ESSA Pharma

NASDAQ: EPIX

2021 Bloom Burton & Co Healthcare Investor Conference

ESSA

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 December 15, 2020 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.

ESSA Corporate Overview

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

Company

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

Sites in Houston, South San Francisco and Vancouver

Technology & Products

First-in-class N-terminal domain (NTD) inhibitors of the androgen receptor ("Anitens")

EPI-7386 phase 1 study began 2Q2020

Clinical development initially focused on resistant mCRPC as a single agent with subsequent development in combination with anti-androgens in CRPC and CSPC

Potential in triple-negative androgen receptor-positive breast cancer

Financial Details

Listed on NASDAQ (EPIX)

Completed raise of $150M in 2021

Cash and short term deposits: $74.5M (at December 31, 2020)

Experienced Management Team

David R. Parkinson, MD
President & Chief Executive Officer

NOVARTIS · AMGEN · biogen idec · NIH NATIONAL CANCER INSTITUTE · nodality revealing biology

Peter Virsik, MS, MBA
EVP & Chief Operating Officer

GILEAD · Genentech · XenoPort · J.P.Morgan · EY

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

Celator Pharmaceuticals · CUBIST PHARMACEUTICALS

Alessandra Cesano, MD
Chief Medical Officer

nanoString · CLEAVE THERAPEUTICS · biogen idec · AMGEN · nodality revealing biology

Prostate Cancer Disease Landscape

PUBLIC HEALTH PROBLEM	LARGE MARKET	VALIDATED THERAPEUTIC TARGET	NEED FOR NEW THERAPEUTIC STRATEGIES
• 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 2021[1]	• Over $7.5B in global sales generated in 2019 by leading anti-androgens, Zytiga® (abiraterone acetate), Xtandi® (enzalutamide) and Erleada (apalutamide)[2]	• Prostate cancer disease progression is associated with androgen receptor (AR) signaling. [3,4,5] • An estimated ~60% of mCRPC tumors post-Xtandi or Zytiga failure may still be AR-driven [6]	• Despite new therapies, mCRPC anti-androgen resistance is inevitable [7,8]

1. American Cancer Society. (2021). *Key Statistics for Prostate Cancer.* Retrieved from https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html
2. 2019 financial reports from www.sec.gov
3. *Robinson D, et al. Cell. 2015.*
4. *Katsogiannou M, et al. Cancer Treat Rev. 2015.*
5. *Azad AA, et al. Clin Cancer Res. 2015.*
6. *Wyatt. JAMA. 2016.*
7. *Watson PA, et al. Nat Rev Cancer. 2015*
8. *Attard G, et al. ASCO Annual Meeting. 2017.*

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

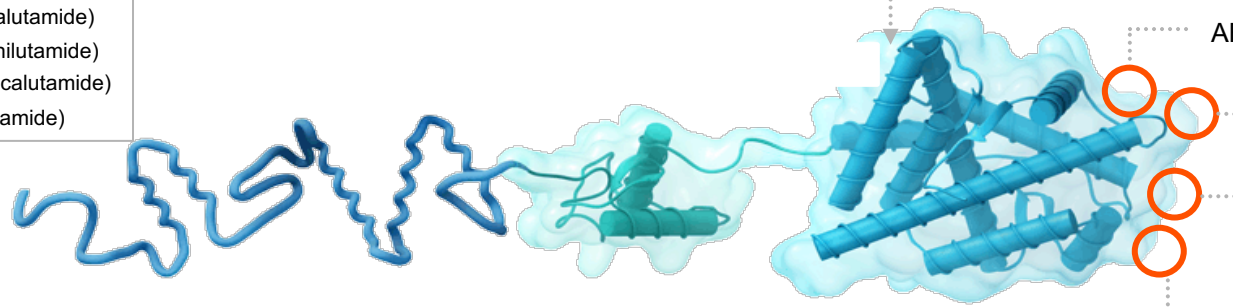
Zytiga® (abiraterone acetate)
Eligard™, **Lupron®** (leuprolide)
Zoladex® (goserelin)
Firmagon® (degarelix)

