

ESSA

CORPORATE PRESENTATION
October 2023

Forward Looking Statements

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Forward-looking statements and information are subject to various known and unknown risks and uncertainties, many of which are beyond the ability of ESSA to control or predict, and which may cause ESSA’s actual results, performance or achievements to be materially different from those expressed or implied thereby. Such statements reflect ESSA’s current views with respect to future events, are subject to risks and uncertainties and are necessarily based upon a number of estimates and assumptions that, while considered reasonable by ESSA as of the date of such statements, are inherently subject to significant medical, scientific, business, economic, competitive, political and social uncertainties and contingencies, many of which, with respect to future events, are subject to change. In making forward-looking statements, ESSA may make various material assumptions, including but not limited to the market and demand for the securities of ESSA, general business, market and economic conditions, obtaining positive results of clinical trials, and obtaining regulatory approvals.

Forward-looking information is developed based on assumptions about such risks, uncertainties and other factors set out herein and in ESSA’s Annual Report on Form 10-K filed on December 13, 2022 under the heading “Risk Factors”, a copy of which is available on ESSA’s profile on the SEDAR website at www.sedar.com, ESSA’s profile on EDGAR at www.sec.gov, and as otherwise disclosed from time to time on ESSA’s SEDAR profile and EDGAR profile. Forward-looking statements are made based on management’s beliefs, estimates and opinions on the date that statements are made and ESSA undertakes no obligation to update forward-looking statements if these beliefs, estimates and opinions or other circumstances should change, except as may be required by applicable Canadian and United States securities laws. Investors are cautioned that forward-looking statements are not guarantees of future performance and investors are cautioned not to put undue reliance on forward-looking statements due to their inherent uncertainty.

Focused on the development of novel therapies for the treatment of prostate and other androgen-driven cancers

Company

- Experienced management team with deep expertise in oncology and drug development
- Headquartered in South San Francisco and Vancouver

Technology & Products

- Lead candidate **masofaniten** (EPI-7386) is a first-in-class oral, small molecule androgen receptor N-terminal domain inhibitor (“Aniten”)
- Masofaniten is being developed as a monotherapy in late-stage metastatic castration-resistant prostate cancer (“PC”) and in antiandrogen combinations in earlier stage PC
- The on-going phase 1 masofaniten monotherapy study shows the drug is well tolerated while the completed masofaniten+ enzalutamide (“ENZ”) clinical data demonstrate that 81% of patients achieved a PSA90 with durable PSA responses
- First generation AR NTD protein degrader (ANITAC) in preclinical development

Financial Details

- Listed on NASDAQ (EPIX)
- Cash and short-term deposits: \$152M (June 30, 2023); runway through 2025

Experienced Management Team



David R. Parkinson, MD
President & Chief Executive Officer



Peter Virsik, MS, MBA
EVP & Chief Operating Officer



David S. Wood, MBA, CPA, CMA
Chief Financial Officer



Alessandra Cesano, MD
EVP & Chief Medical Officer



Prostate Cancer Disease Landscape

PUBLIC HEALTH PROBLEM

- Prostate cancer is the 2nd most common cause of male cancer deaths
- American Cancer Society estimates 268,000 new cases and 34,500 deaths in 2022¹

LARGE MARKET

- Over \$9B in global sales generated in 2022 by leading antiandrogens²
- Newest antiandrogens: Zytiga[®] (abiraterone acetate), Xtandi[®] (enzalutamide), Erleada[®] (apalutamide) and Nubeqa[®] (darolutamide)²

VALIDATED THERAPEUTIC TARGET

- Androgen receptor (AR) signaling is critical for prostate cancer development and progression^{3,4,5}
- Mounting evidence that progression to CRPC remains dependent upon persistent AR signaling driven by AR resistance mechanisms^{3,5}

NEED FOR NEW THERAPEUTIC STRATEGIES

- Resistance to second-generation antiandrogens is common and on average occurs within a year of starting therapy⁶
- Clinical results suggest that more potent AR inhibition used earlier in therapy may provide improved clinical outcomes for patients⁷

1. American Cancer Society. (2022). *Key Statistics for Prostate Cancer*. Retrieved from <https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html>.

2. 2022 financial reports from www.sec.gov.

3. Robinson D, et al. *Cell*, 2015.

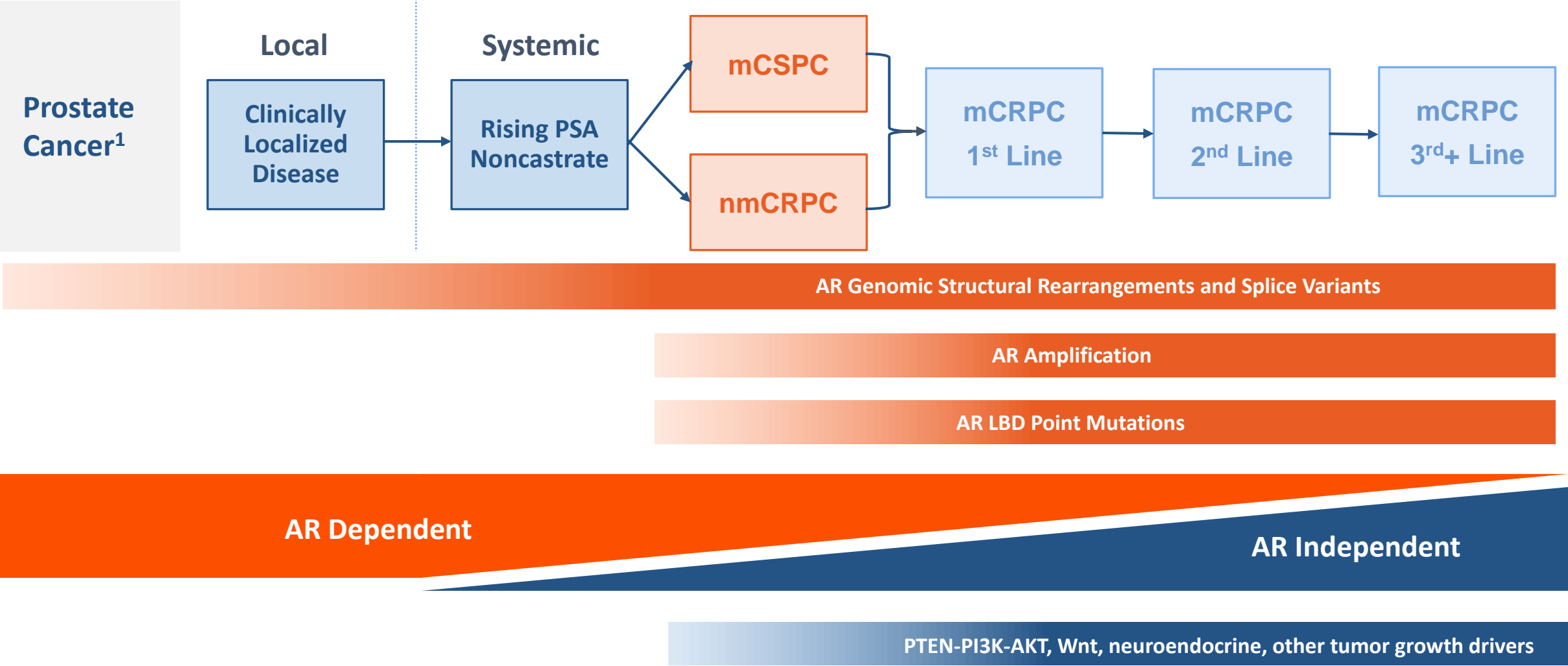
4. Chen CD, et al. *Nat Med*, 2004.

