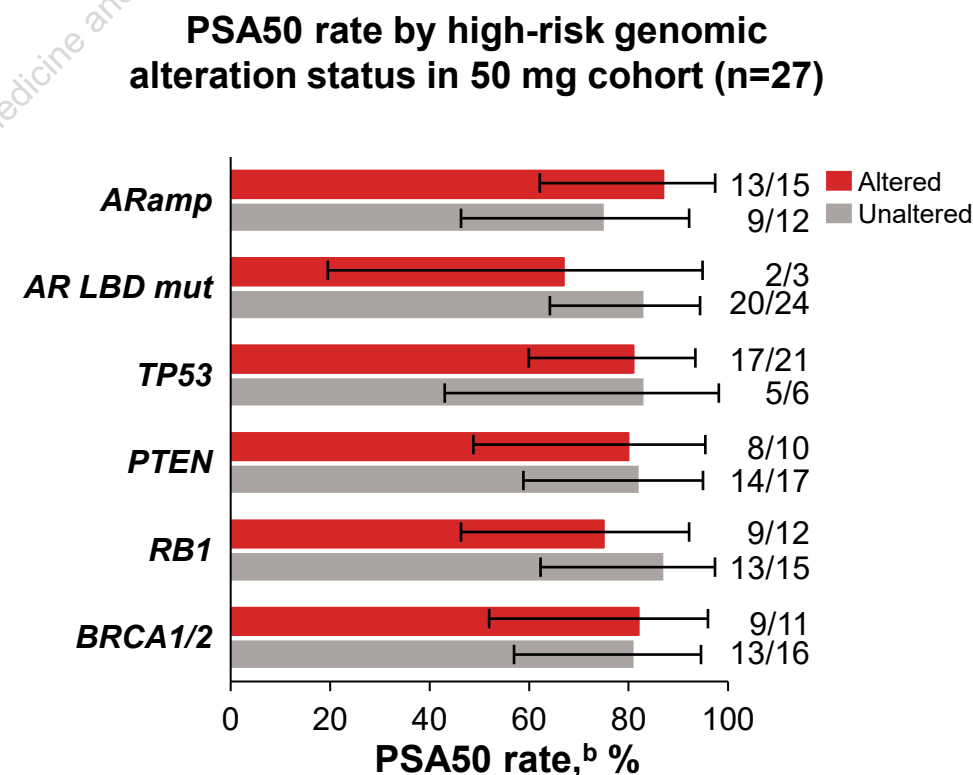
