ESSA Pharma

NASDAQ: EPIX

September 2021

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.

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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 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 study began 2Q2020

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

Potential in triple-negative androgen receptor-positive breast cancer

Financial Details

Listed on NASDAQ (EPIX)

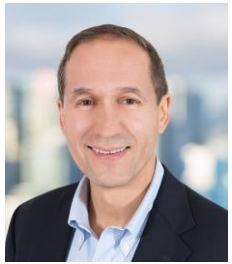
Completed raise of $150M in 2021

Cash and short term deposits: $202M (at June 30, 2021)

Experienced Management Team

David R. Parkinson, MD
President & Chief Executive Officer

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

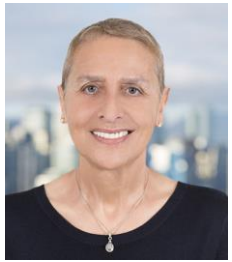


Peter Virsik, MS, MBA
EVP & Chief Operating Officer

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 antiandrogens, 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 antiandrogen 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 Antiandrogen Therapies Only Target the Androgen Receptor Ligand Binding Domain

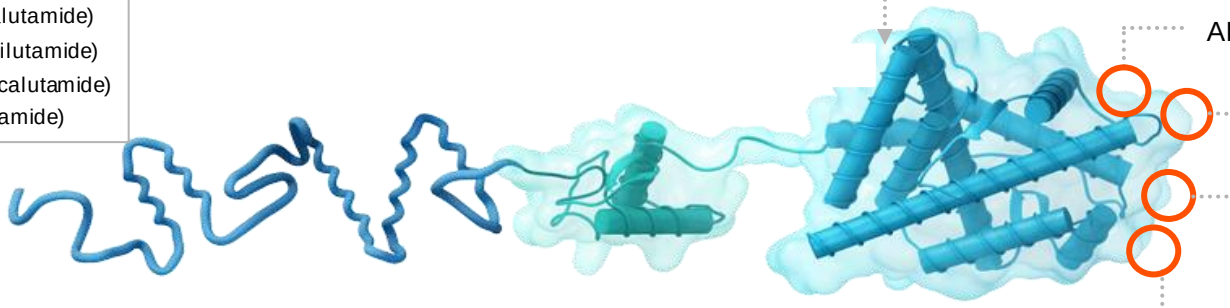
Zytiga® (abiraterone acetate)
Eligard™, **Lupron®** (leuprolide)
Zoladex® (goserelin)
Firmagon® (degarelix)

Inhibit androgen synthesis

ANDROGEN

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

Block androgen binding



Antiandrogen Resistance Mechanisms

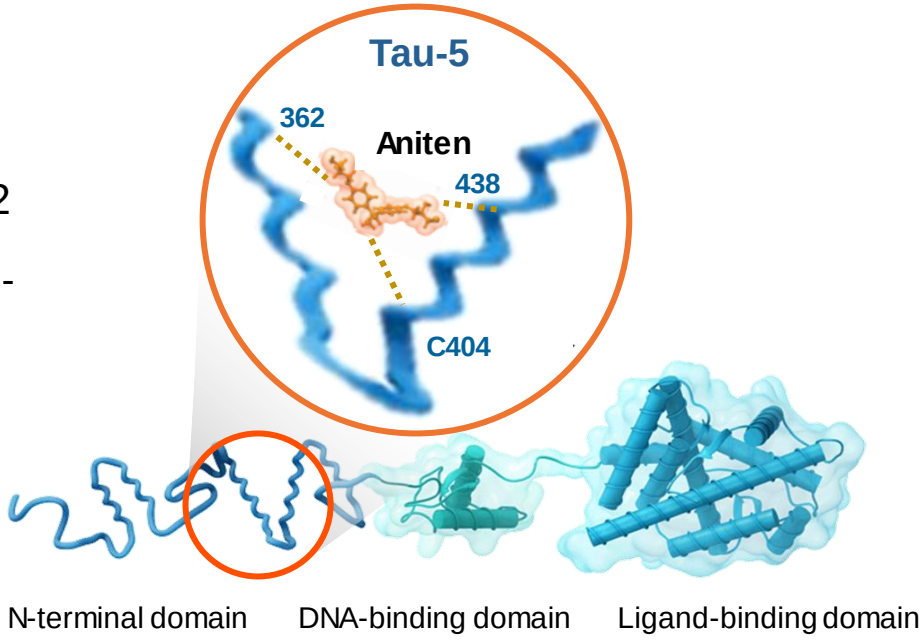
- AR Amplification[1]
- Gain-of-function mutations[1,2]
- Splice variants[3,4,5]
- Promiscuous activation (i.e., glucocorticoids, progesterone)[6,7]