5. Kumar A, et al. *Nat Med*, 2016.

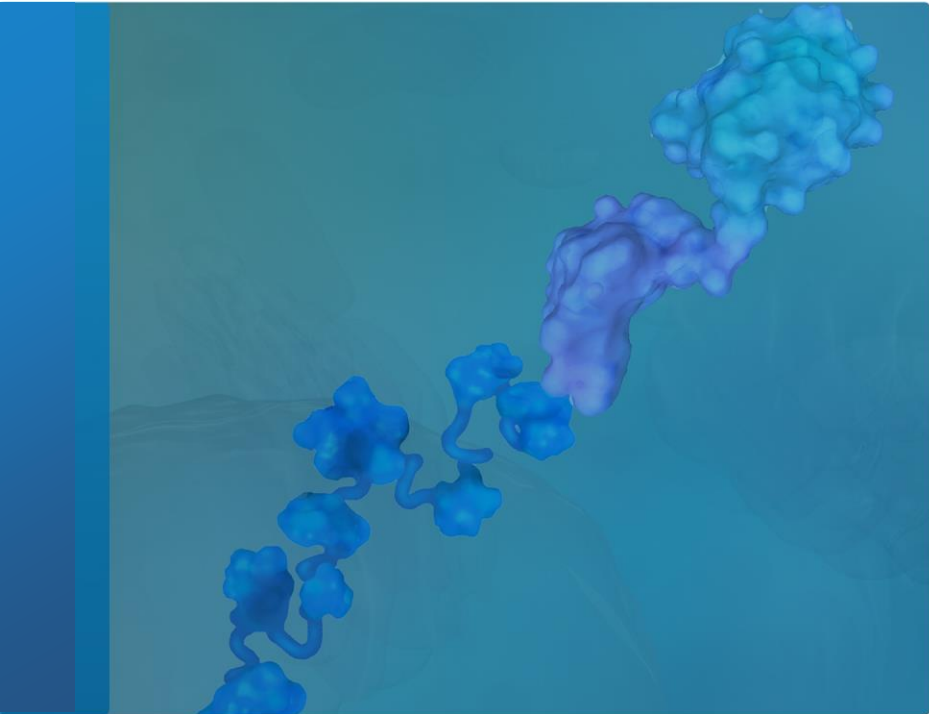
6. Sharp A, et al. *JCI*, 2019.

7. ESMO 2021.

Prostate Cancer Evolution and AR Dependency



1. Adopted from Scher, HI, et al. J Clin Oncol, 2016.

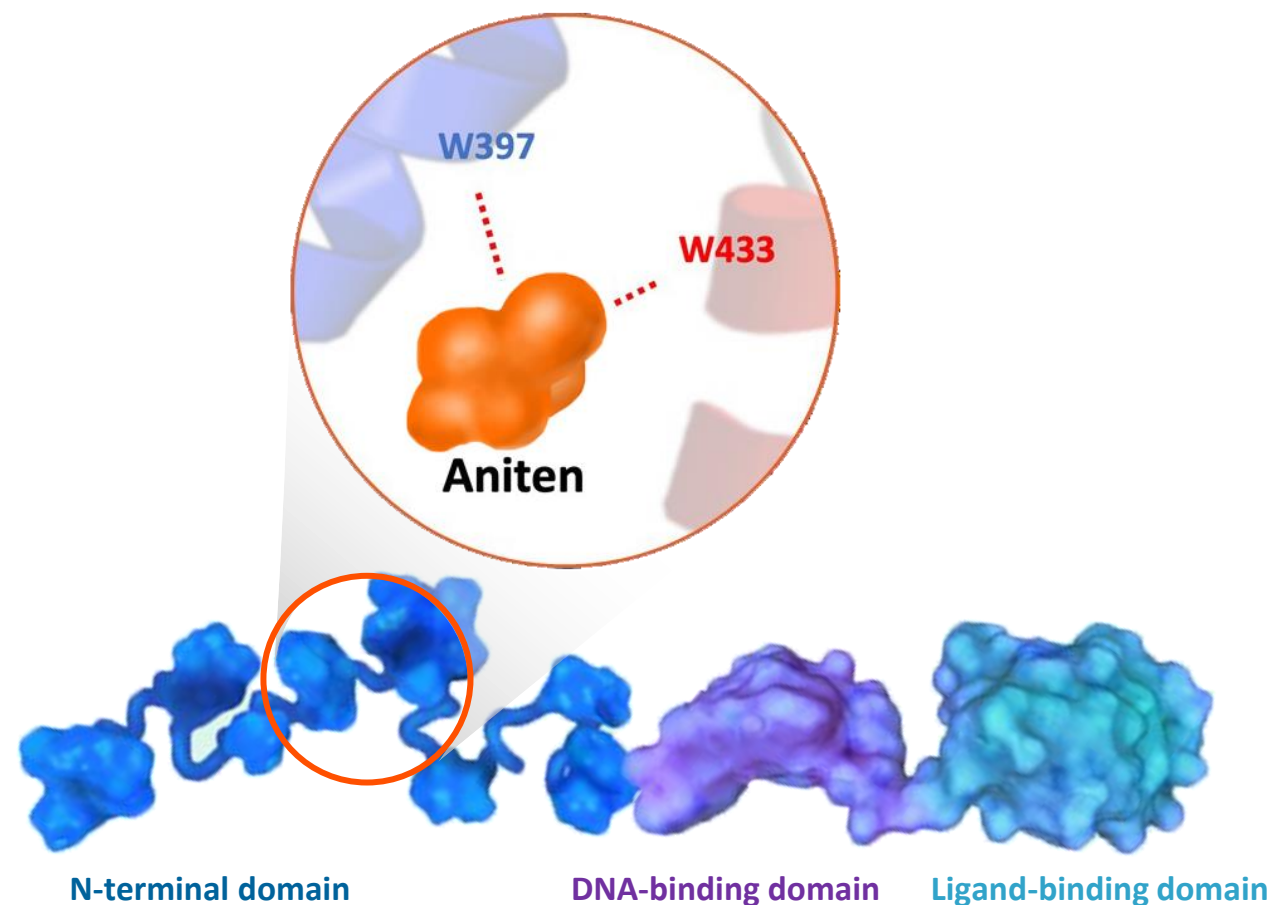


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Masofaniten (EPI-7386)
First-in-Class NTD AR Inhibitor

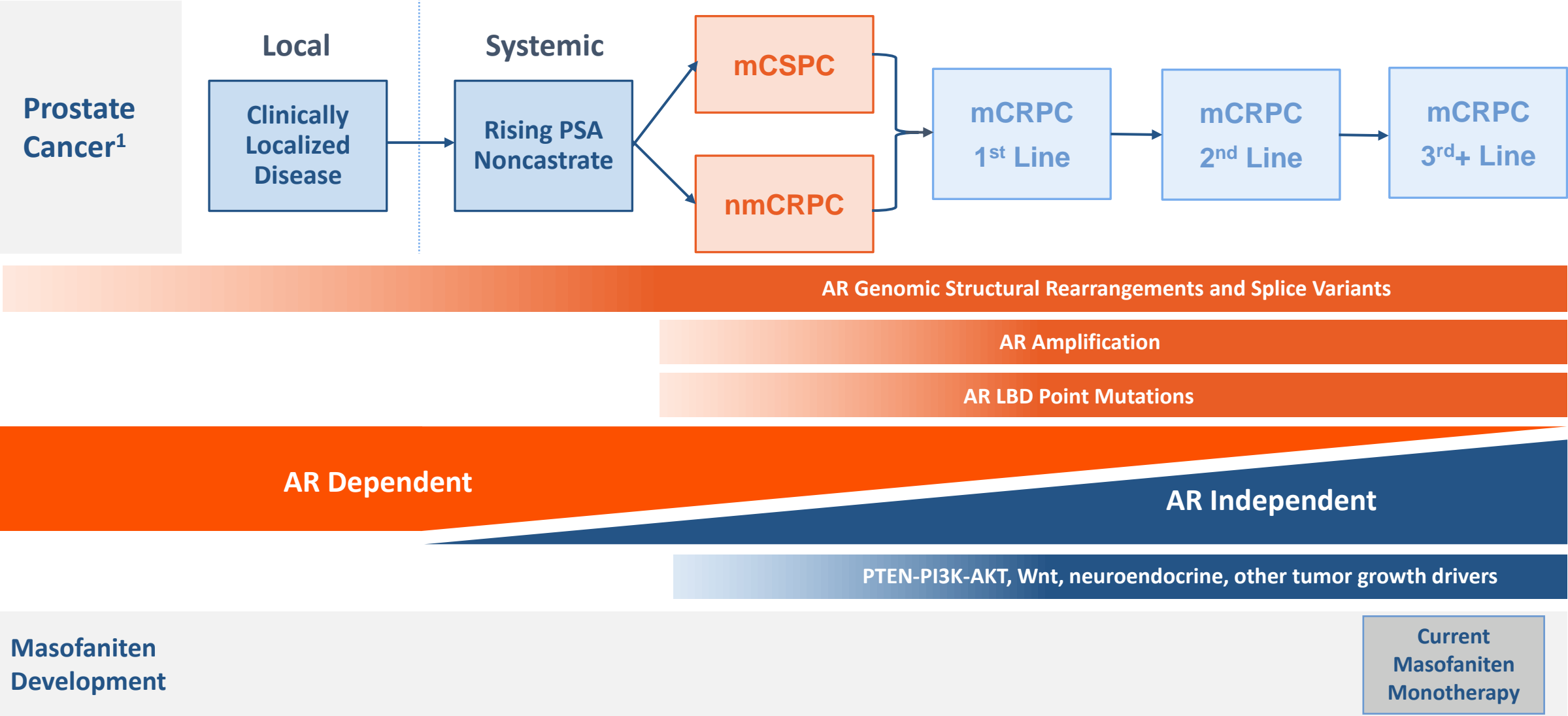
Masofaniten's Novel MoA Uniquely Inhibits the NTD of the Androgen Receptor, Potentially Overcoming Resistance to Standard-of-Care

