

ESSA

March 2022

Forward Looking Statements

Certain written statements in and/or oral statements made in connection with this presentation may be considered forward-looking statements within the meaning of applicable Canadian securities laws and the United States securities laws, that may not be based on historical fact, including, without limitation, statements containing the words “believe”, “may”, “plan”, “will”, “estimate”, “continue”, “anticipate”, “predict”, “project”, “intend”, “expect”, “potential” and similar expressions. Forward-looking statements in this presentation include, but are not limited to: the mortality rate of prostate cancer; ESSA’s upcoming milestones; potential treatments for EPI-7386; EPI-7386’s Phase 1 study and its success; clinical trials; and potential market opportunities for EPI-73896.

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 November 18, 2021 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

Founded with technology licensed from The University of British Columbia and the British Columbia Cancer Agency

Sites in South San Francisco, Vancouver, and Houston

Technology & Products

- First-in-class N-terminal domain (NTD) inhibitors of the androgen receptor (“Anitens”)
- EPI-7386 phase 1 monotherapy study in patients with mCRPC who are resistant to standard of care treatments began in 2020
- First phase 1/2 study of EPI-7386 in combination with antiandrogens in patients with earlier mCRPC disease began in 1Q2022
- Emerging research pipeline focused on prostate and other androgen-driven cancers

Financial Details

- Listed on NASDAQ (EPIX)
- Completed raise of \$150M in 2021
- Cash and short-term deposits: \$189.2M (December 31, 2021)

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
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 248,000 new cases and 34,000 deaths in 2021¹

LARGE MARKET

- Over \$7.5B in global sales generated in 2020 by leading antiandrogens
- 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. (2021). *Key Statistics for Prostate Cancer*. Retrieved from <https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html>.

2. 2020 financial reports from www.sec.gov.

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

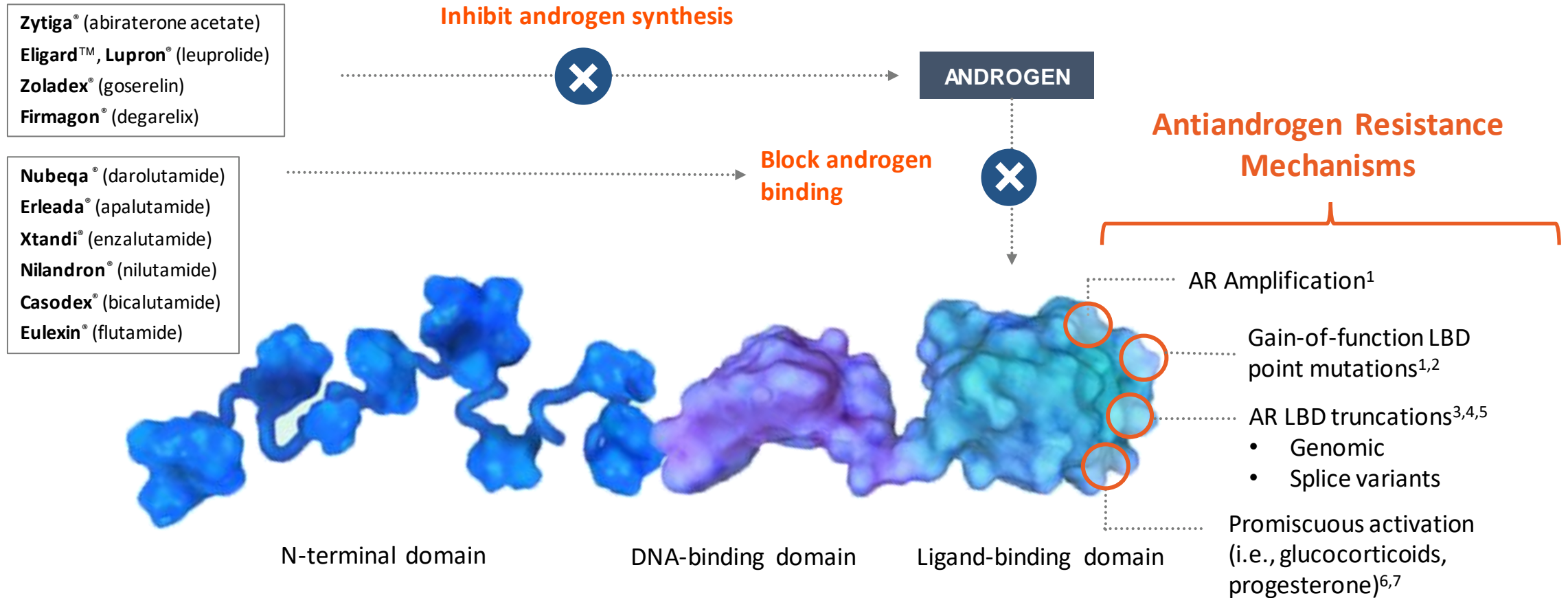
4. Chen CD, et al. *Nat Med*, 2004.

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

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

7. ESMO 2021.

Current Antiandrogen Therapies Only Target the Androgen Receptor Ligand-Binding Domain



- All current antiandrogens function through the ligand-binding domain (LBD) of the androgen receptor
- Known antiandrogen resistance mechanisms develop at the LBD