Inhibit androgen synthesis

ANDROGEN

Nubeqa® (darolutamide)
Erleada® (apalutamide)
Xtandi® (enzalutamide)
Nilandron® (nilutamide)
Casodex® (bicalutamide)
Eulexin® (flutamide)

Block androgen binding



N-terminal domain

DNA-binding domain

Ligand-binding domain

Anti-androgen Resistance Mechanisms

- AR Amplification[1]
- Gain-of-function mutations[1,2]
- Splice variants[3,4,5]
- Promiscuous activation (i.e., glucocorticoids, progesterone)[6,7]

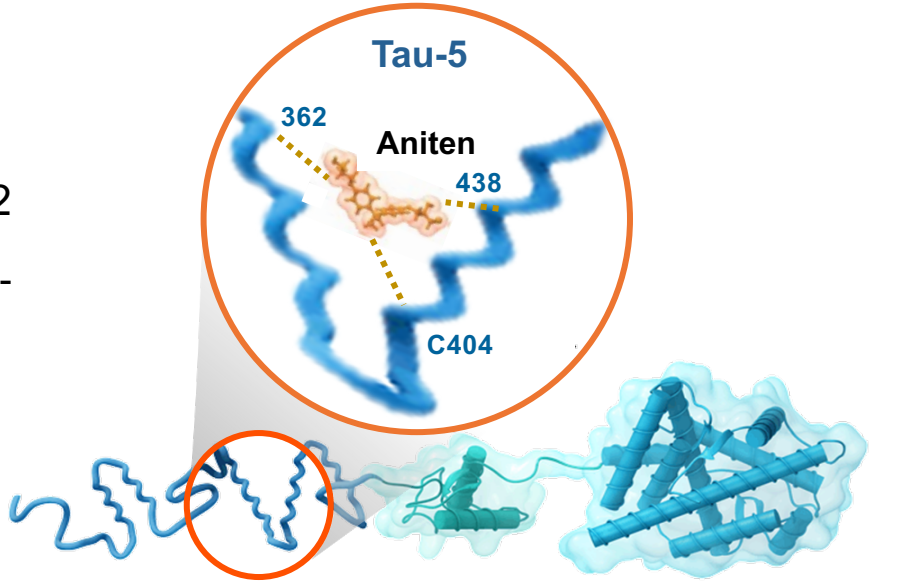
- **All current anti-androgens function through the ligand-binding domain of the androgen receptor**
- **Known anti-androgen resistance mechanisms develop at the ligand-binding domain**

ESSA

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. Sun S, et al. J Clin Invest, 2010
6. Chen EJ, et al. Clin Cancer Res, 2015
7. Culig Z, et al. Cancer Res, 1994

Targeting the AR NTD: Novel Transcription Factor Inhibition of Androgen-Driven Prostate Cancer Biology

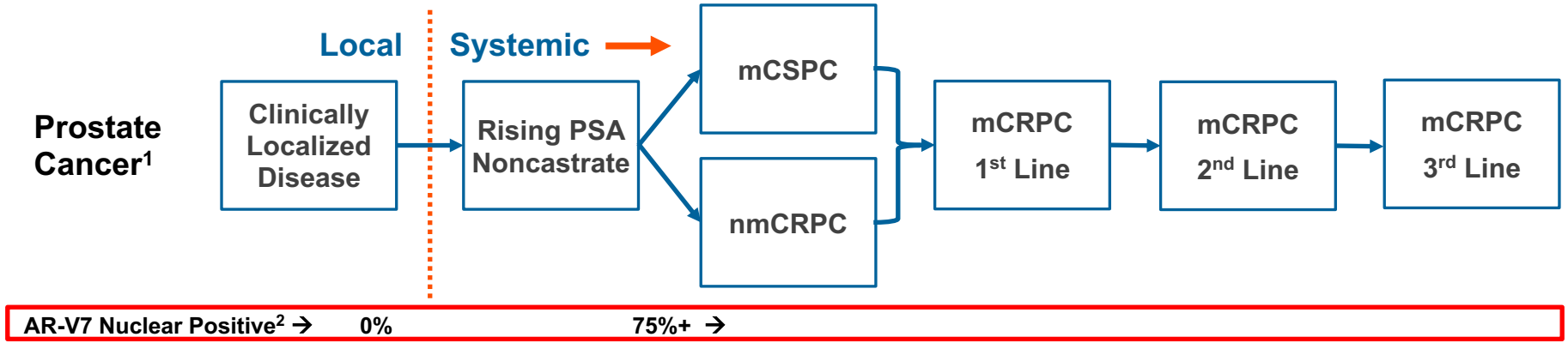
- Novel method of inhibiting the AR
- Binding formally demonstrated for EPI-001, the racemic form of EPI-002
  - Proposed binding of Anitens to the Tau-5 region of AF1 [1]
- Anitens showed activity against multiple forms of AR:
  - Wild-type AR, LBD mutant AR, and splice-variant AR[2,3,4]