- All current antiandrogens function through the ligand-binding domain (LBD) of the androgen receptor (AR)
 - Known antiandrogen resistance mechanisms develop at the LBD
- Masofaniten specifically binds to the N-terminal domain (NTD) of the AR, a region of the androgen receptor required for AR activity
- As a result of this binding, masofaniten is active against multiple AR forms, including those resistant to current antiandrogens
- Masofaniten's novel method of inhibiting the AR may lead to greater AR suppression when used in combination with current antiandrogen therapies



Granted unique USAN drug stem of “Aniten” as a AR NTD inhibitor

EPI-7386 Monotherapy Clinical Development for AR-Driven CRPC



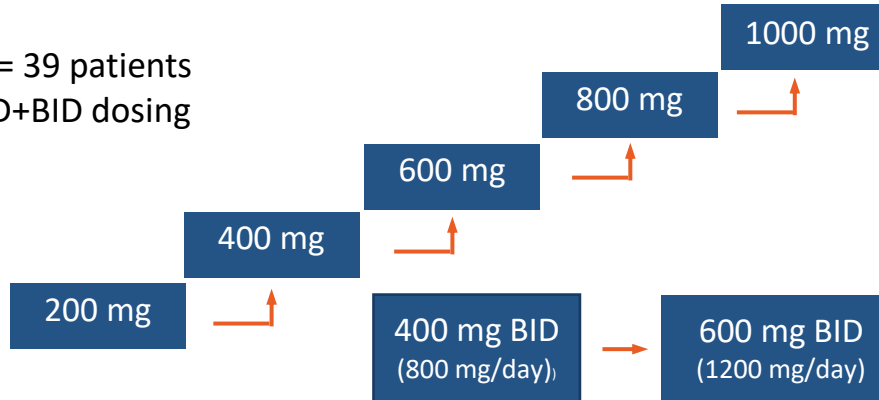
1. Adopted from Scher HI, et al. J Clin Oncol, 2016.

Masofaniten Phase 1 Monotherapy Study in mCRPC Patients: Study Design

- First-in-human Phase 1 multi-center open-label study enrolling mCRPC patients failing standard-of-care therapy
- Two-part study: Phase 1a dose-escalation (Completed) followed by Phase 1b dose expansion (Currently enrolling)

Phase 1a Clinical Study

N = 39 patients
QD+QD dosing



Results

- Masofaniten was safe and well-tolerated
- Masofaniten has a long half life (>24hrs) and all doses reached target drug exposures
- Some signals of clinical anti-tumor activity observed in less experienced patients (e.g. PSA, PSA_{dt}, ctDNA, etc)