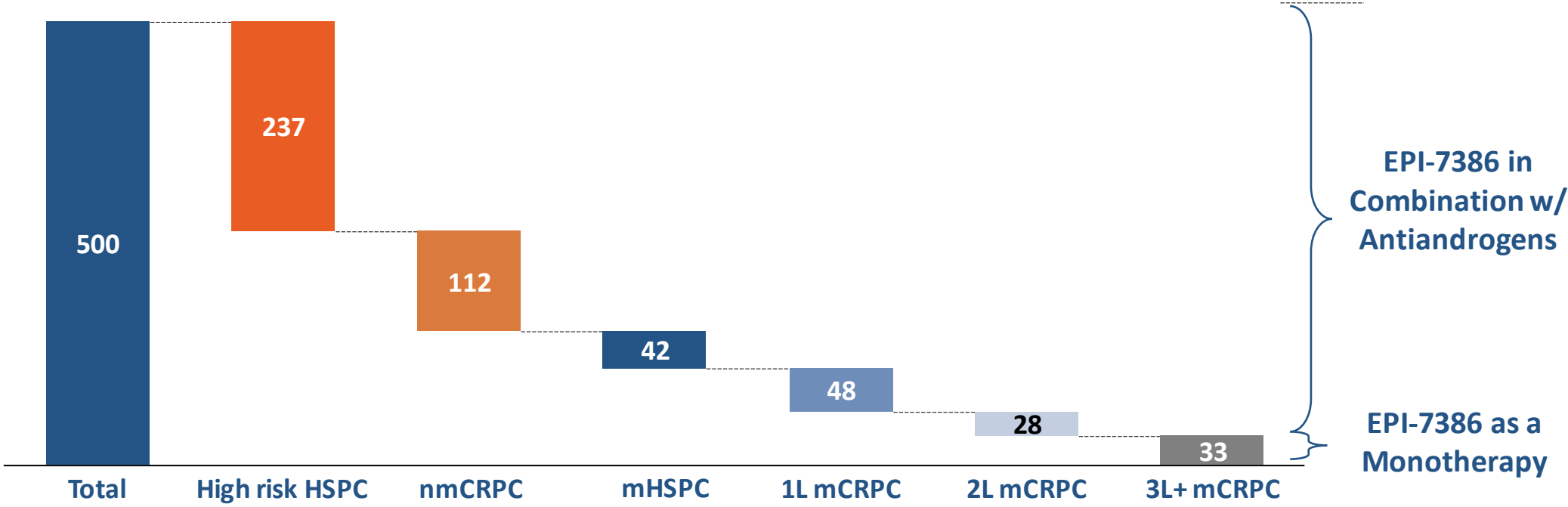
1. Azad AA, et al. *Clin Cancer Res*, 2015.
 2. Joseph JD, et al. *Cancer Discov*, 2013.
 3. Antonarakis ES, et al. *NEJM*, 2014.

4. Mostaghel EA, et al. *Clin Cancer Res*, 2011.
 5. Annala, et al. *Cancer Discov*, 2018.
 6. Chen EJ, et al. *Clin Cancer Res*, 2015.

7. Culig Z, et al. *Cancer Res*, 1994.

EPI-7386: US Prostate Cancer Market Opportunity is Large*

US Prostate Cancer Prevalence Estimated in 2020 by Stage of Disease* (in thousands)



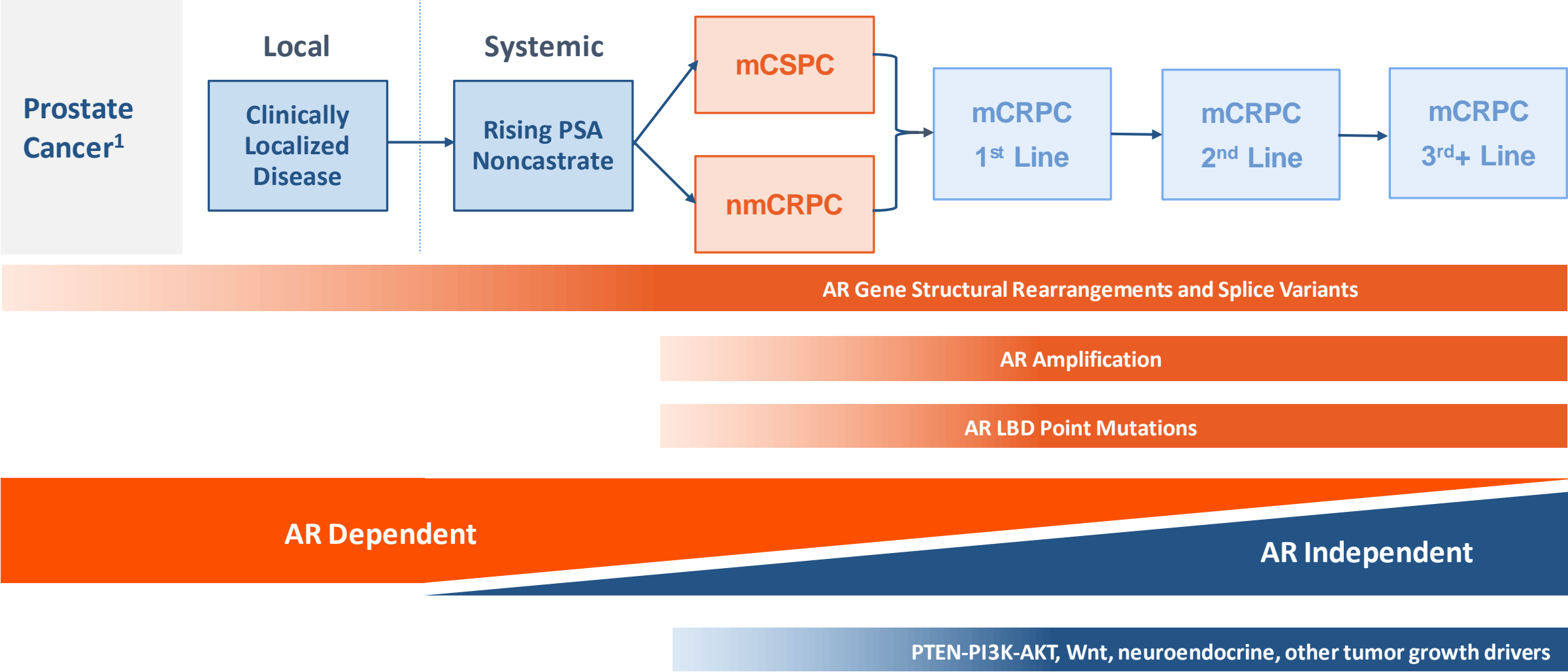
Antiandrogens Approved or in a Pivotal Phase 3 Study