Granted unique USAN drug stem of "Aniten" as an N-terminal inhibitor of AR

1. De Mol E, et al. ACS Chem Biol. 2016.
2. Andersen RJ, et al. Cancer Cell. 2010.
3. De Mol E, et al. ACS Chem Biol. 2016.
4. Yang YC, et al. Clin Cancer Res. 2016.

Prostate Cancer Clinical Treatment Model



Currently Approved Treatments

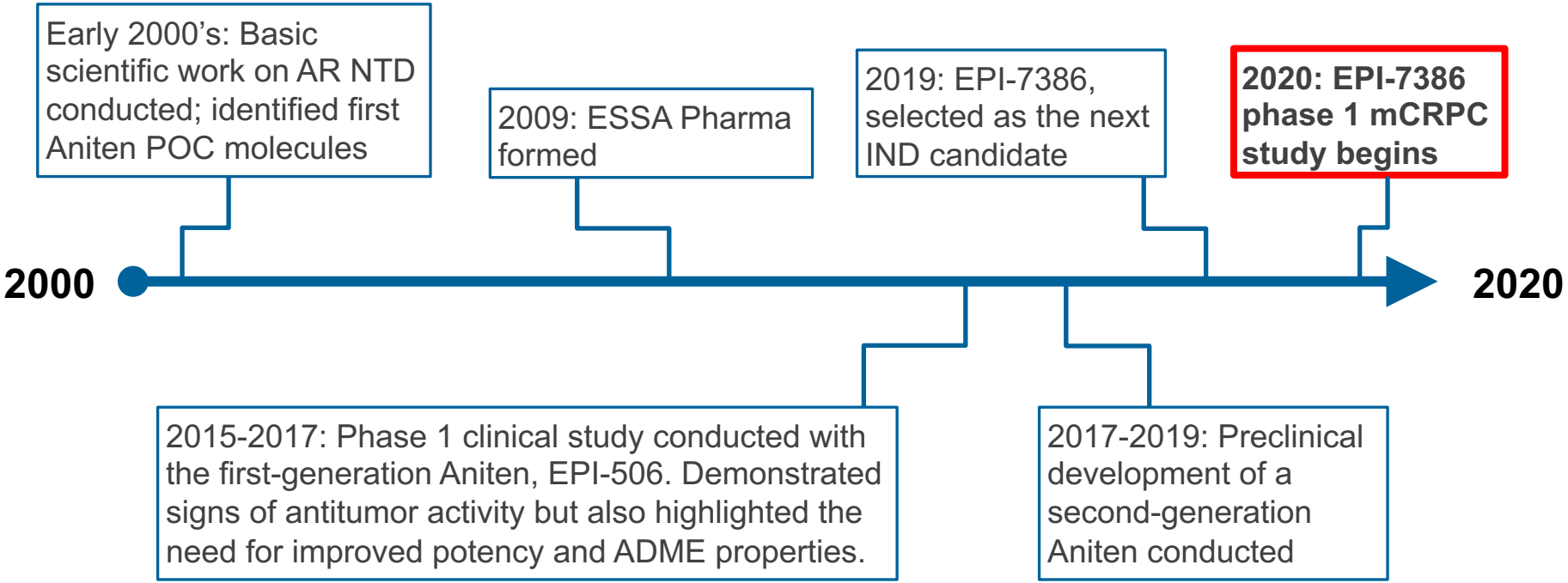
- Surgery Radiation +/- ADT
- ADT+/- lutamides
- Abiraterone Enzalutamide Apalutamide Darolutamide
- Abiraterone / -lutamides Docetaxel/Cabazitaxel/Radium / Olaparib
- Rucaparib / Experimental Agents

