ESSA Pharma
NASDAQ: EPIX; TSX-V: EPI

37th Annual J.P. Morgan Healthcare Conference
Forward Looking Statement

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Focus on the development of novel therapies for the treatment of metastatic castrate resistant prostate cancer

Company
Founded in 2009 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) transcription inhibitors of the androgen receptor (“Anitens”) overcome resistance to current anti-androgens
First generation EPI-506 clinical trial established clinical proof-of-concept
Advancing next-generation Aniten compounds to IND

Financial Details
Listed on NASDAQ & TSXV
Cash balance of $14.8 M (Sept 30, 2018)
### Investment Highlights

**FIRST-GENERATION**
- EPI-506 established clinical safety and proof-of-mechanism for NTD inhibition of the androgen receptor in mCRPC

**POTENCY & ADME IMPROVED**
- Next-generation Aniten compounds have increased potency, longer half-lives and improved ADME properties compared to EPI-506

**MARKET OPPORTUNITY**
- mCRPC represents a significant market opportunity - 165,000 new cases of prostate cancer each year in the US and annual global sales of over $5B

**MANAGEMENT TEAM**
- Highly experienced management team with significant oncology experience

**IND FILING**
- IND filing of next-generation Aniten compound anticipated 9-12 months following IND candidate selection in 1Q19
Experienced Management Team

David R. Parkinson, MD
President & Chief Executive Officer, Director

Peter Virsik, MS, MBA
EVP & Chief Operating Officer

David S. Wood, MBA, CPA, CMA
Chief Financial Officer
ESSA’s Goal

**THE CHALLENGE**

New approach to the inhibition of androgen receptor (AR)-driven biology in anti-androgen resistant prostate cancer

**ESSA’S APPROACH**

N-terminal domain (NTD) inhibition of the androgen receptor:

- Single-agent therapy of anti-androgen resistant mCRPC
- Future combination with anti-androgens for early-stage patients

**PROGRESS TO DATE**

- Phase I clinical trial confirmed the safety and POC of NTD inhibitors
- More potent & stable compounds needed for optimal efficacy
- Final stages of selecting a next-generation Aniten
Metastatic Castration-Resistant Prostate Cancer (mCRPC)
An Unmet Medical Need

PUBLIC HEALTH PROBLEM

- Prostate cancer is the 2nd most common cause of male cancer deaths\(^1\)
- Each year in the US, 165,000 men are diagnosed and 29,000 die due to prostate cancer

LARGE MARKET

- Over $5B in global sales generated in 2017 by leading anti-androgens, Zytiga\(^\circledR\) (abiraterone acetate) and Xtandi\(^\circledR\) (enzalutamide)

VALIDATED THERAPEUTIC TARGET

- Prostate cancer disease progression is associated with androgen receptor (AR) signaling. \(^2,3,4\)
- An estimated ~60% of mCRPC tumors post-Xtandi or Zytiga failure may still be AR-driven \(^5\)

NEED FOR NEW THERAPEUTIC STRATEGIES

- Despite new therapies, mCRPC anti-androgen resistance is inevitable \(^6,7\)

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\(^1\) Surveillance Research, American Cancer Society. 2018.
Current Anti-androgen Therapies
Target the AR Ligand Binding Domain

- The AR is comprised of 3 distinct, independently acting domains
- Current therapies target the ligand-binding domain (LBD) of the AR

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

Inhibit synthesis

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

ANDROGEN

Block ligand binding

N-terminal domain
DNA-binding domain
Ligand-binding domain
Mechanisms of AR Resistance Occur in the Ligand Binding Domain

AR Amplification

Gain-of-function mutations

Splice variants

Promiscuous activation (i.e., glucocorticoids, progesterone)

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

- Proposed binding of Anitens to Tau-5 region of AF1 \(^1\)
- Anitens inhibit wild-type, LBD mutant, and splice-variant AR activity \(^2,3,4\)
- Anitens inhibit AR transcriptional activity by blocking interaction with key transcriptional proteins (RAP74 & CBP) \(^5,6\)

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Granted unique USAN drug stem of “Aniten” as an N-terminal inhibitor of AR
First Generation NTD Inhibition:
Summary of the EPI-506 Experience
**EPI-506: First Generation NTD Inhibitor**