- ▶ Approved
- ◆ In P3 Study

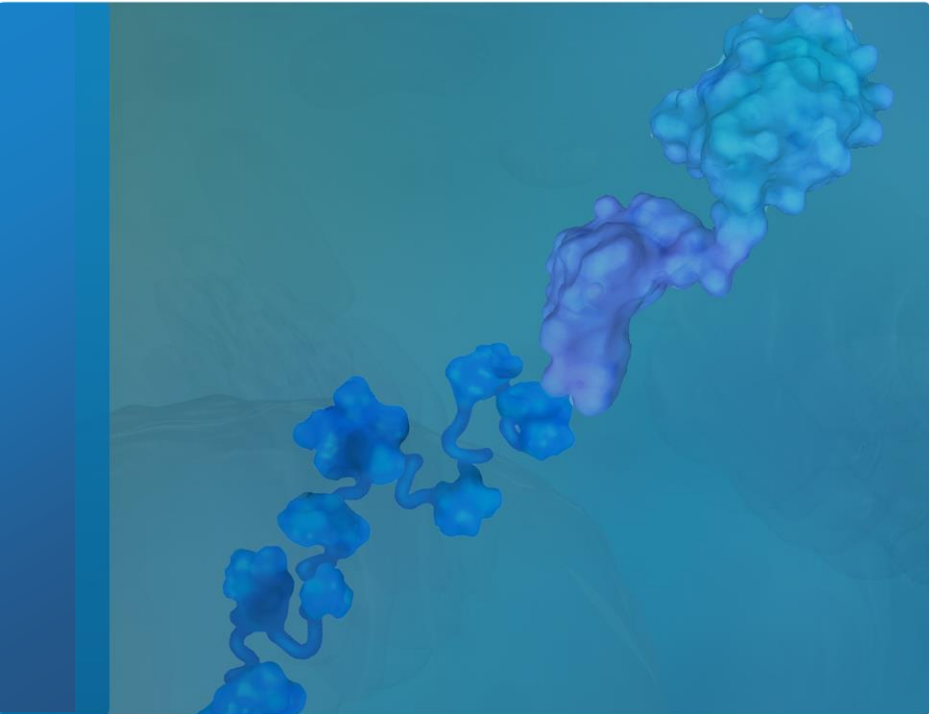
◆ Erleada (apalutamide) tablets	▶ Xtandi (enzalutamide)	▶ Xtandi (enzalutamide)	▶ Xtandi (enzalutamide)
◆ NUBEQA (darolutamide) tablets	▶ Erleada (apalutamide) tablets	▶ Zytiga (abiraterone acetate) 250 mg, 300 mg tablets	▶ Zytiga (abiraterone acetate) 250 mg, 300 mg tablets
	▶ NUBEQA (darolutamide) tablets	◆ Erleada (apalutamide) tablets	◆ NUBEQA (darolutamide) tablets

* Sher, H, et al. PLOS One, 2015. 3L mCRPC patients are estimated as the yearly mortality incidence due to prostate cancer.