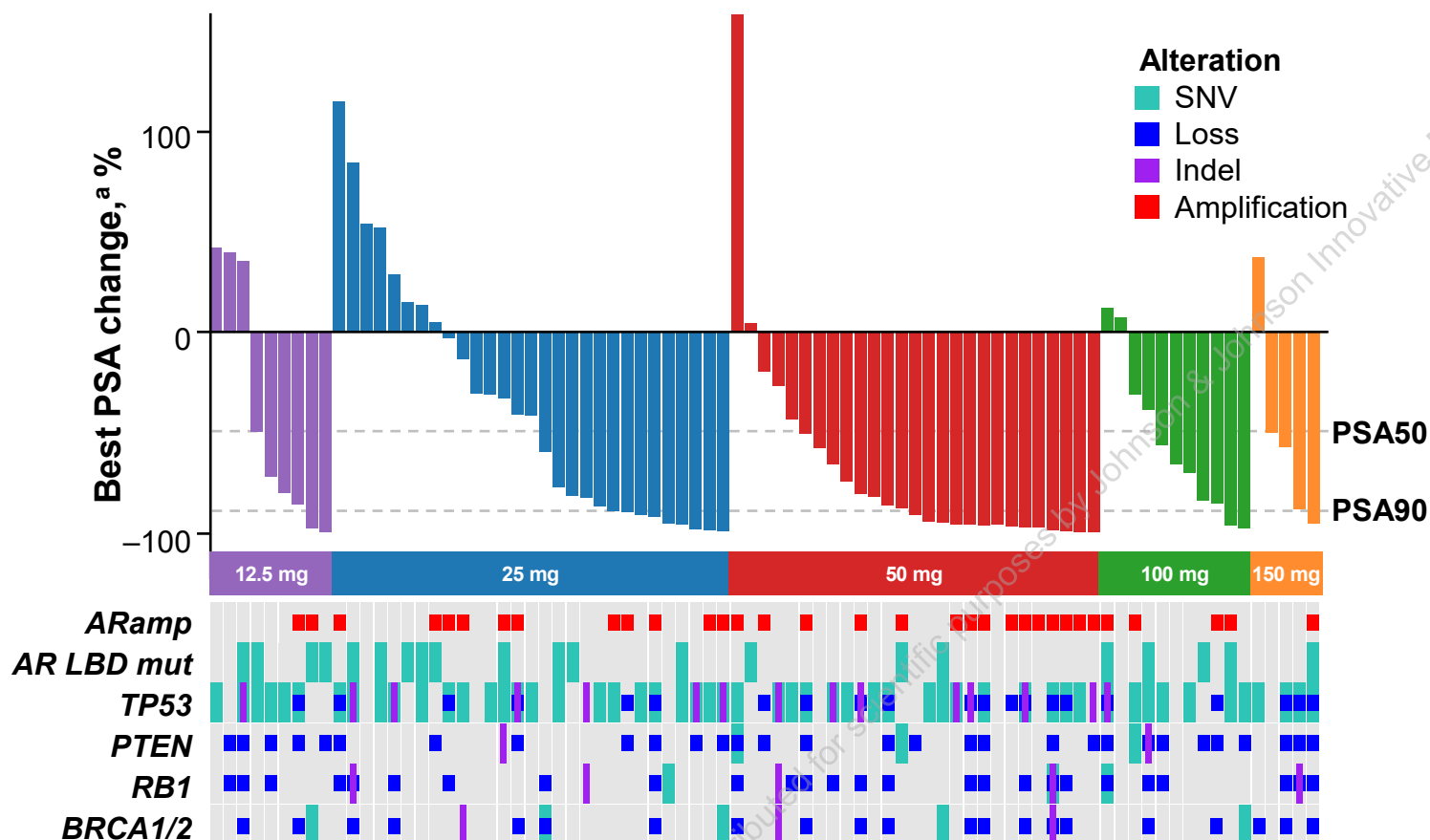