Potential EPI-7386 Treatments

EPI-7386 Combo ← EPI-7386 Combo ← EPI-7386 Combo ← EPI-7386 Combo ← EPI-7386 Monotherapy

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

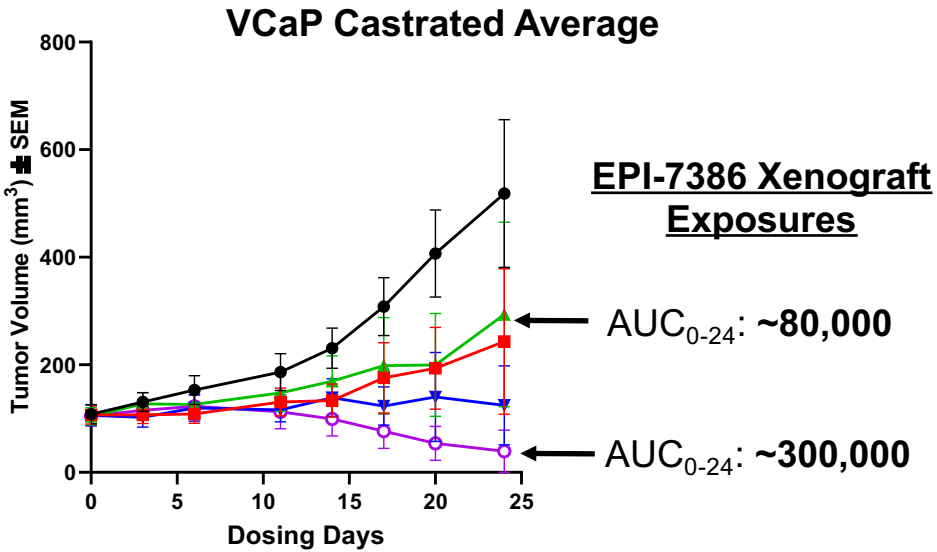
The Development of N-Terminal Domain Inhibitors of the Androgen Receptor



EPI-7386 Next Generation NTD Inhibitor of the AR: Comparison to First Generation EPI-506

EPI-7386	EPI-506 (EPI-002)	Target Criteria	Description
☒	☐	**Potency**	*In vitro* potency similar to second generation 'lutamide anti-androgens
☒	☒	**Activity**	*In vivo* xenograft activity in both anti-androgen-sensitive & resistant models
☒	☐	**ADME**	Preclinical studies showed low *in vitro* metabolism, good animal ADME & long predicted human T1/2
☒	☒	**Selectivity**	Specific NTD on-target activity with minimal off-target binding
☒	☐	**DDI**	Appropriate properties to combine with other drugs (e.g. drug-drug interactions (DDI), etc.)
☒	☐	**CMC**	Simple synthesis of drug substance and favorable pharmaceutical properties for the drug product

Favorable IND-enabling Toxicology Studies Allowed a Relatively High Starting Dose of EPI-7386 in the Clinic



Projected EPI-7386 Human Exposures

Dose (mg)	Cmax (ng/mL)	AUC0-24 (ng*hr/mL)
50	1,729	34,320
100	3,458	68,639
200	**6,915**	**137,278**
400	13,830	274,556
800	27,659	549,113

- The 200 mg EPI-7386 human starting dose is projected to deliver a similar drug exposure as biologically relevant exposures in the VCaP xenograft model
- Patient target EPI-7386 exposures are >300,000 AUC_{0-24}

EPI-7386-CS-001: A phase 1, open-label study to evaluate the safety, PK and anti-tumor activity of oral EPI-7386 in patients with mCRPC

Phase 1, multi-center, open-label, ascending multiple-dose study

First in-human, 2-part study
Part 1a (dose escalation) and Part 1b (dose expansion)

Patients with metastatic castration-resistant prostate cancer (CRPC) resistant to standard of care treatment:

- Progression on at least 2 approved systemic therapies for mCRPC, including ≥1 second generation anti-androgen drug