Prostate Cancer Evolution and AR Dependency



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

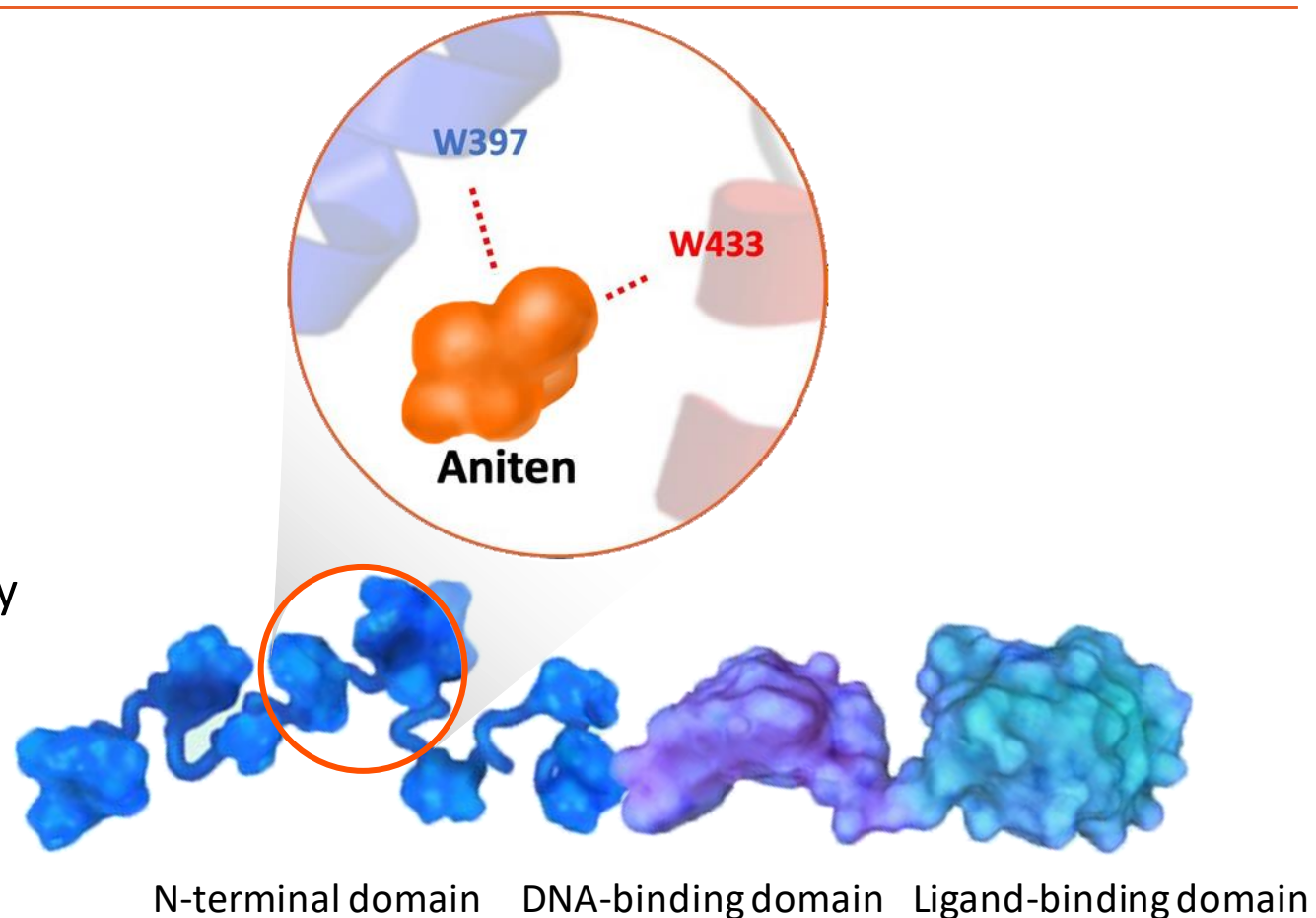


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**EPI-7386, First-in-Class NTD AR
Inhibitor**

EPI-7386 is Uniquely Designed to Prevent AR Transcription by Binding to the NTD

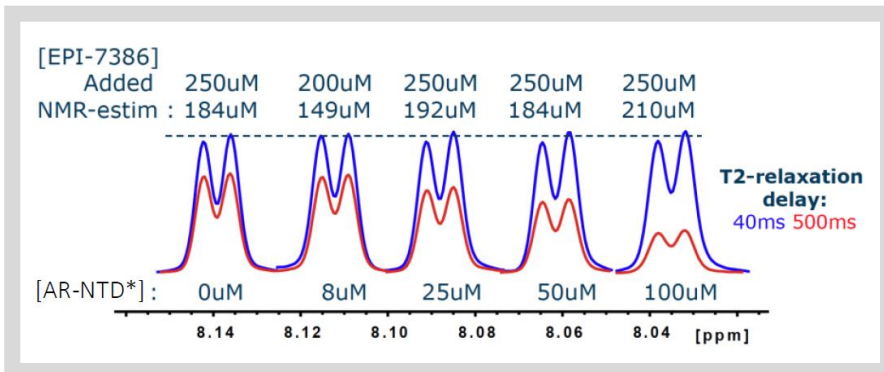
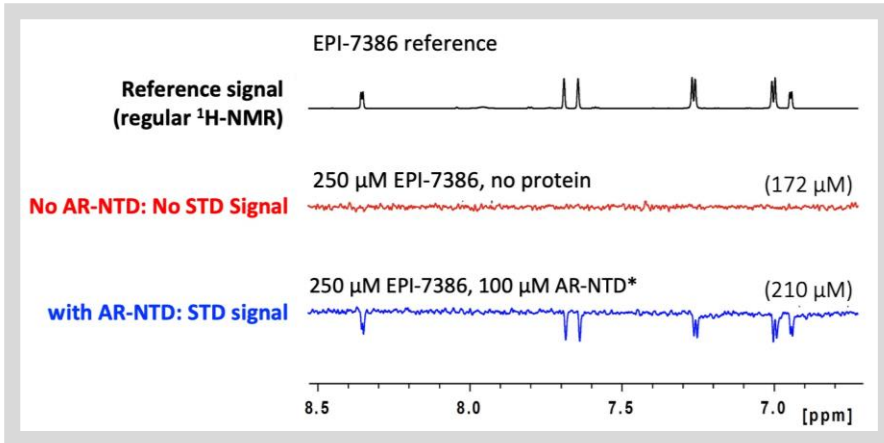
- EPI-7386 specifically binds to the NTD of the AR, unlike current therapies which bind to the LBD, a site with multiple known resistance mechanisms
- Unlike current antiandrogens, EPI-7386 is active against multiple forms of the AR, including those resistant to current antiandrogens
- EPI-7386's novel 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 an N-terminal domain inhibitor of AR

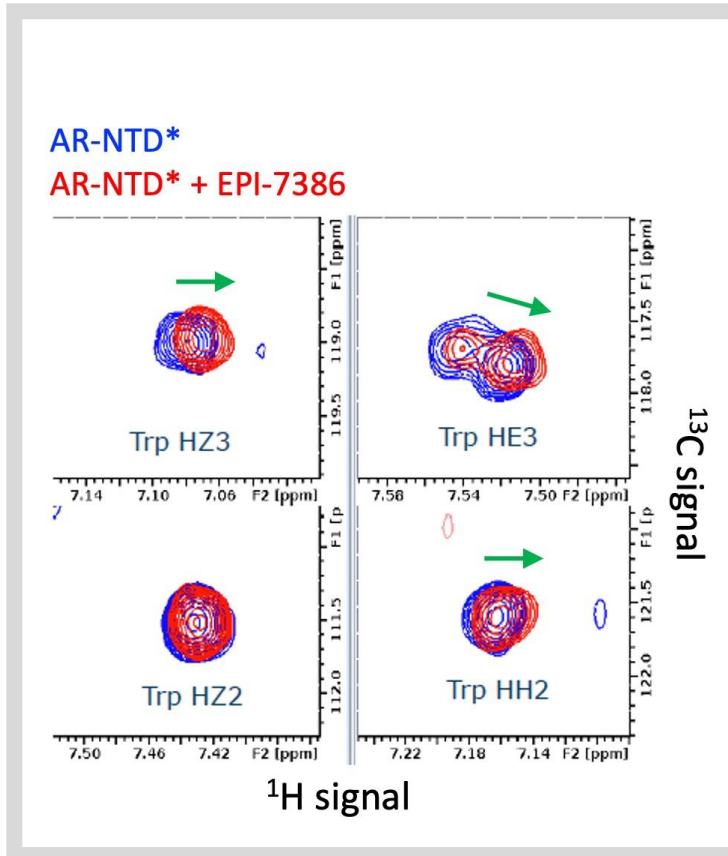
Three NMR Approaches Confirm Binding of EPI-7386 to the AR NTD¹