Phase 1b Clinical Study

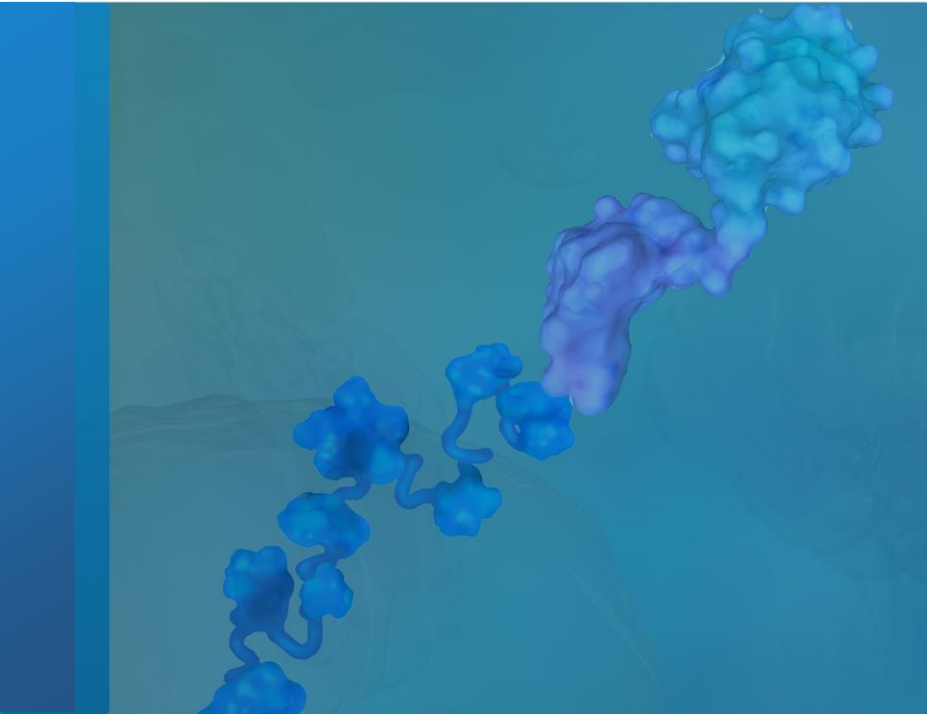
600 mg BID
N=12



600 mg QD
N=12

Results

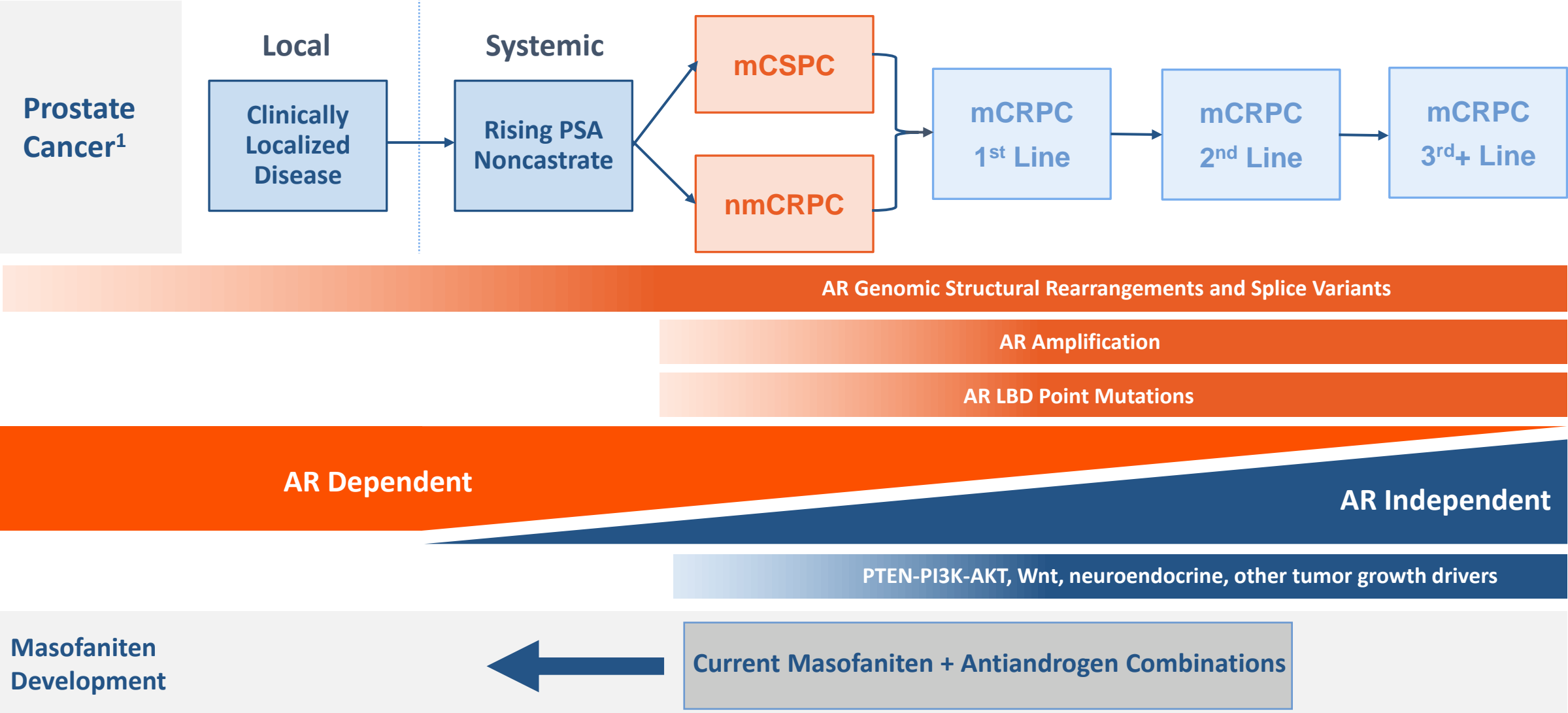
- Currently enrolling patients



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**Masofaniten (EPI-7386) in Combination
with Second Generation Antiandrogens**

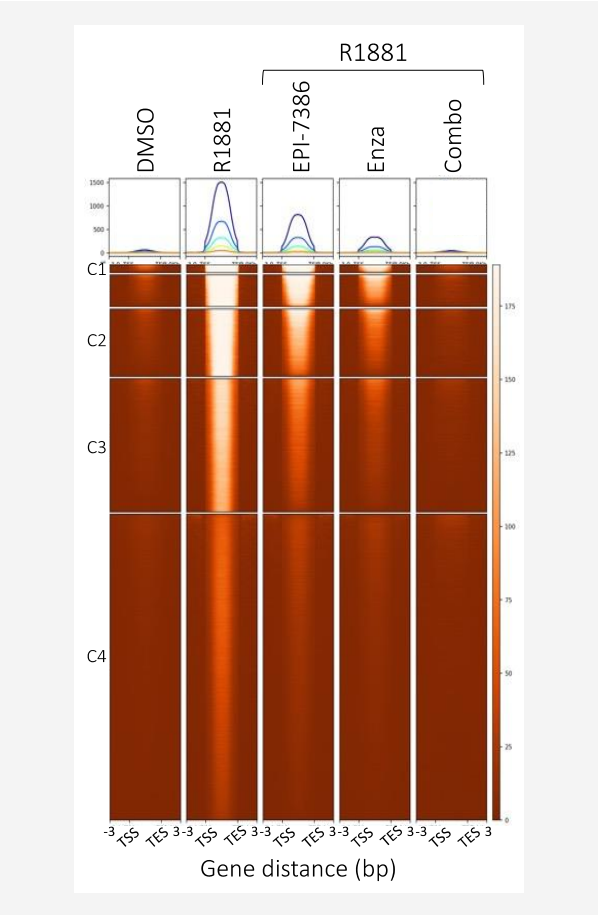
Masofaniten Combination Study Clinical Program for AR-Driven CRPC



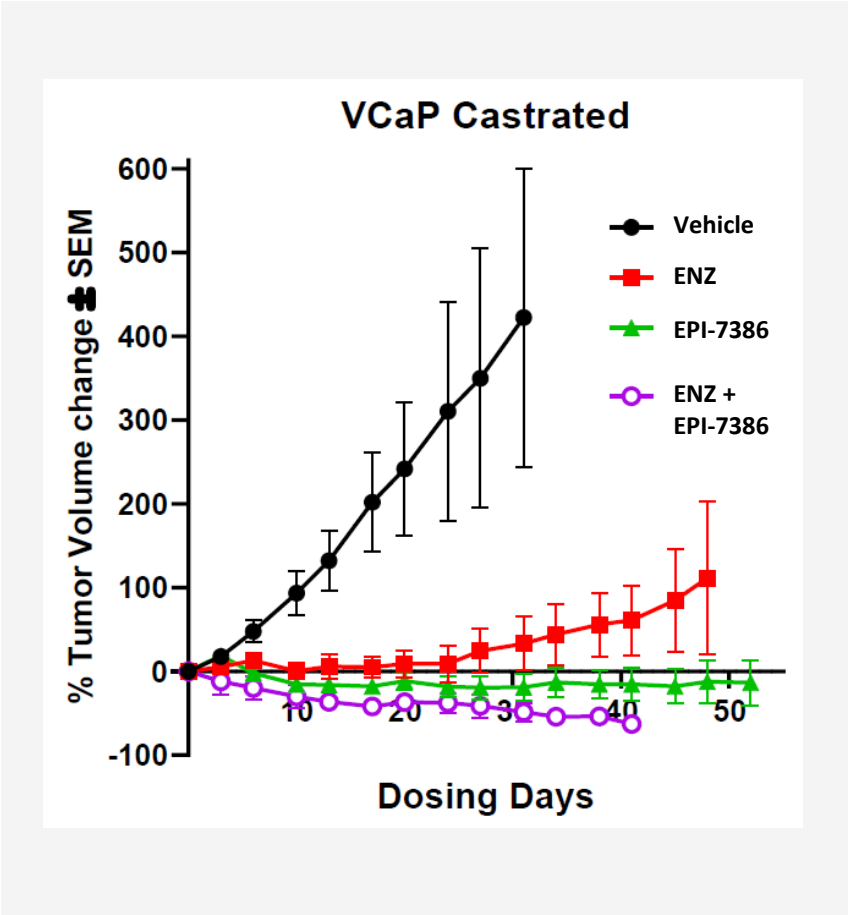
1. Adopted from Scher, HI, et al. J Clin Oncol, 2016.

Preclinical Rationale for the Combination of Masofaniten with Antiandrogens

AR Binding to Genomic DNA



Mouse VCaP Xenograft Efficacy



- Decades of clinical research link improved clinical results with deeper AR axis suppression
- Combining an AR NTD-inhibitor with an LBD-inhibitor provides two complementary ways of inhibiting AR biology
- Preclinical studies support deeper and broader suppression of AR-driven biology by combining masofaniten with antiandrogens

Masofaniten Combination Development Program with Second-Generation Antiandrogens



ESSA collaboration with Astellas to evaluate masofaniten in combination with Xtandi[®] (enzalutamide) in an ESSA-sponsored Phase 1/2 clinical study in mCRPC patients naïve to second generation antiandrogens (study began 1Q2022)



ESSA collaboration with Janssen to evaluate masofaniten in combination with Erleada[®] (apalutamide) and Zytiga[®] (abiraterone acetate) + prednisone in Phase 1 clinical study cohorts evaluating apalutamide + masofaniten in nmCRPC patients and also abiraterone and prednisone in combination with masofaniten in mCRPC patients naïve to second generation antiandrogens and in mCSPC patients.