Part 1a

Primary objective

- Evaluate the safety and tolerability of EPI-7386

Secondary objectives

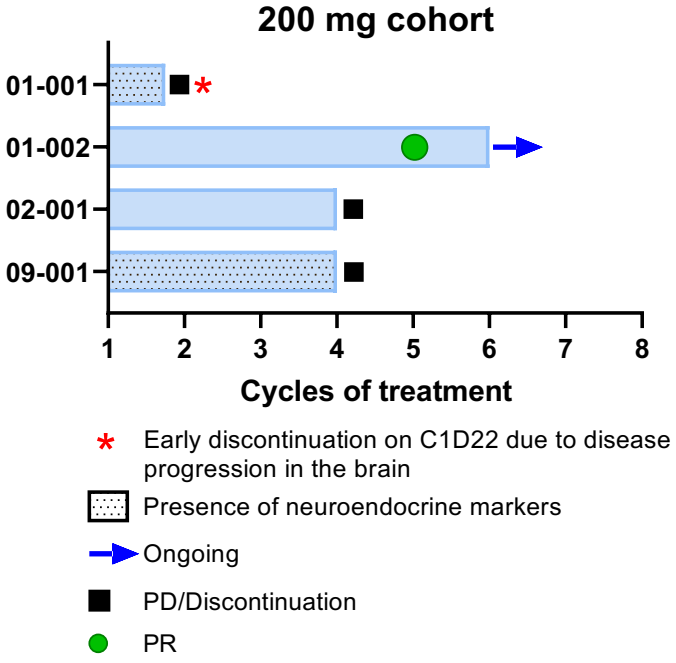
- Determine the maximum tolerated dose of EPI-7386
- Define the recommended phase 2 dose of EPI-7386
- Evaluate the PK of EPI-7386 following single- and multiple-dose oral administration
- Assess EPI-7386's potential for drug-drug interactions
  - Measuring 4β hydroxycholesterol as cytochrome P450 3A induction marker

Dose (mg/day)	Day	N	t1/2 (hr)*	C_{max} (ng/mL)	C_{last} (ng/mL)	AUC_{0-24} (ng•h/mL)
200	1	4	22.0	3,295	1,808	53,850
	28	3	24.8	8,020	4,593	146,833

- **Drug accumulation observed with repeat QD dosing**
  - EPI-7386 half life (~24 hrs) observed in humans, supporting QD dosing
- **Average Day 28 AUC ~ 147K was similar to preclinical projections for the AUC (137K) in patients at the 200mg dose**
- **Doses ≥ 600 mg of EPI-7386 are projected to achieve the AUC goal of >300K, corresponding to drug exposures in mouse xenograft studies that showed antitumor activity**
- **No signs of CYP3A induction observed at the 200 mg level, as measured by 4β-OH cholesterol / total cholesterol ratios**
- **Currently dosing patients in the 800mg cohort**

EPI-7386-CS-001: Patient treatment history, duration of therapy and safety results from the 200mg cohort*

- Four patients enrolled into cohort
- Three patients evaluable for DLT assessment
  - One patient discontinued before D28 due to disease progression
- Prior lines of treatment for mCRPC: 2 to 7
  - 2 patients received both abiraterone and enzalutamide
  - 3 patients received prior chemotherapy (taxanes)
- 2 patients showed high levels of neuroendocrine markers
  - Neuron-specific enolase (NSE) used as a marker