Data cutoff date: September 21, 2026.

Presented by B Garmezay at the European Society for Medical Oncology (ESMO) Annual Congress; October 23–27, 2026; Madrid, Spain



JNJ-6143: High PSA Response Rate Irrespective of High-Risk Molecular Features



PSA50 was achieved in 5/6 (83%) ARv7+ patients with evaluable CTCs (n=7)

Data cutoff date: September 21, 2026.

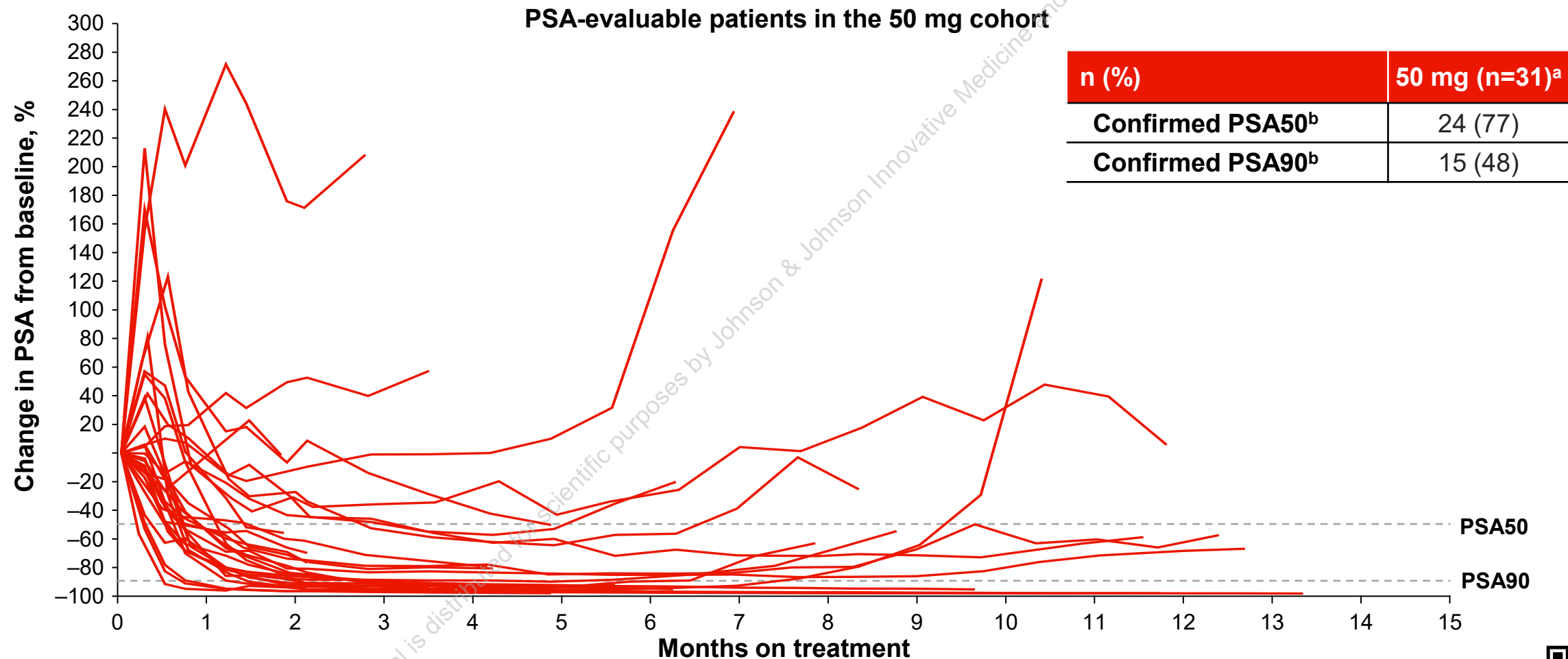
^aPatients with both baseline and ≥ 1 postbaseline PSA assessment and available C1D1 ctDNA data from Guardant Reveal (Guardant Health, Palo Alto, CA).

^bError bars represent Wilson 95% CI.

ARamp, androgen receptor amplification; AR LBD mut, androgen receptor ligand binding domain mutation; ARv7, androgen receptor splice variant 7; BRCA, breast cancer gene; CTC, circulating tumor cell; Indel, insertion or deletion; PSA50, 50% reduction in prostate-specific antigen from baseline; PSA90, 90% reduction in prostate-specific antigen from baseline; PTEN, phosphatase and tensin homolog; RB1, RB transcriptional corepressor 1; SNV, single nucleotide variant; TP53, tumor protein p53.



JNJ-6143: PSA Responses Were Rapid, Deep, and Durable at the RP2D in Advanced mCRPC