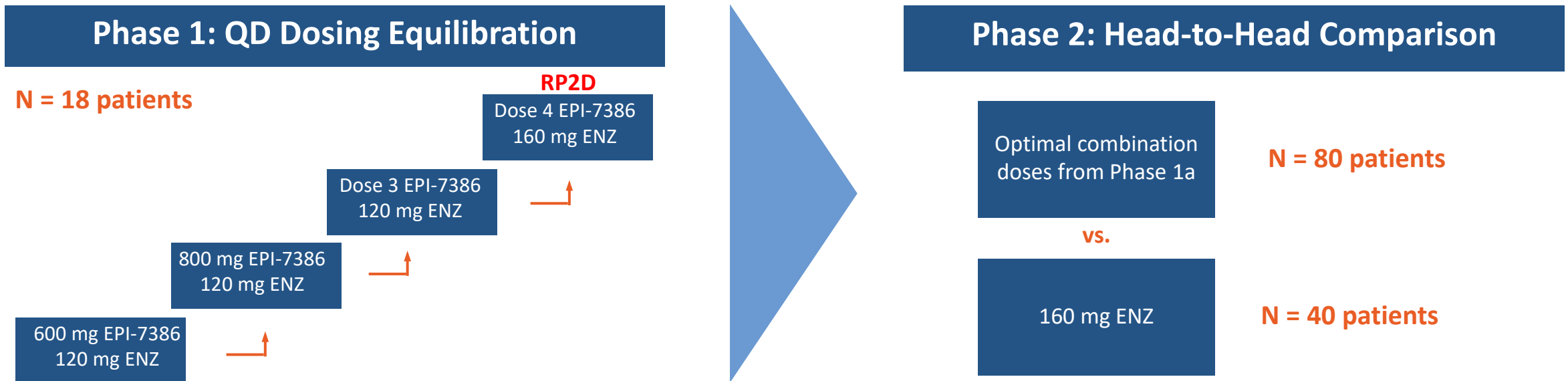
Bayer collaboration with ESSA to evaluate masofaniten in combination with Nubeqa[®] (darolutamide) in a Phase 1/2 clinical study in mCRPC patients

**Investigator-Sponsored
Neoadjuvant Study**

A 12-week two-arm randomized study of Nubeqa vs. masofaniten + Nubeqa in PC patients undergoing prostatectomy for high risk localized prostate cancer

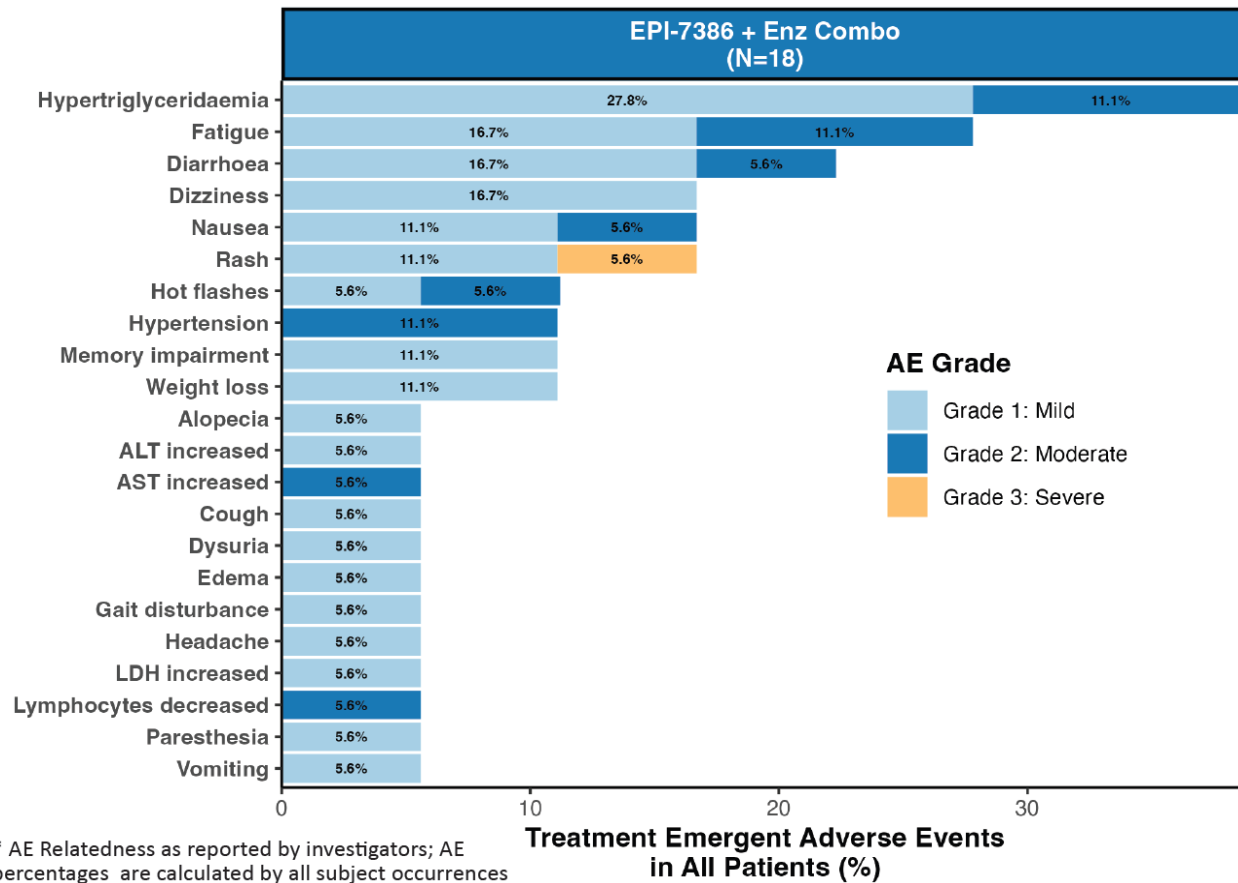
Phase 1/2 Masofaniten + Enzalutamide (ENZ) Combination Study Trial Design in mCRPC Patients Naïve to Second-Generation Antiandrogens

- Phase 1/2 multi-center open-label study enrolling mCRPC patients naïve to second-generation antiandrogens
- Two-part study: Phase 1 dose-equilibration followed by Phase 2 open-label randomized study



- Phase 1 study focused on the PK and safety of masofaniten and enzalutamide when administered in combination along with establishing the RP2D for both drugs to address any possible drug-drug interactions
- Phase 2 study will assess the anti-tumor activity of the combination of masofaniten and enzalutamide versus single agent enzalutamide at the standard of care dose

Phase 1/2 Masofaniten + ENZ Combination Study Results: Safety



* AE Relatedness as reported by investigators; AE percentages are calculated by all subject occurrences

Safety

- The combination of masofaniten and ENZ was well-tolerated
- Most adverse events (AE) reported were grade 1 and 2
 - One grade 3 drug-related AE (rash) occurred in cohort four & was observed after ENZ was added to masofaniten
- Otherwise, the combination safety profile was consistent with second generation antiandrogens