- *In vitro & in vivo* inhibited AR-driven gene expression in both wild-type AR (LNCaP, VCaP) and androgen-resistant AR settings (LNCaP95)

- Specific binding (imaging, protein-binding studies) w/ moderate potency (>10 μM IC50)

- Toxicology unremarkable (minor weight loss & reversible)

- Combination with anti-androgens revealed activity greater than either NTD inhibitor or anti-androgen alone
## First-Generation EPI-506 Phase 1 Study in Patients w/mCRPC

<table>
<thead>
<tr>
<th><strong>DESIGN</strong></th>
<th>An adaptive Phase 1 first-in-man dose escalation / dose expansion study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DOSE</strong></td>
<td>EPI-506 (EPI-002 active) oral once-daily or twice-daily dosed as a soft-gel capsule</td>
</tr>
<tr>
<td><strong>POPULATION</strong></td>
<td>mCRPC patients progressing after abiraterone, enzalutamide, or both; allowed to have also failed one regimen of docetaxel chemotherapy</td>
</tr>
<tr>
<td><strong>STUDY SIZE</strong></td>
<td>26 patients</td>
</tr>
<tr>
<td><strong>ENDPOINTS</strong></td>
<td>Safety, PK, maximum tolerated dose, recommended Phase 2 dose</td>
</tr>
<tr>
<td><strong>STUDY STATUS</strong></td>
<td>Completed at 5 sites in US and Canada</td>
</tr>
</tbody>
</table>
First-Generation EPI-506 Phase 1 Pharmacokinetic Data

Minimal time with drug concentrations >IC50

Mean Steady-State EPI-002 Plasma Concentration-vs-Time Profiles

Short effective $T_{1/2}$

Significant first-pass metabolism seen
First-Generation EPI-506 Interim PSA Response
Maximal PSA Change at Any Time from Start of Multi-dose Period (N=25)*

%PSA Change

-30
-20
-10
0
10
20
30
40
50

Pts receiving <1280 mg
Pts receiving ≥1280 mg

*ESMO 2017
# EPI-506: Safe and Well-tolerated Until Very High Doses

## Most Commonly Reported Adverse Event > 10%

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>All Grades, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea, nausea</td>
<td>13 (46%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7 (25%)</td>
</tr>
<tr>
<td>Decreased appetite, pain in extremity</td>
<td>6 (21%), each</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5 (18%)</td>
</tr>
<tr>
<td>Back Pain</td>
<td>4 (14%)</td>
</tr>
<tr>
<td>Abdominal distension, anemia, arthralgia, musculoskeletal pain, UTI</td>
<td>3 (11%), each</td>
</tr>
</tbody>
</table>

## Adverse Events ≥ Grade 3

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>N (%)</th>
<th>Relationship to Study Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>3 (11%)</td>
<td>Not related.</td>
</tr>
<tr>
<td>AST elevated</td>
<td>2 (7%)</td>
<td>Probably related, Possibly related.</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>2 (7%)</td>
<td>Not related.</td>
</tr>
<tr>
<td>Abdominal pain, diarrhea</td>
<td>1 (4%), each</td>
<td>Possibly related.</td>
</tr>
<tr>
<td>ALT elevated, amylase elevated, angina, hypertension, dizziness postural</td>
<td>1 (4%), each</td>
<td>Probably related.</td>
</tr>
<tr>
<td>Arthralgia, gastrointestinal hemorrhage, pain in extremity, syncope, thrombocytopenia, urinary retention</td>
<td>1 (4%), each</td>
<td>Not related.</td>
</tr>
</tbody>
</table>
Lessons From the Phase 1 Experience With EPI-506

EPI-506 was well-tolerated with evidence of a successful POC, but was not potent enough and was metabolized rapidly with a short half-life.