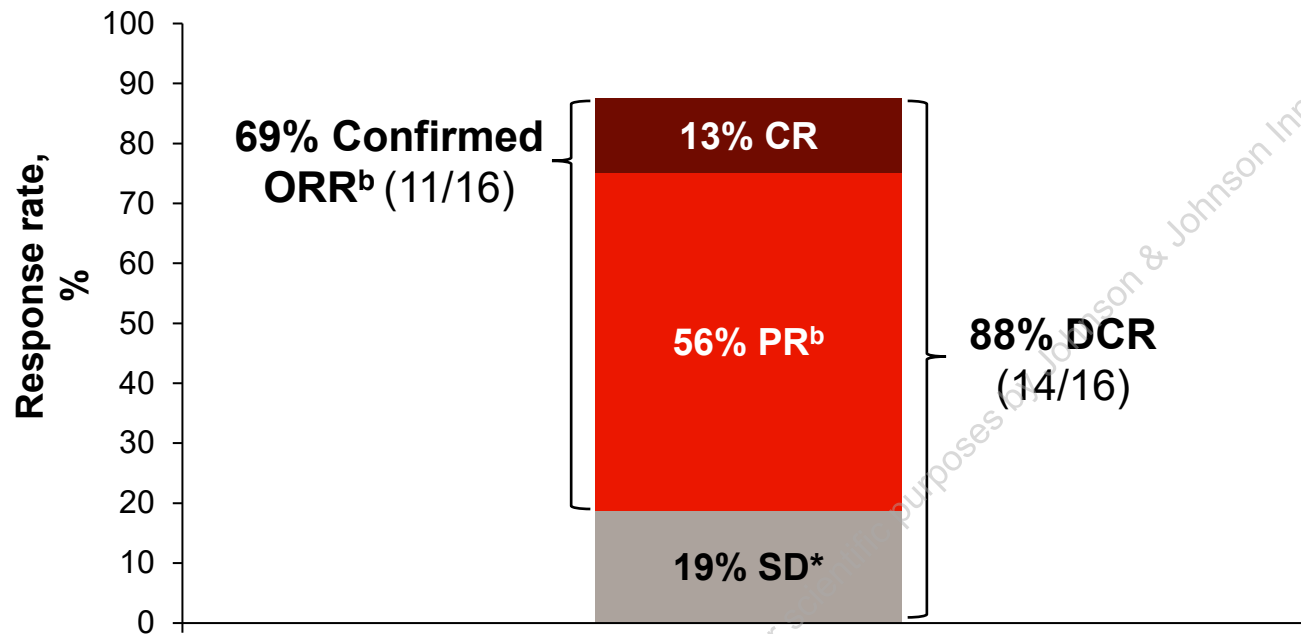


Data cutoff date: September 21, 2026.
^aSeven ongoing patients are excluded for not having completed ≥ 1 postbaseline PSA assessment and ≥ 2 cycles of treatment.
^bPSA decreases confirmed by a subsequent measurement 3 weeks or later.



JNJ-6143: High Rate of Radiographic Responses at the RP2D in Advanced mCRPC

ORR-evaluable patients in the 50 mg cohort



	50 mg (n=16) ^a
DOR, median (95% CI), months	11.0 (5.9, NE)

*After the data cutoff, 1 patient with SD converted to confirmed PR.

Data cutoff date: September 21, 2026.

^aPatients with measurable disease at baseline and either off-study or with ≥1 postbaseline assessment.

^bResponses are based on best overall response per RECIST version 1.1. CR and PR are confirmed and without bone progression by PCWG3.

^cThree patients with PR had visceral disease.

CR, complete response; CI, confidence interval; DCR, disease control rate; DOR, duration of response; NE, not evaluable; ORR, objective response rate; PCWG3, Prostate Cancer Working Group 3; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.



JNJ-6143: Conclusions

- **JNJ-6143 is a first-in-class RIPTAC™ molecule that forms a targeted dual-protein lock between AR (PC-selective tumor antigen) and BRD4 (essential cell survival protein) to trigger cell death**
- JNJ-6143 was highly active with an encouraging safety profile in this phase 1 study of patients with heavily pretreated mCRPC
- At the RP2D of 50 mg once daily (oral):
 - <60% any-grade TRAEs
 - 77% confirmed PSA50 rate and 48% confirmed PSA90 rate
 - High PSA response rate irrespective of high-risk molecular features
 - 69% confirmed ORR
- **A Phase 2 study (NCT07832292) initiated with 50 mg once daily**

These early data suggest that JNJ-6143 has the potential to combine high tumor selectivity and robust efficacy with a favorable safety profile and convenient oral administration



Acknowledgments

- The investigators and study sponsor would like to thank the patients for their participation, and the site caregivers and staff for their support of the study
- The study is sponsored by Johnson & Johnson



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