STD-NMR



LO-NMR T2-CPMG

2D ¹³C, ¹H-NMR

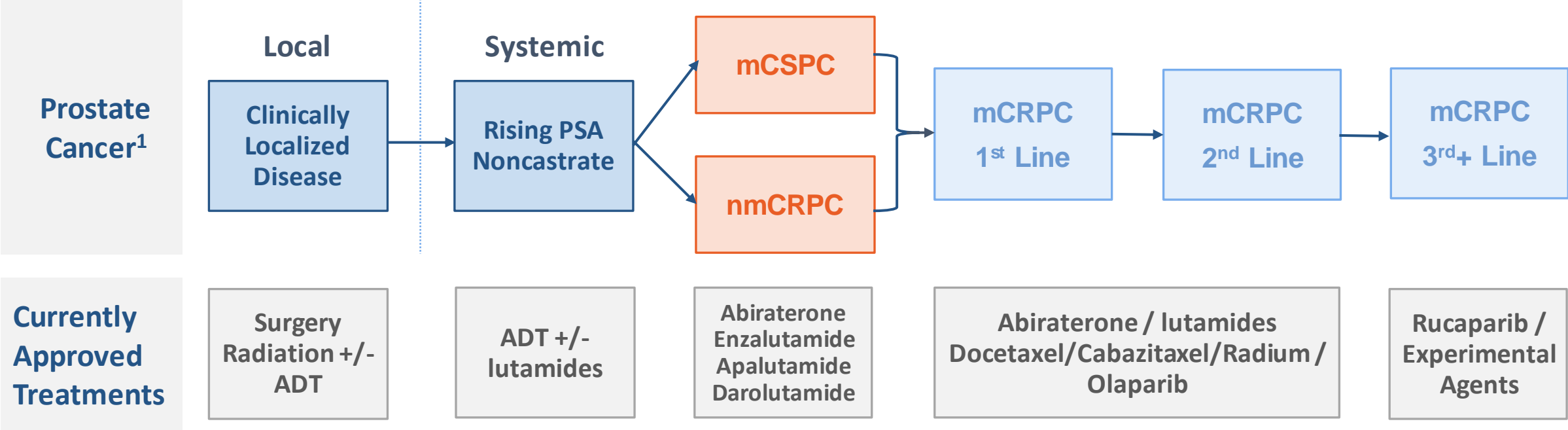


- Preclinical data in antiandrogen-sensitive and resistant models demonstrate impact of EPI-7386 on AR biology and suggest EPI-7386 binding to AR NTD:
 - AR reporter screening assays
 - AR transcriptional activity (RNA-seq)
 - AR dependent cell growth
 - AR binding to cistrome (ChIP-seq)
 - Cellular AR engagement (CETSA)
 - Prostate cancer xenograft activity
- Recent nuclear magnetic resonance (NMR) studies conclusively demonstrate EPI-7386 engagement and binding to AR NTD

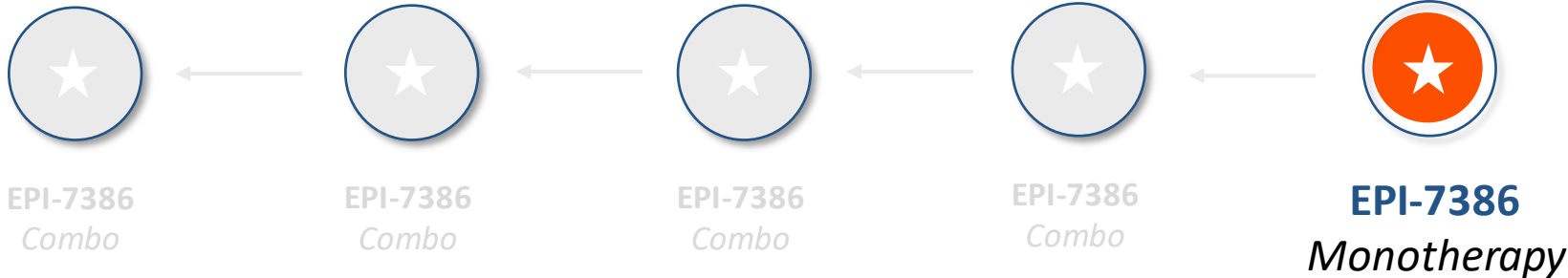
In Vitro Target Product Profile of EPI-7386 Next Generation AR NTD Inhibitor

EPI-7386	Target Criteria	Description
<input checked="" type="checkbox"/>	Potency	<i>In vitro</i> potency similar to second generation lutamide antiandrogens
<input checked="" type="checkbox"/>	Activity	<i>In vivo</i> xenograft anti-tumor activity in both antiandrogen-sensitive & resistant models
<input checked="" type="checkbox"/>	ADME	Low <i>in vitro</i> metabolism, good animal ADME & long predicted human T1/2
<input checked="" type="checkbox"/>	Selectivity	Specific NTD on-target activity with minimal off-target binding
<input checked="" type="checkbox"/>	DDI	Appropriate properties to combine with other drugs (e.g. drug-drug interactions (DDI), etc.)
<input checked="" type="checkbox"/>	CMC	Simple synthesis of drug substance and favorable pharmaceutical properties for the drug product

Prostate Cancer Clinical Treatment Model: Patient Population for Monotherapy



Potential EPI-7386 Development



1. Adopted from Scher, HI, et al. J Clin Oncol, 2016.
2. Sharp, A, et al. J Clin Invest, 2019.

Phase 1a/1b Monotherapy Study of EPI-7386 in Patients with mCRPC

Phase 1a Monotherapy EPI-7386 Dose Escalation Study Design

- Dose escalation 3+3 monotherapy clinical trial initiated in 3Q2020
- mCRPC patients who have failed ≥ 2 prior systemic therapies with ≥ 1 second-generation antiandrogen
- Initial EPI-7386 cohorts planned as 200, 400, 600, 800 and 1000 mg dosed QD
- Primary Objective:
 - Safety and tolerability of EPI-7386
- Secondary Objectives:
 - Determine MTD, evaluate the PK profile, define the recommended phase 2 dose (RP2D)
- Biomarker characterization of patients
- Initial results from the first cohort of patients presented at ASCO-GU 2021