Phase 1/2 Masofaniten + ENZ Combination Study Results: Pharmacokinetics

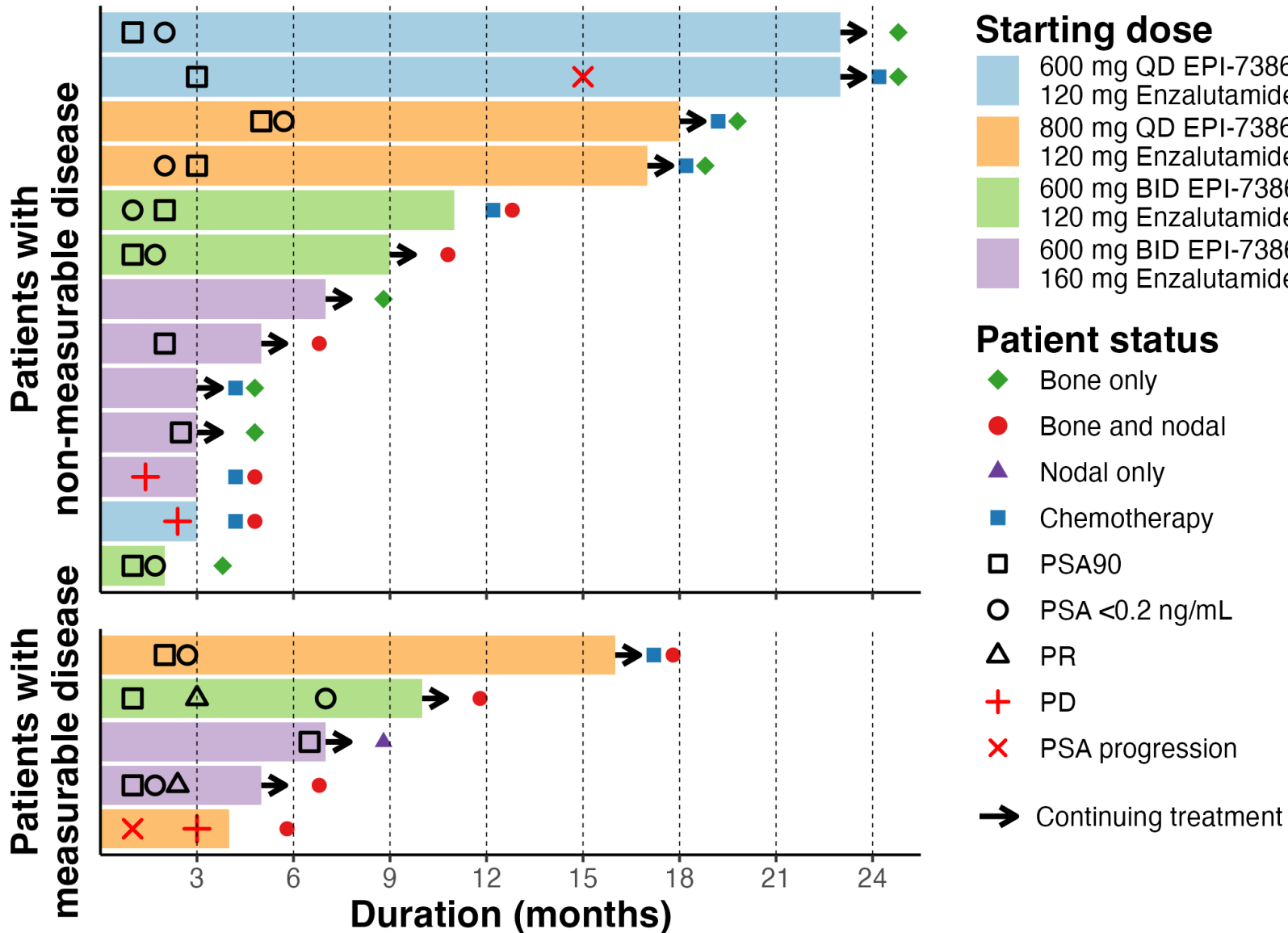
Masofaniten Dose	Timepoint	ENZ Dose	Masofaniten AUC	Masofaniten AUC Decline	ENZ AUC	ENZ M2 AUC
600mg BID	7-Day Run-in	--	508,250	--	--	--
600mg BID	28 Days	120 mg	233,000	-54%	304,750	208,725
600mg BID	7-Day Run-in	--	435,833	--	--	--
600mg BID	28 Days	160 mg	189,600	-56%	300,600	278,300

- Clinically relevant concentrations of masofaniten seen across all dose cohorts and are well within the predicted efficacious range based upon preclinical studies
 - Masofaniten concentrations >15 uM in both dose arms
- The reduction in masofaniten AUC was similar in both the 120mg ENZ cohort and the 160mg ENZ cohort, indicating the 160mg ENZ dose can be used in the phase 2 clinical study

Pharmacokinetics (PK)

- ENZ exposure minimally impacted by masofaniten administration
- Masofaniten exposure reduced but BID dosing can partially compensate
 - Clinically relevant concentrations of masofaniten in all cohorts
- Cohort four dose selected for RP2D
 - 600mg BID masofaniten
 - 160mg ENZ

Phase 1 Masofaniten + ENZ Combination Study: Swimmer Lane Plot with PSA and Radiographic Responses



Clinical Activity

13/18 ongoing, 5/18 discontinued

- Disease progression = 3
- Brain abscess = 1 (non-related)
- Non-cancer-related death = 1 (patient w/ PSA90 and <0.2 ng/mL)

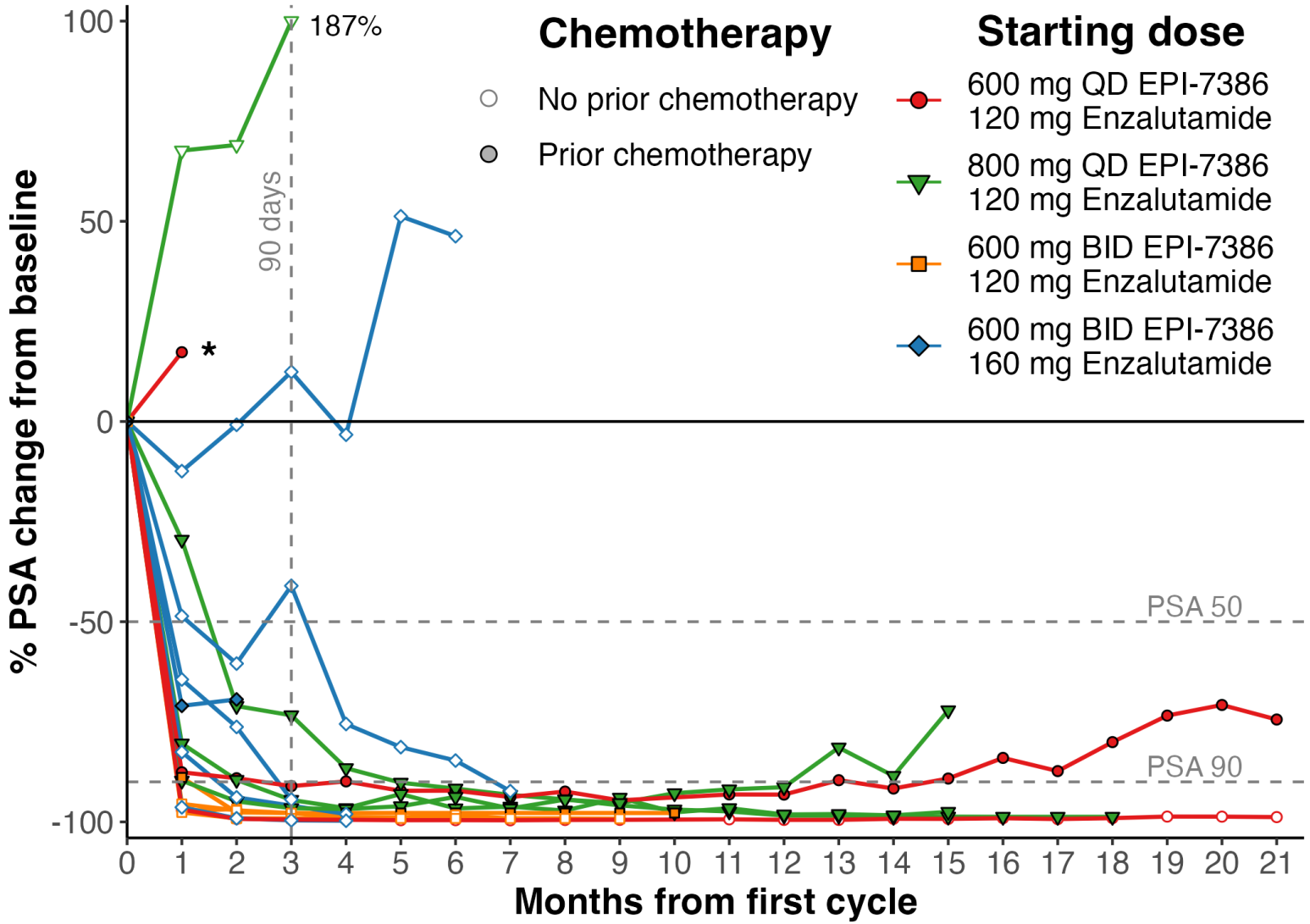
13/18 non-measurable disease:

- Bone only or bone + non-target lesions:
 - 11/13 SD ; 2/13 PD
- 2 non-evaluable for efficacy (per protocol, insufficient drug exposure)

5/18 measurable disease (RECIST v1.1):

- 2/5 PR ; 2/5 SD ; 1/5 PD

Phase 1 Masofaniten + ENZ Combination Study: Longitudinal PSA Changes



Clinical Activity

- Data not fully mature
- Rapid, deep and durable PSA reductions observed
- 13 of 16 (81%) patients achieved a PSA90 regardless of prior chemotherapy status
- 11 of 16 (69%) patients achieved a PSA90 in 90 days and 9 of 16 (56%) have achieved a PSA < 0.2ng/mL
- PSA responses appear durable