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

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

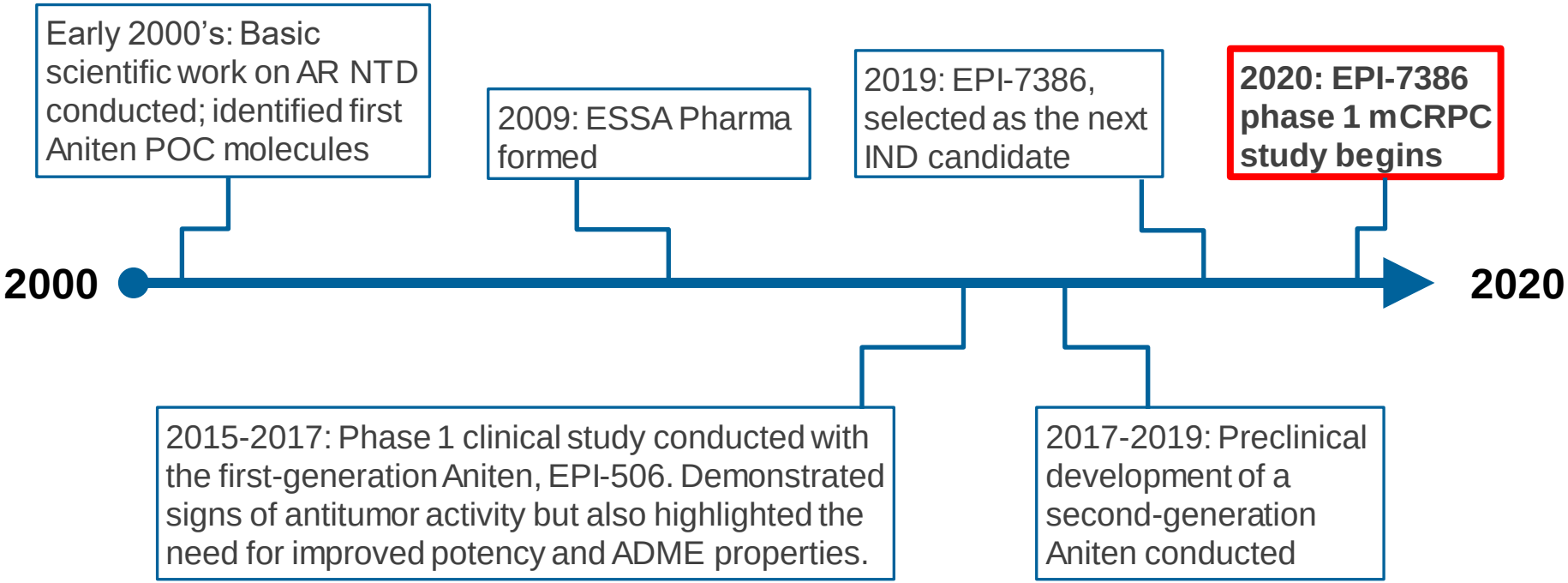
- Novel method of inhibiting the AR
- Binding formally demonstrated for EPI-001, the racemic form of EPI-002
  - Proposed binding of Anitens to the Tau-5 region of AF1 [1]
- Anitens active against multiple forms of AR:
  - Wild-type AR, LBD mutant AR, and splice-variant AR[2,3,4]