Experience informed the specifications for a next-generation Aniten compound:

- Higher potency
- Less metabolism with a longer half-life
- Maintain on-target specificity
- Commercial formulation
- Ease of manufacturing / shelf-life stability

New technology enables patient biological characterization and more informative, efficient trial conduct:

- ctDNA to assess tumor AR status and verify continued reliance on AR pathway
- CTC mRNA gene expression to monitor PK/PD
ESSA: Next-Generation Aniten Development: Goals and Process

• **Goals:**
  - To generate potent and specific NTD inhibitors with long half-lives and commercial grade pharmaceutical properties

• **Process:**
  - Strengthened ESSA’s chemistry and preclinical team in early 2018
  - Augmented external chemistry efforts to expand the synthesis of new molecules
    - >350 new compounds designed; >200 compounds screened *in vitro* for potency and ADME profile
  - Preclinical ADME characterization of molecules
    - Comprehensive molecule profiling program
# ESSA Next-Generation Aniten Program: Status

<table>
<thead>
<tr>
<th>TPP CRITERIA</th>
<th>STATUS</th>
<th>SPECIFICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased potency</td>
<td>✔</td>
<td><em>In vitro</em> potency goal achieved (&gt;15X more potent than EPI-506 / 002)</td>
</tr>
<tr>
<td>ENZ-resistant activity</td>
<td>✔</td>
<td><em>In vitro</em> cellular activity in ENZ-resistant cell lines</td>
</tr>
<tr>
<td>Xenograft <em>in vivo</em> activity</td>
<td>✔</td>
<td>Equal anti-tumor activity to ENZ at similar doses in ENZ-sensitive xenograft model</td>
</tr>
<tr>
<td>Clean off-target profile</td>
<td>✔</td>
<td>CEREP screening indicates minimal off-target binding</td>
</tr>
<tr>
<td>Reduced metabolism</td>
<td>✔</td>
<td>Major metabolic pathways blocked (&gt; 5X less metabolized <em>in vitro</em> than EPI-506 / 002)</td>
</tr>
<tr>
<td><em>In vivo</em> PK profile</td>
<td>✔</td>
<td>Mouse PK studies support once-daily dosing and predict significant human exposures</td>
</tr>
<tr>
<td>Strong IP coverage</td>
<td>✔</td>
<td>IP broadly filed on new Anitens; patent expirations anticipated 2037+</td>
</tr>
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</table>
**In Vitro Potency and Stability of Next-Generation Anitens**

- Significant gains made in *in vitro* potency and stability compared to EPI-002
- Preclinical characterization limited to only the most potent and stable compounds

![Graph showing in vitro cellular IC50 potency and stability](image)

- **Enzalutamide**
- EPI-002 potency is >> 4500nM
- Stability threshold
- Potency threshold
- Target compounds

CONFIDENTIAL
<table>
<thead>
<tr>
<th>Date</th>
<th>Potency</th>
<th>ADME</th>
<th>Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 2018</td>
<td>&gt;1μM</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>September 2018</td>
<td>&lt;500nM</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>January 2019</td>
<td>200-500nM</td>
<td>+++</td>
<td>++</td>
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</table>
Financial History and Highlights

- $12M Cancer Prevention Research Institute of Texas (CPRIT) grant awarded
- $16.3M IPO included Deerfield, Omega, Special Situations Fund
- Commenced trading on NASDAQ (EPIX) and TSX-V (EPI)

<table>
<thead>
<tr>
<th>2010–12</th>
<th>2014–15</th>
<th>2016</th>
<th>2018</th>
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<tbody>
<tr>
<td>• $3.7M seed financing</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>• $20M financings included Clarus, Deerfield, Omega, Eventide</td>
<td></td>
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<tr>
<td></td>
<td>• $10M Silicon Valley Bank loan facility; $8M drawn</td>
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Cash reported at Sept 30, 2018: $14.8M
Common Shares 8.0M (fully diluted)
# ESSA Upcoming Milestones

<table>
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<th>STATUS</th>
<th>SPECIFICS</th>
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<tbody>
<tr>
<td>✔️</td>
<td>Select final Aniten molecules for selectivity and xenograft preclinical studies</td>
</tr>
<tr>
<td>✔️</td>
<td>Medical conference presentation(s) of the initial preclinical findings of Aniten molecules</td>
</tr>
<tr>
<td>✔️</td>
<td>IND candidate selection and initiation of IND-enabling studies</td>
</tr>
<tr>
<td></td>
<td>Medical conference presentation of the preclinical findings of Aniten molecules in antiandrogen-resistant prostate models and in combination with antiandrogens</td>
</tr>
<tr>
<td>✔️</td>
<td>IND filing of the next-generation Aniten</td>
</tr>
<tr>
<td>✔️</td>
<td>First patient dosed in phase 1 mCRPC study with next-generation Aniten</td>
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