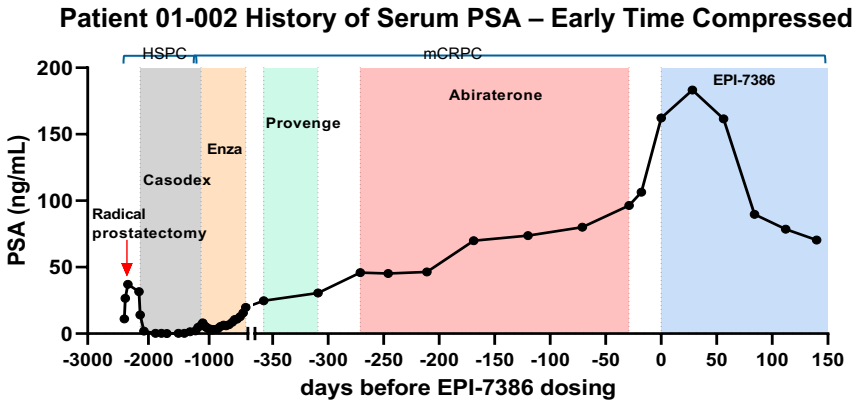
Safety Assessment

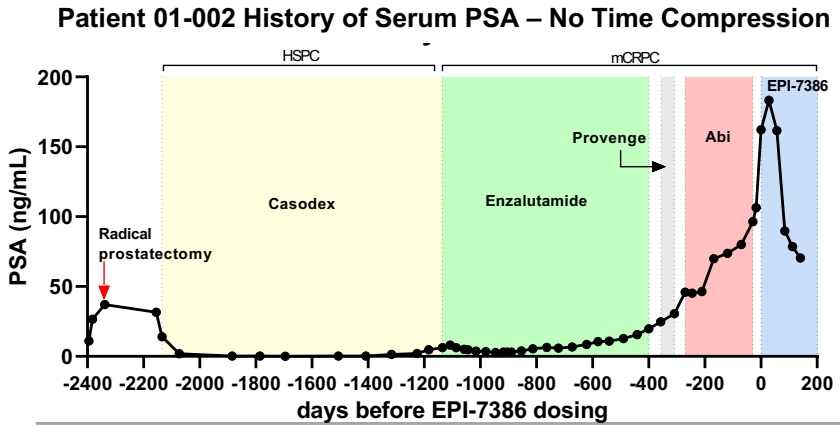
- No DLTs observed
- Possible related adverse events (AEs):

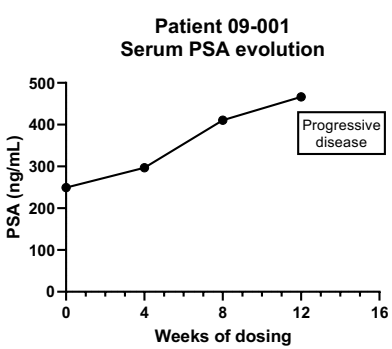
Patient	Grade	AE	Comment
01-001	1	Anemia	Ongoing at time of death
01-002	2	Hot flashes	Ongoing
02-001	2	Neutropenia*	Resolved
02-001	1	Hyperkalemia	Resolved
09-001	1	Weight loss	Ongoing at time of PD

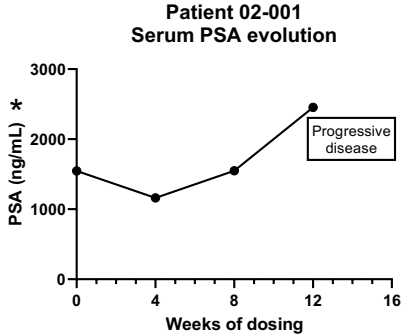
* Patient had baseline Grade1 neutropenia secondary to chemotherapy