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

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

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



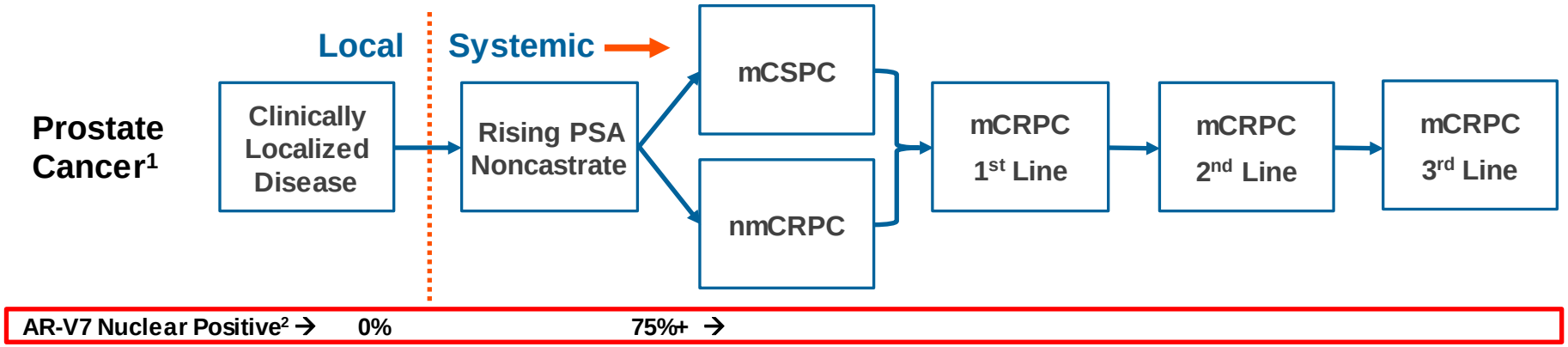
EPI-7386 Next Generation NTD Inhibitor of the AR: Comparison to First Generation EPI-506

EPI-7386	EPI-506 (EPI-002)	Target Criteria	Description
☒	☐	**Potency**	*In vitro* potency similar to second generation ‘lutamide antiandrogens
☒	☒	**Activity**	*In vivo* xenograft activity in both antiandrogen-sensitive & resistant models
☒	☐	**ADME**	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

EPI-7386: Towards Confirmation of Specific Binding to the AR NTD

- EPI-7386 is derived from earlier generation Anitens, which were confirmed to bind to the Tau5 region within the AF1 region of the AR NTD
- *In vitro* and *in vivo* xenograft studies with EPI-7386 are consistent with AR NTD-based transcriptional inhibition
- Extensive *in vitro* transcriptomic studies indicate overlapping but distinct AR inhibition characteristics differentiated from ligand-based AR inhibition
- CETSA (cellular thermal shift assay) studies are consistent with NTD binding
- Definitive confirmatory NMR studies to be presented at the AACR/NCI/EORTC meeting in October 2021

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

ESSA

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

Status of Clinical Development of EPI-7386

- **Phase 1 EPI-7386 monotherapy clinical trial initiated in 3Q/2020**
- **Initial EPI-7386 PK data presented at ASCO-GU 2021:**
  - Confirmation of favorable pharmaceutical characteristics based initial 200 mg cohort experience
  - Drug was safe and well-tolerated with evidence for mechanism POC from patient 01-002
  - Initial experience with the biological complexities of late stage mCRPC patients
- **Recent clinical program update:**
  - Confirmation of safety and tolerability through 1000 mg cohort
  - Goal is to establish monotherapy RP2D by first half 2022
  - New protocol amendment will focus monotherapy development on less heavily pretreated patients and explore the effects of even higher drug exposures
    - » Plan to further characterize individual patient biology: DNA & RNA liquid biopsy
- **Combination trials on track; RP2D for combo studies established; initial trials to begin 4Q/2021**
- **Full phase 1 clinical update planned for H1/2022**

EPI-7386-CS-001 Monotherapy: A phase 1 study to evaluate the safety, tolerability and anti-tumor activity of EPI-7386 in mCRPC