Phase 1b Monotherapy EPI-7386 Dose Expansion Study Design

- Confirmation of EPI-7386 safety and tolerability of the RP2D from the phase 1a study
- Evaluate the clinical effects of EPI-7386 at the RP2D in a select group of mCRPC patients

Expanding Patient Biology Characterization Through Biomarker Exploration

- **Patient biomarker characterization of circulating tumor DNA (ctDNA) is currently being conducted on all patients entering the monotherapy study^{1,2,3}**
 - Provides genomic characterization of patient tumor biology focusing on both AR and non-AR pathways
 - Can help provide insight into disease heterogeneity and AR pathway dependency
 - Changes in ctDNA can be used to measure tumor burden changes in response to treatment
- **Caris and ESSA are utilizing Caris' Whole Transcriptome Sequencing (WTS) and Whole Exome Sequencing (WES) platform in clinical studies of EPI-7386**
 - Caris' platform may allow ESSA to more fully characterize patient biological profiles as well as monitor the biological effects of EPI-7386
- **Ultimately, these approaches may facilitate more efficient development of EPI-7386 in patients through the identification of relevant tumor biological subpopulations**

1. Annala M. et al. *Cancer Discov.* 2018.

2. Vandekerkhove G. et al. *Eur Urol.* 2019.

3. Warner E. et al. *Clin Cancer Res.* 2021.

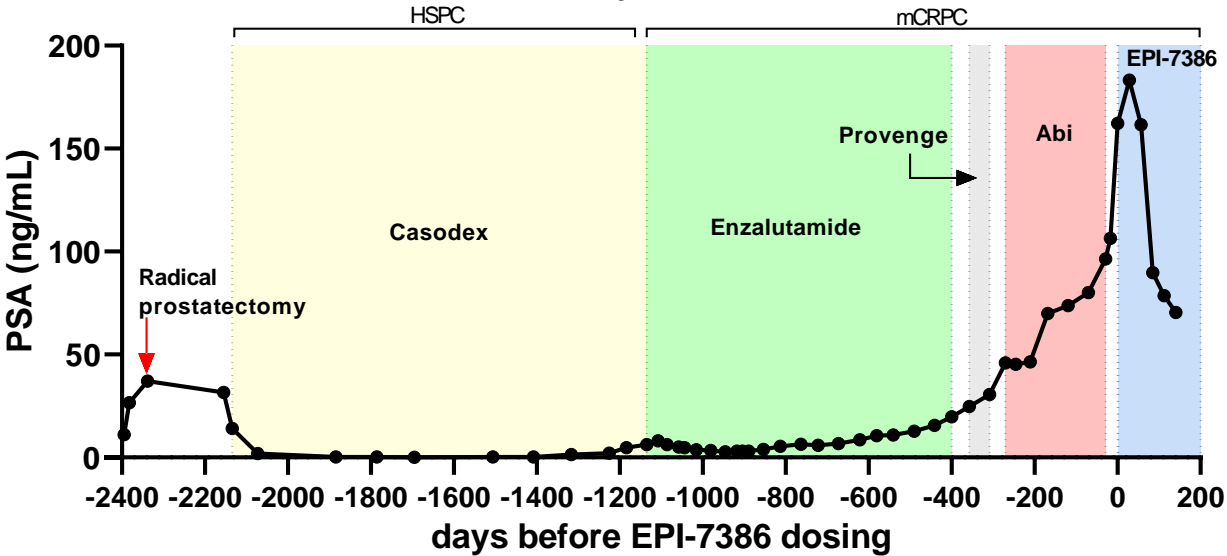
EPI-7386 Phase 1 Monotherapy Study Update

ASCO-GU 2021 Presentation

Cohort 1 Pharmacokinetic Profile

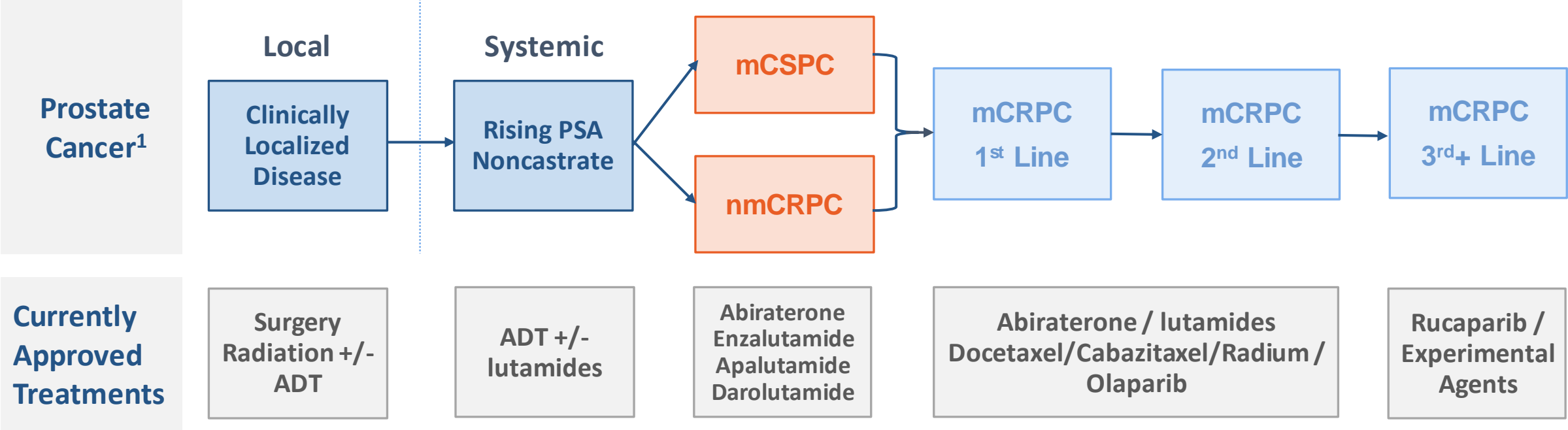
Dose (mg/day)	Day	N	t1/2 (hr)*	C _{max} (ng/mL)	C _{last} (ng/mL)	AUC ₀₋₂₄ (ng•h/mL)
200 mg	28	3	24.8	8,020	4,593	146,833