EPI-7386-CS-001: Patient PSA level changes observed in the 200 mg cohort*







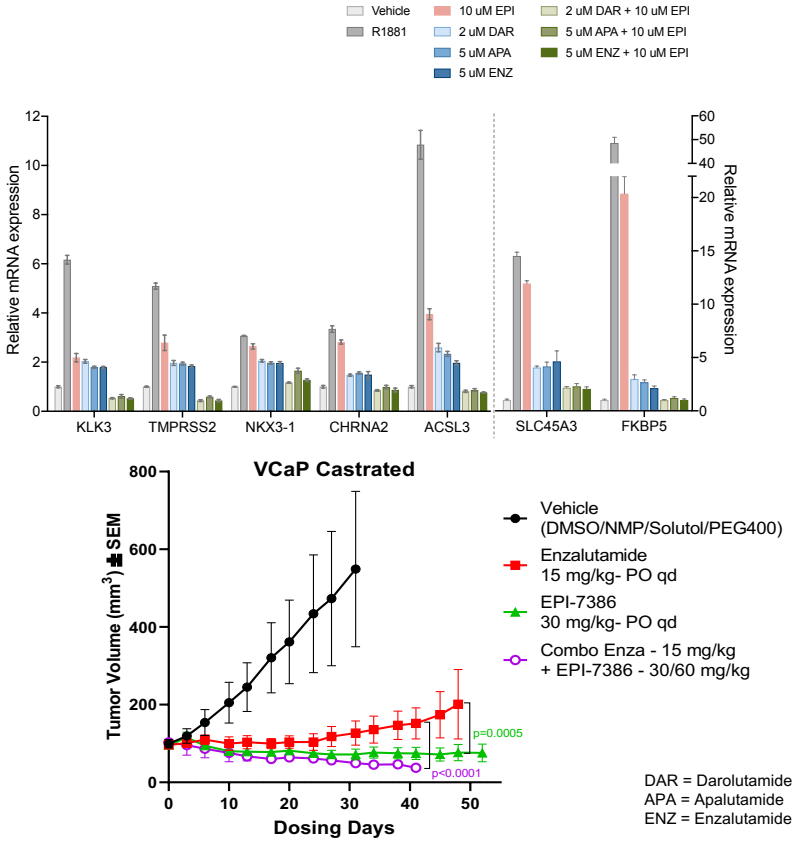


* 18 days before study patient started ADT (degarelix)

- At 200 mg, EPI-7386 levels were still below the target exposures that led to antitumor activity in animal models
- PSA response (patient 01-002) first observed at the end of Cycle 3. Radiologic assessment at 12 weeks showed SD (bone and pelvic lymph nodes)
- Patient 01-002 was dose escalated to 400 mg when starting cycle 7

* Interim data as of January 21st, 2021

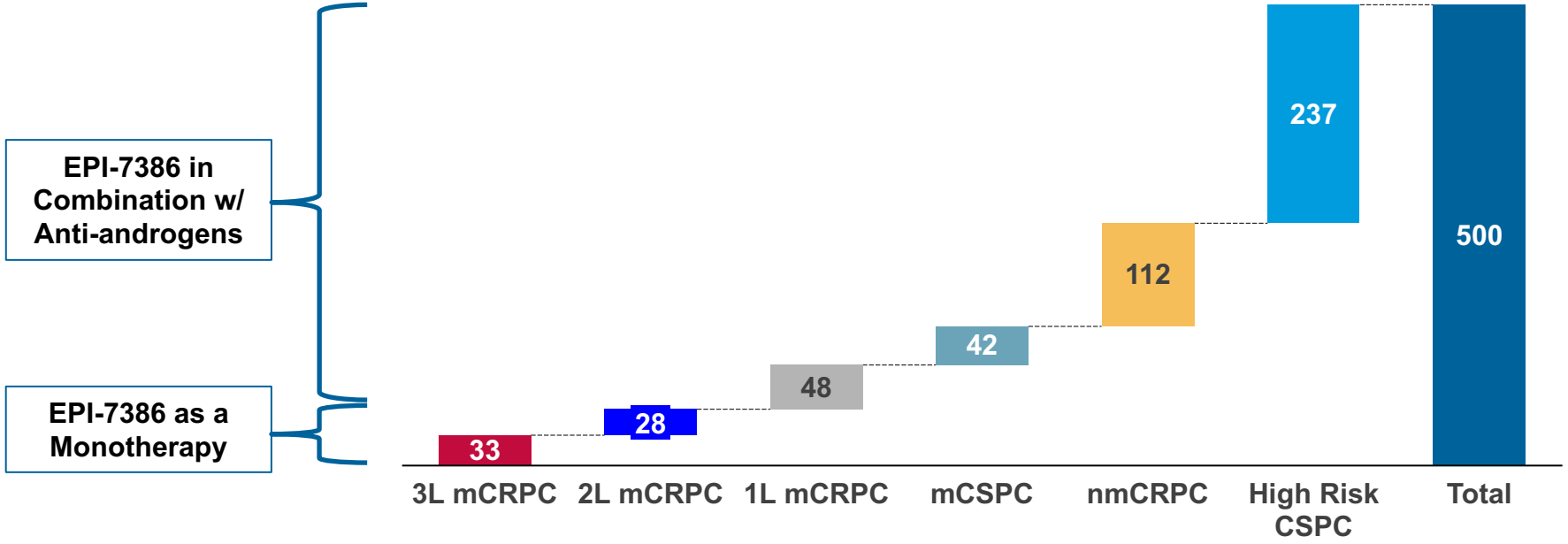
Preclinical Data Support Combining EPI-7386 with Anti-Androgens