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

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 antiandrogen drug

Part 1a

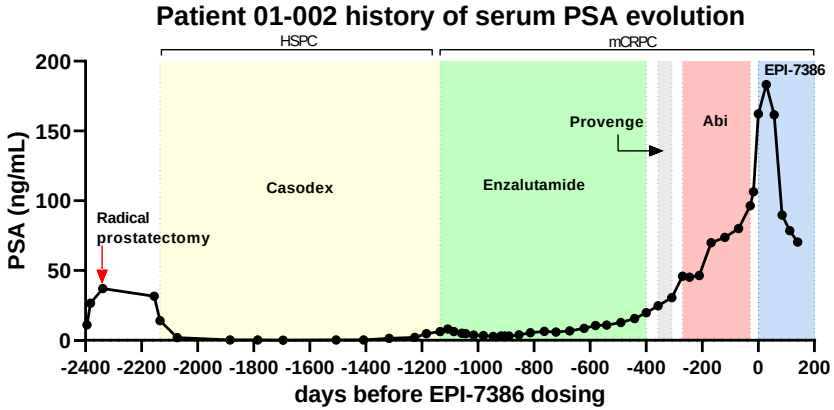
Primary objective

- Evaluate the safety and tolerability of EPI-7386 in patients failing current AR therapies

Secondary objectives

- Determine the maximum tolerated dose of EPI-7386
- Define the recommended phase 2 dose of EPI-7386
- Evaluate the PK profile of EPI-7386 following single- and multiple-dose oral administration

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



- **Favorable pharmacokinetic profile with long T1/2**
- **Safe and well-tolerated**
- **Patient (01-002) achieved PSA50 response by Cycle 3 and showed stable disease at 12 weeks by radiologic assessment (bone and pelvic lymph nodes)**
  - **Patient achieved deeper and extended PSA response**
  - **Dose escalated and continues on therapy through 9/1/2021**

Rationale for the Combination of EPI-7386 with Antiandrogens

- Decades of clinical research link improved clinical results with better suppression of the AR axis

- Combining an NTD-inhibitor such as EPI-7386 with an LBD-inhibitor such as enzalutamide, provides two complementary ways of inhibiting AR biology
  - Greater suppression of androgen activity through two distinct mechanisms may potentially delay the emergence of drug resistance

- Preclinical studies support deeper and broader suppression of AR-driven biology by combining EPI-7386 with antiandrogens (e.g. enzalutamide)
  - *In vitro* gene expression studies
  - *In vivo* preclinical androgen-responsive animal models

Clinical Collaborations: EPI-7386 With Approved Antiandrogens

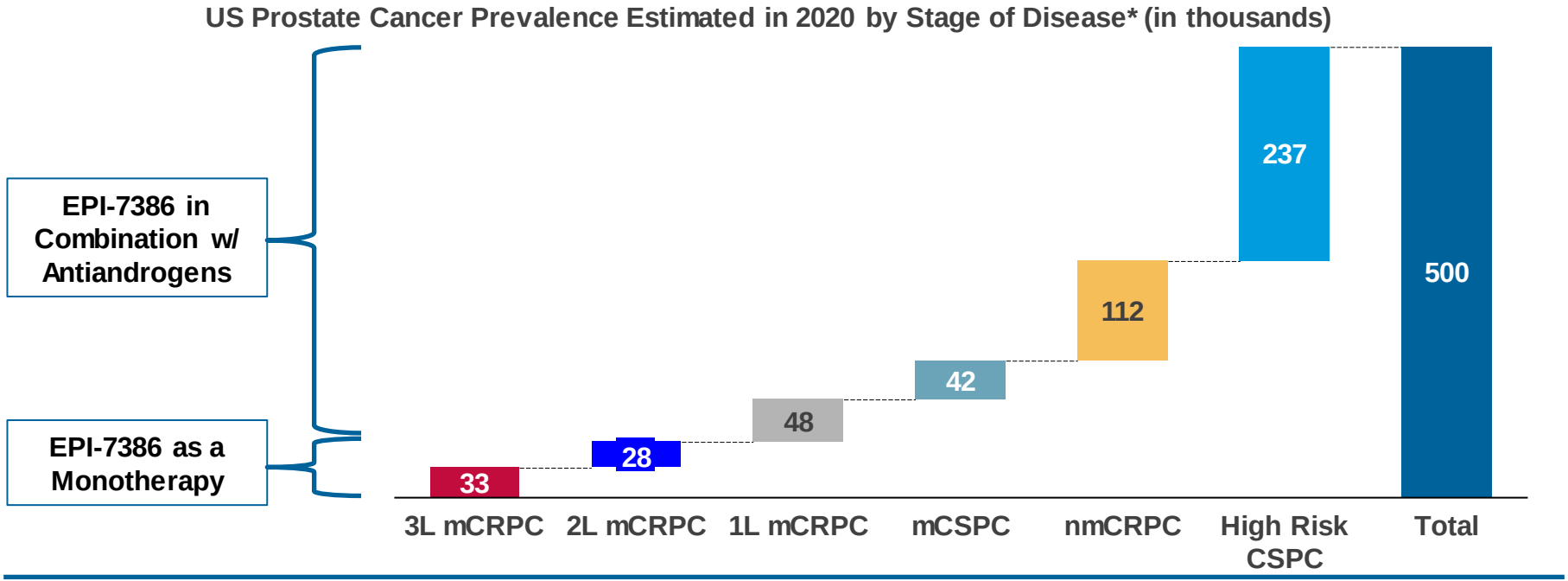
ESSA partnered with Astellas to evaluate EPI-7386 in combination with Astellas and Pfizer's androgen receptor inhibitor Xtandi (enzalutamide) in a phase 1/2 clinical study in mCRPC patients:

- Initial phase I "dose equilibration" followed by randomized ENZ vs ENZ/7386
- Patient population: mCRPC patients naïve to second-generation antiandrogens
- Starting dose: 800 mg QD EPI-7386
- Initiation 4Q/2021

Janssen partnered with ESSA to evaluate EPI-7386 in combination with Erleada (apalutamide) and Zytiga (abiraterone acetate) in a series of phase 1/2 clinical studies in mCPRC patients

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

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



Antiandrogens Approved or in a Pivotal P3 Study

(▶= Approved)

(♦= In P3 Study)

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)	

** 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	$202M reported at June 30th, 2020 (no debt O/S); $150M gross proceeds from public offering Feb 22nd, 2021
Share Price (Sept 3, 2021)	$9.66
Shares	~47M – 44M I/O common shares and 3M prefunded warrants
Stock Options	~6.8M @ $5.20
Top Shareholders	BVF, Pfizer Inc, Blackstone, Soleus, RTW, Avidity, Eventide, Vivo, Bellevue, Janus, Adage, Fidelity
Covering Analysts	Mark Breidenbach, *Oppenheimer;* Maury Raycroft, *Jefferies;* David Martin, *Bloom Burton;* Joe Cantanzaro, *Piper Sandler*

Current cash funds completion of phase 1 dose-escalation & expansion studies, phase 1 combination studies with antiandrogens, 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
☒	Completed all preclinical studies needed for IND filing
☒	EPI-7386 IND filed by 1Q20
☒	First patient dosed July 2020 in EPI-7386 phase 1 study in mCRPC patients failing second generation antiandrogens
☒	Established the recommended phase 2 dose (RP2D) for the combination studies
☐	Establish the RP2D for the monotherapy study
☐	Expand phase 1 monotherapy cohort to enroll more patients at the RP2D
☐	Begin combination study w/ one or more antiandrogens in first-line mCRPC patients

Summary

- EPI-7386 is a unique AR NTD inhibitor with activity against both wild-type and mutated AR
- The agent is more potent, has a longer half-life, and has improved pharmaceutical properties over the first-generation NTD inhibitor, EPI-506
- Combining EPI-7386 with antiandrogens suppresses AR-driven biology more broadly and deeply than with either approach alone
- Initial clinical development is as monotherapy treatment in mCRPC patients resistant to current antiandrogens; under FDA Fast Track designation
    - The focus of the phase 1 clinical trial is to establish a monotherapy RP2D, and to identify those antiandrogen-resistant mCRPC patients whose tumors are still predominantly driven by the AR axis
- Subsequent development, initiating shortly, involves combining EPI-7386 with antiandrogens in mCPRC patients as an earlier line of therapy

For further information, please contact:

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