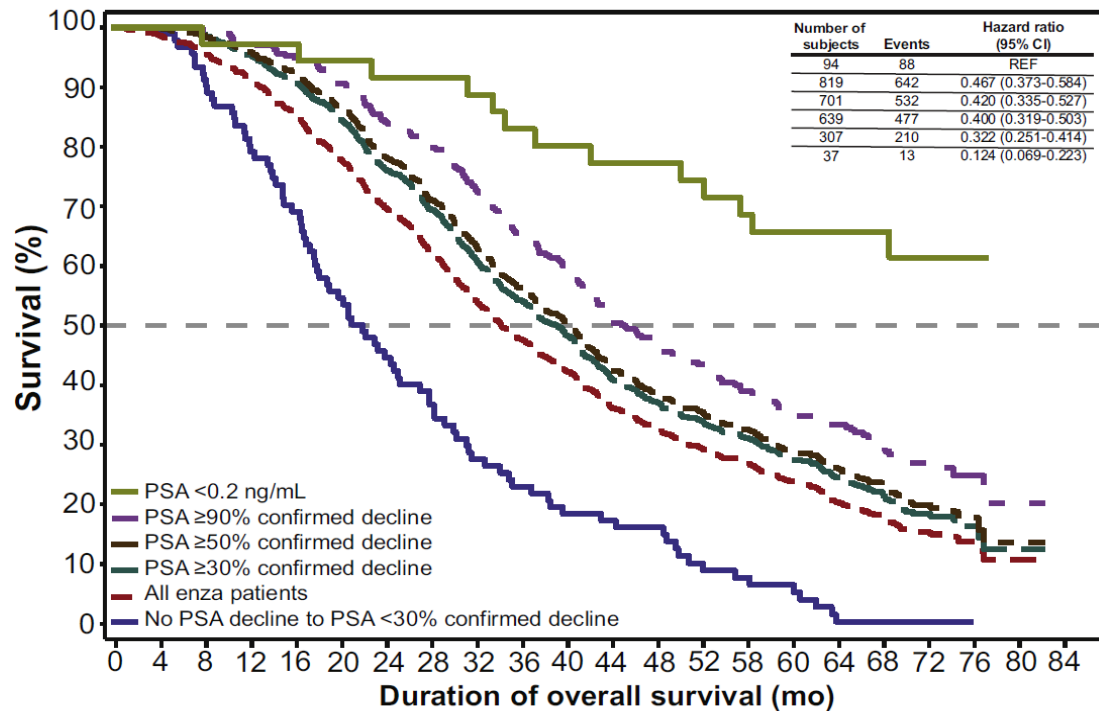
Phase 1 Masofaniten + ENZ Combination Study: PSA Data Compare Favorably to Pivotal ENZ and other mCRPC Antiandrogen Studies

mCRPC Patient Population	Agent	PSA90 (Overall)	Study Type	PSA90 (90 Days)	PSA <0.2 ng/mL (Overall)	Time to PSA Progression (months)	Reference
Pre-Chemo Setting							
PREVAIL Study	ENZ	47%	Pivotal	37%	12%⁺	11.2	Beers et al., NEJM, 2014; Armstrong et al., Eu Assoc of Uro, 2020; Armstong, et al. Eu Urol Onc_2019
PREMISE Study	ENZ	45%	Observational	--	--	--	Payne et al., Int J of Canc, 2021.
ACIS Study	ABI	47%	Pivotal	--	19%	12.0	Saad et al., Lancet Onc, 2021.
ACIS Study	ABI+APA	53%	Pivotal	--	25%	13.8	Saad et al., Lancet Onc, 2021.
Post-Chemo Setting							
AFFIRM Study	ENZ	25%	Pivotal	13%	--	8.3	Scher et al., NEJM, 2012; Armstrong et al., Cancer 2017.
PREMISE Study	ENZ	31%	Observational	--	--	--	Payne et al., Int J of Canc, 2021.
Masofaniten P1		81%		69%	56%	--	Prostate Cancer Foundation Scientific Retreat, 2023

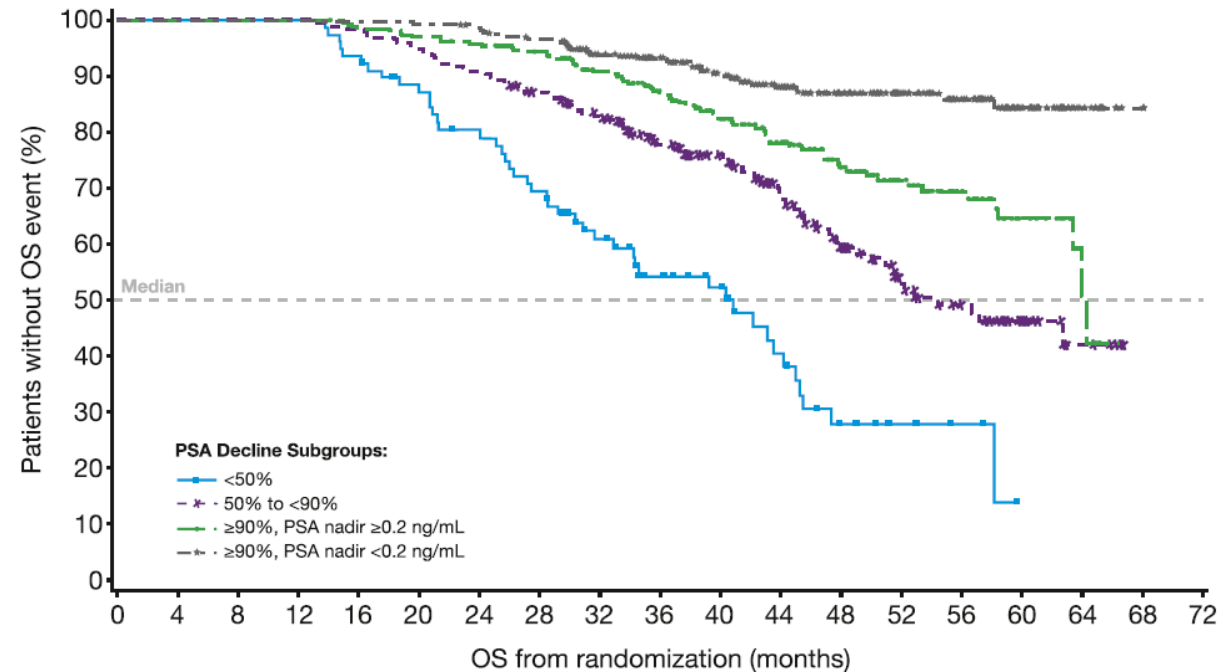
- Phase 1 data are not yet mature, so the above estimates may not fully represent Phase 1 results

* Armstong, et al. Eu Urol Onc_2019.; * Estimate derived from Armstong, et al. Eu Urol Onc_2019

In Prior Studies of ENZ in CRPC Patients, Deep PSA Declines were Associated with Better Long-Term Overall Survival*



From the PREVAIL study of mCRPC patients, the deeper the PSA decline during the initial 13-week period, the better the long-term overall survival



From the PROSPER study of nmCRPC patients, the deeper the 12-month PSA nadir, the better the long-term overall survival

*Armstrong, et al. *Eu Urol*_2020; Hussain, et al. *The J of Uro*_2023.