- *In vitro* gene expression data support combining EPI-7386 with LBD-targeted anti-androgens
- *In vivo* VCaP xenograft data support combining EPI-7386 with LBD-targeted anti-androgens
- Clinical collaborations signed to study EPI-7386 with different LBD-targeted anti-androgens
  - Janssen will study EPI-7386 with Erleada® (apalutamide) in a phase 1/2 study as well as with Zytiga® (abiraterone acetate plus prednisone) in a separate parallel Phase 1/2 study
  - ESSA with Astellas/Pfizer will study EPI-7386 with Xtandi (enzalutamide) in a phase 1/2 study
  - All combo studies will be in earlier lines of mCRPC than ESSA's current monotherapy mCRPC study

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

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



Anti-androgens Approved or in a Pivotal Phase 3 Study

(▶= Approved)

(♦= In Phase 3 Study)

3L mCRPC	2L mCRPC	1L mCRPC	mCSPC	nmCRPC	High Risk CSPC
	▶ Xtandi (enzalutamide)	▶ Xtandi (enzalutamide)	▶ Xtandi (enzalutamide)	▶ Xtandi (enzalutamide)	♦ Erleada (apalutamide) tablets
	▶ Zytiga (abiraterone acetate)	▶ Zytiga (abiraterone acetate)	▶ Zytiga (abiraterone acetate)	▶ Erleada (apalutamide) tablets	♦ NUBEQA (darolutamide)
		♦ Erleada (apalutamide) tablets	▶ Erleada (apalutamide) tablets	▶ NUBEQA (darolutamide)	

ESSA

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

Financial Position & Capitalization

Nasdaq: EPIX	
Cash	$74.5M reported at Dec 31st, 2020 (no debt O/S); $150M gross proceeds from public offering Feb 22nd, 2021
Share Price (April 19, 2021)	$24.87
Shares	~46M – 39.6 I/O common shares and 6.4 prefunded warrants
Stock Options	~6.7M @ $3.75
Top Shareholders	Pfizer Inc, BVF, Soleus Capital, Avidity Partners, Blackstone, Eventide Healthcare, Vivo, Driehaus, Omega, Janus Capital
Covering Analysts	Mark Breidenbach, *Oppenheimer;* Joe Pantginis, *HCW;* Maury Raycroft, *Jefferies;* David Martin, *Bloom Burton;* Tyler van Buren, *Piper Sandler*

Current cash funds completion of Phase 1 dose-escalation & expansion studies, Phase 1 combination studies with anti-androgens, Phase 2 pivotal study, and preparatory work for a Phase 3 confirmatory study. ESSA also is planning additional pipeline work including preclinical studies w/ Anitens in breast & other AR driven tumors.

ESSA Upcoming Milestones

STATUS	SPECIFICS
☒	Complete all preclinical studies needed for IND filing
☒	IND filing of EPI-7386 by 1Q20
☒	First patient dosed July 2020 in EPI-7386 Phase 1 study in mCRPC patients failing second generation anti-androgens
☐	Establish the recommended phase 2 dose (RP2D)
☐	Expand phase 1 cohort to enroll more patients at the RP2D
☐	Begin combination study w/ one or more anti-androgens in first-line mCRPC patients

Summary

- EPI-7386 is a unique investigational inhibitor of the N-terminal domain of the AR, with single agent activity observed in preclinical studies against both wild-type and mutated AR
- In preclinical studies, EPI-7386 has shown more potency, a longer half-life, and improved pharmaceutical properties over first-generation compound, EPI-506
- Combining EPI-7386 with anti-androgens suppresses AR-driven biology more broadly and deeply than with either approach alone in preclinical studies
- Initial proof-of-concept established for EPI-7386 in phase 1 study of mCRPC patients failing standard-of-care therapies
- Subsequent development will be in earlier lines of treatment in combination with anti-androgens