Patient 01-002 history of serum PSA evolution



- Favorable pharmacokinetic profile: long T1/2 with patient plasma concentrations of EPI-7386 >10uM for 24 hours
- EPI-7386 was well tolerated with no SAE’s observed
- Patient (01-002) achieved PSA50 response and showed stable disease at 12 weeks by radiologic assessment (bone and pelvic lymph nodes)
 - Patient achieved a deeper (PSA80) and extended PSA response, dose escalated several times and remained on therapy for a total of 72 weeks.
- At dose cohorts >800 mg QD, saturation of absorption may be present but AUC >300K ng*hr/mL
- Most patients entering the study were heavily pretreated and 80% exhibited non-AR mutations, suggesting possible non-AR related tumor growth dependence
- Protocol Amendment:
 - Protocol amendment limits prior therapy to no more than 3 prior systemic therapies for mCRPC
 - Also excludes patients with visceral metastases
 - Twice-daily dosing at 400mg BID (800mg daily) will be tested initially with 600mg BID potentially to follow

Prostate Cancer Clinical Treatment Model: Patient Population for Combination Therapy



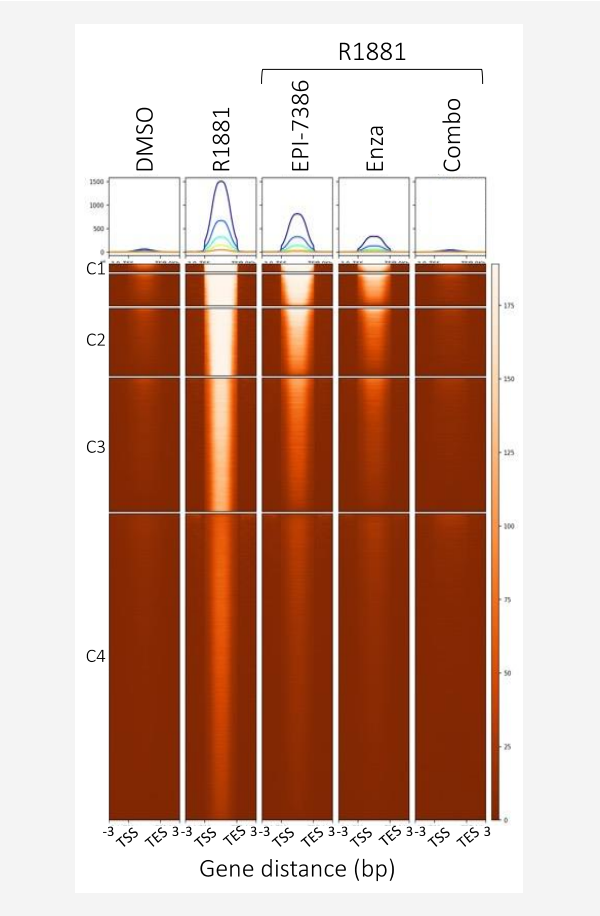
Potential EPI-7386 Development



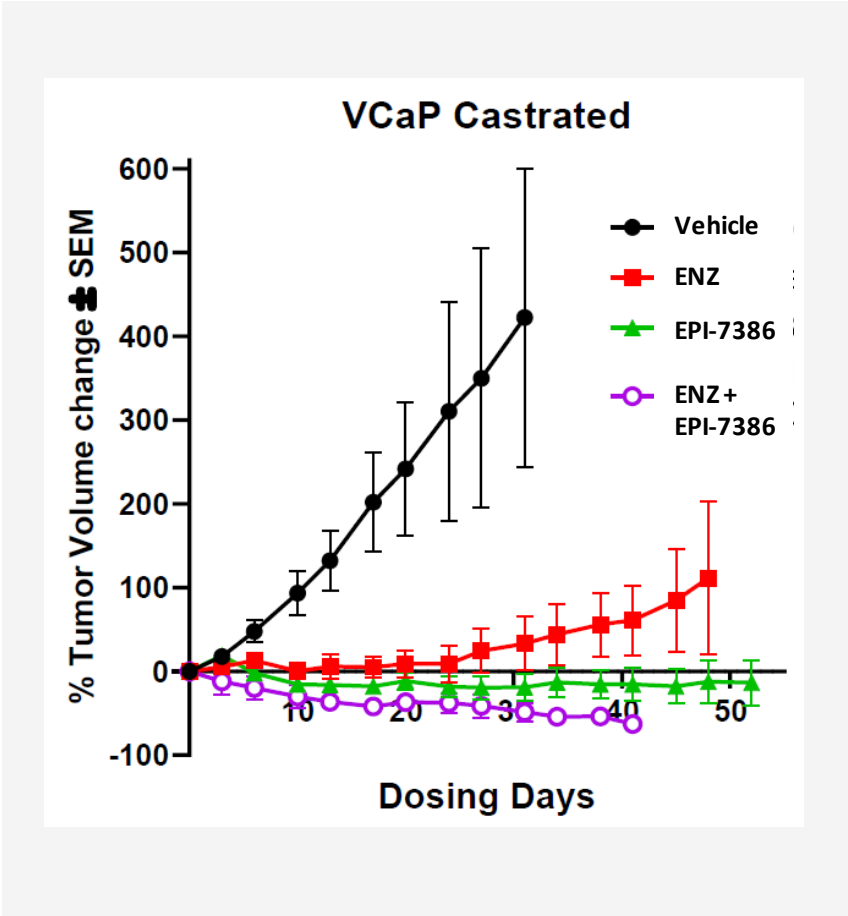
1. Adopted from Scher, HI, et al. J Clin Oncol, 2016.
2. Sharp, A, et al. J Clin Invest, 2019.