Additional Masofaniten Phase 1 Combination Studies

ESSA + Janssen Combinations

Phase 1 Masofaniten + Abiraterone Acetate

600mg QD 800mg QD 600mg BID

- **Metastatic castration-sensitive PC (mCSPC)**
- **mCRPC**
 - 1st line (no-prior 2nd gen antiandrogens) but prior docetaxel in mCSPC allowed
- Cohorts: 600mg + 800mg QD & 600mg BID dosing

Phase 1 Masofaniten + Apalutamide

600mg QD 800mg QD 600mg BID

- **Non-metastatic CRPC (nmCRPC) patients**
 - 12 weeks of EPI-7386 monotherapy treatment before combining with apalutamide
- Cohorts: 600mg + 800mg QD & 600mg BID dosing

Investigator Sponsored Studies

Phase 1 Masofaniten + Darolutamide (DAR)

600mg BID

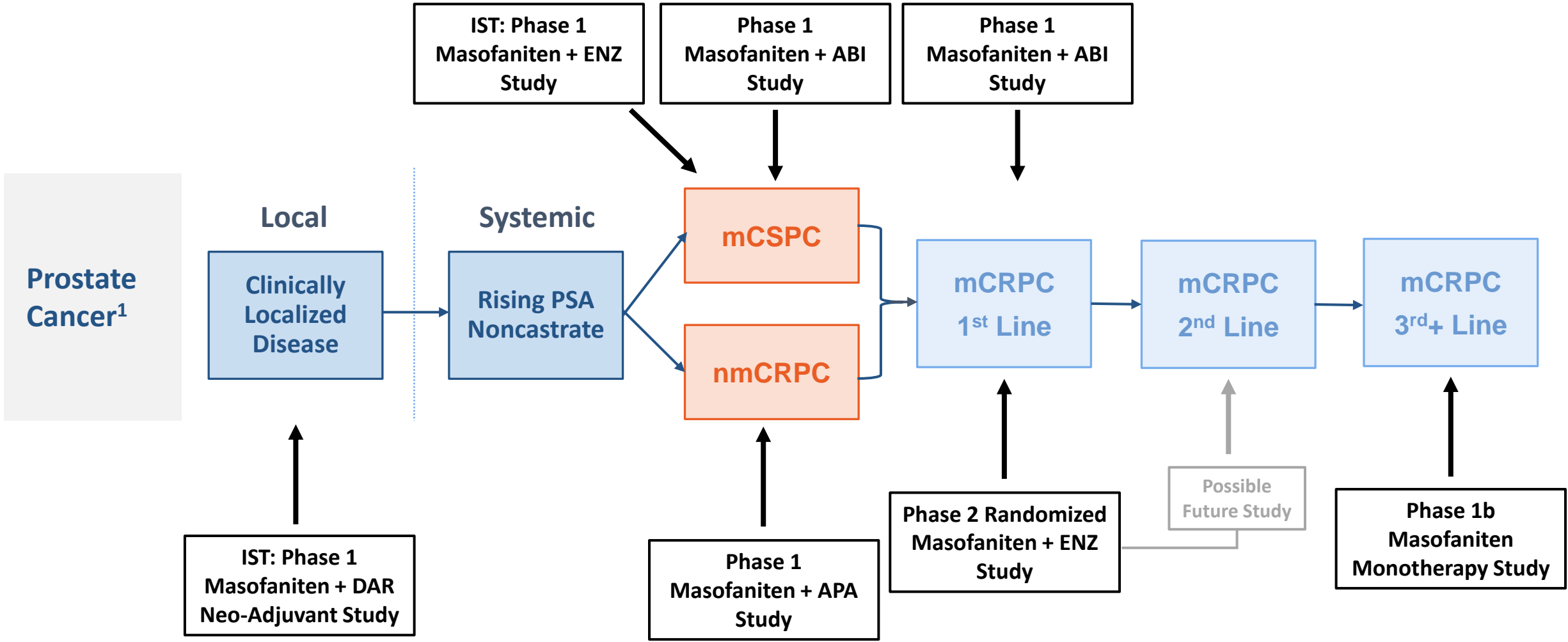
- **Neoadjuvant Therapy in High-Risk Patients Undergoing Prostatectomy**
 - 12-Weeks treatment of DAR vs. Masofaniten + DAR

Phase 1 Masofaniten + Enzalutamide

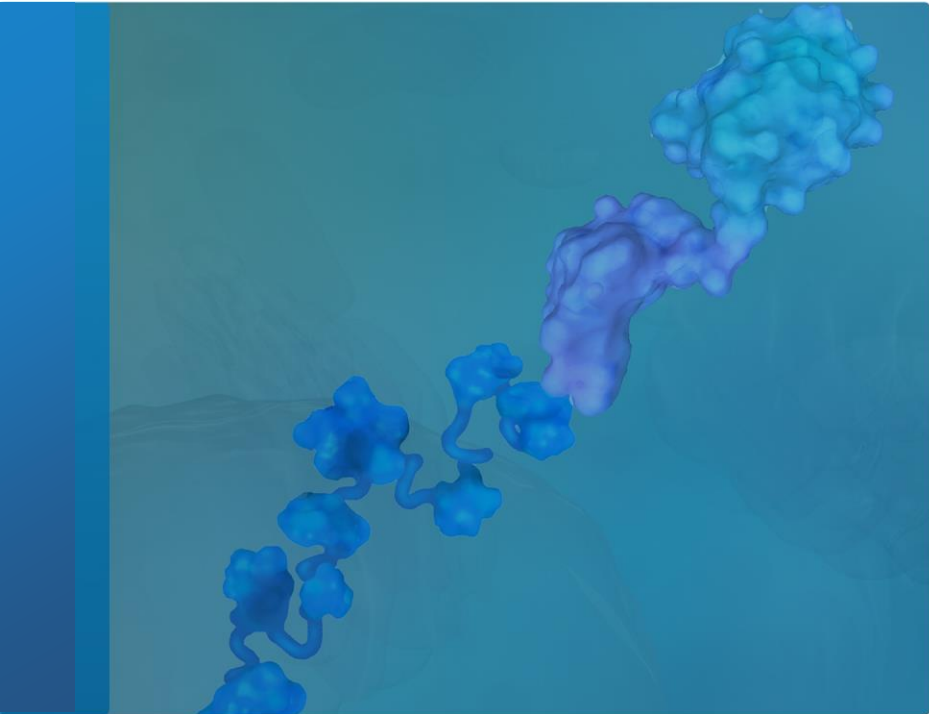
600mg BID

- **Metastatic castration-sensitive PC (mCSPC)**
 - ENZ combination study examining PSA <0.2 ng/mL
 - Starting Year-End

Masofaniten Clinical Program Will Generate Significant New Data in the Near-term



1. Adopted from Scher, HI, et al. J Clin Oncol, 2016.



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Milestones and Cash Flow

ESSA Research and Development Pipeline

EPI-7386

PROGRAM	INDICATION	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	COLLABORATIONS
EPI-7386 monotherapy	mCRPC – Resistant to standard of care treatments						
	Non-PC AR-driven Cancers						
EPI-7386 + enzalutamide	mCRPC						
EPI-7386 + abiraterone acetate + prednisone	mCRPC + mCSPC						
EPI-7386 + apalutamide	nmCRPC						
EPI-7386 + darolutamide	mCRPC						

Discovery

PROGRAM	INDICATION	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	COLLABORATIONS
3rd-Generation AR N-Terminal Domain Inhibitor	Prostate Cancer						
AR N-Terminal Domain Degradar (“ANITAC”)	Prostate Cancer						
AR N-Terminal Domain Tau-1 Site Inhibitor	Prostate Cancer						

ESSA Upcoming Milestones

EPI-7386 Programs	Timing
Monotherapy	
Present clinical update on Phase 1 trial	Completed
Establish the recommended Phase 2 dose (RP2D)	Completed
Initiate Phase 1b expansion study	Completed
Complete enrollment into the Phase 1b expansion study	2023
Combination	
Complete Phase 1 study	Completed
Establish the RP2D for EPI-7386/enzalutamide combination trial	Completed
Initiate Phase 2 portion of EPI-7386/enzalutamide combination trial	Completed
Enrollment of apalutamide and abiraterone acetate cohorts	2H2023
Discovery	
Initiate IND-enabling studies for an ANITAC NTD degrader or an Aniten	2023

Financial Position & Capitalization

Nasdaq: EPIX

Cash

\$152M reported at August 8, 2023 (no debt O/S)

Shares

~47M (44M I/O common shares and 3M prefunded warrants)

Covering Analysts

Bloom Burton - *David Martin* | Jefferies - *Maury Raycroft*
Oppenheimer – *Leland Gershell* | Piper Sandler - *Joe Catanzaro*

Current cash runway through 2025 funds:

- Completion of Phase 1 dose escalation & expansion monotherapy studies
- Completion of Phase 1/2 combination studies with antiandrogens
- Phase 2 monotherapy pivotal study
- Phase 2 combination study with enzalutamide and Phase 1 combination study with abiraterone and apalutamide
- Pipeline work including preclinical studies with Anitens in other AR-driven tumors



For further information, please contact:

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