Rationale for the Combination of EPI-7386 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 EPI-7386 with antiandrogens

Clinical Collaborations: EPI-7386 With Approved Second-Generation Antiandrogens



ESSA collaboration with Astellas to evaluate EPI-7386 in combination with Xtandi (enzalutamide) in a phase 1/2 clinical study in mCRPC patients (study began 1Q2022)



Janssen collaboration with ESSA to evaluate EPI-7386 in combination with Erleada (apalutamide) and Zytiga (abiraterone acetate) in two phase 1/2 clinical studies in mCRPC patients



Bayer collaboration with ESSA to evaluate EPI-7386 in combination with Nubeqa (darolutamide) in a phase 1/2 clinical study in mCRPC patients

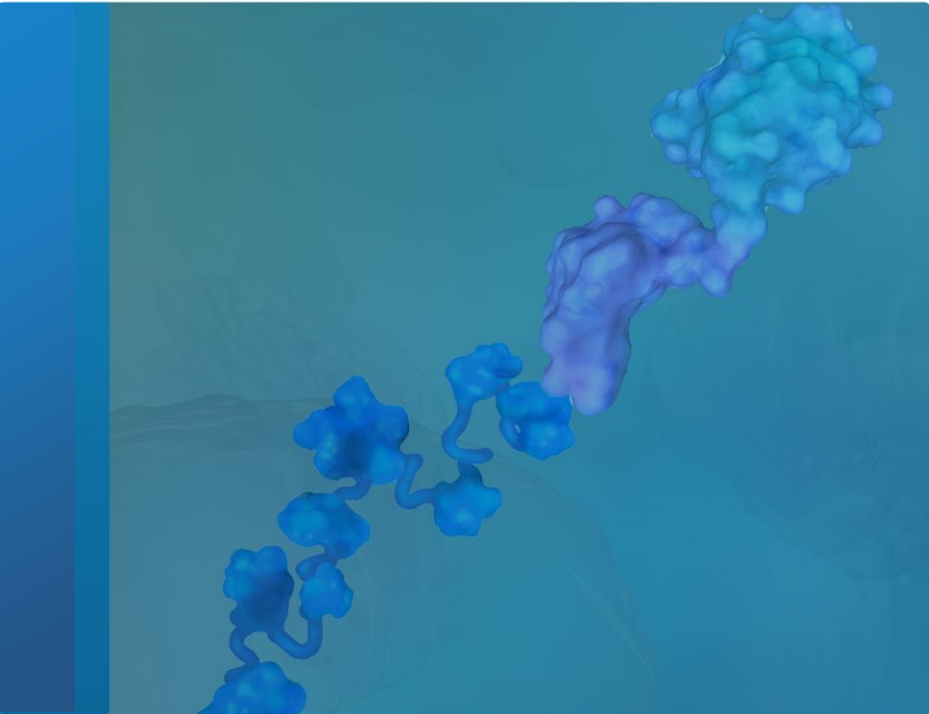
ESSA-Led Phase 1/2 Study of EPI-7386 in Combination with Enzalutamide in Patients with mCRPC

Phase 1 Single-Arm Dose Escalation Study Combining EPI-7386 and Enzalutamide

- Dose escalation 3+3 combination clinical trial began 1Q2022
- mCRPC patients who have not yet been treated with a second-generation antiandrogen
- Initial EPI-7386 cohort planned as 600 mg QD EPI-7386 and 120mg QD enzalutamide
- Primary Objective:
 - Safety and tolerability of the combination of EPI-7386 and enzalutamide
 - Establish the recommended phase 2 combination dose (RP2CD) of each of the two agents
- Secondary Objectives:
 - Evaluate the pharmacokinetics of each of the two agents

Phase 2 Two-Arm Randomized Study Combining EPI-7386 and Enzalutamide

- mCRPC patients who have not yet been treated with a second-generation antiandrogen
- Two-arm randomized (2:1) open label study design of ~120 patients
- Primary Objective:
 - Evaluate the antitumor activity and safety of the combination compared to single agent enzalutamide
- Secondary Objectives:
 - Evaluate the pharmacokinetics of each of the two agents



ESSA



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-PCAR-driven Cancers						
EPI-7386 + enzalutamide	mCRPC						
EPI-7386 + abiraterone acetate + prednisone	mCRPC						
EPI-7386 + apalutamide	mCRPC						
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	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	1H 2022
Establish the recommended phase 2 dose (RP2D)	1H 2022
Initiate the expansion portion of phase 1 trial	1H 2022
Combination	
Initiate phase 1 portion of EPI-7386 combination trials with all partners	1H 2022
Establish the RP2D for EPI-7386/enzalutamide combination trial	2H 2022
Initiate phase 2 portion of EPI-7386/enzalutamide combination trial	2H 2022
Initiate phase 2 portion of EPI-7386 combination trials with partners	2H 2022
Discovery	
Select next drug candidate and initiate IND-enabling studies	2H 2022

Financial Position & Capitalization

Nasdaq: EPIX

Cash

\$189.2M reported at December 31, 2021 (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 - *Mark Breidenbach* | Piper Sandler - *Joe Catanzaro*

Current cash runway through 2024 funds:

- Completion of phase 1 dose escalation & expansion monotherapy studies
- Completion of phase 1 combination studies with antiandrogens
- Phase 2 pivotal study
- Preparatory work for a phase 3 confirmatory study
- Pipeline work including preclinical studies with Anitens in other AR-driven tumors



For further information, please contact:

Peter Virsik, Chief Operating Officer
pvirsik@essapharma.com