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2. Epigenetic Mechanism Review

3. Prostate Cancer Rationale Review

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5. Enzalutamide Combination Trial – Phase 1b

6. Next Steps

Safe Harbor Statement. This presentation contains forward-looking statements that involve risks and uncertainties, which may cause actual results to differ materially from the statements made. For this purpose, any statements that are contained herein that are not statements of historical fact may be deemed to be forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, the words "believes," "anticipates," "plans," "intends," "will," "should," "expects," "projects," and similar expressions are intended to identify forward-looking statements. You are cautioned that such statements are subject to a multitude of risks and uncertainties that could cause actual results, future circumstances, or events to differ materially from those projected in the forward-looking statements. These risks include, but are not limited to, those associated with the success of research and development programs, the regulatory approval process, competition, securing and maintaining corporate alliances, market acceptance of the Company's products, the availability of government and insurance reimbursements for the Company's products, the strength of intellectual property, financing capability, the potential dilutive effects of any financing, reliance on subcontractors and key personnel. The forward-looking statements are made as of the date hereof, and the Company disclaims any intention and has no obligation or responsibility, except as required by law, to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise. CONTACT: Donald J. McCaffrey, Chairman, President & CEO Suite 300, 4820 Richard Road S.W. Calgary, AB, Canada T3E 6L1 Tel: (403) 254-9252, Fax:(403) 256-8495, http://www.zenithepigenetics.com
# Share Structure Profile

<table>
<thead>
<tr>
<th>Founded</th>
<th>Corporate spin out from Resverlogix in June 2013</th>
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<tbody>
<tr>
<td>Status</td>
<td>Private Company, full reporting issuer</td>
</tr>
<tr>
<td>Cash Raised 2014-2016</td>
<td>Approx. US$44MM @ $1.00 USD per share (all pre-clinical results based)</td>
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<tr>
<td>Enterprise Value est.</td>
<td>$350 to $375MM USD ($2.50 to $3.00 USD/share) est.</td>
</tr>
<tr>
<td>Shares Outstanding</td>
<td>125.2 MM</td>
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<tr>
<td></td>
<td>134.0 MM fully diluted</td>
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<td>10MM additional shares will be sold shortly</td>
</tr>
<tr>
<td>Cash Burn</td>
<td>$2 MM per quarter - Current</td>
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</table>
Epigenetic Mechanism

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7. Intellectual Property
Epigenetics: the Mechanism Behind Our Approach

Early Epigenetic Approach

Advanced Epigenetic Approach

Epigenetics: A mechanism for regulating gene activity independent of DNA sequence that determines which genes are turned on or off:
- in a particular cell type
- in different disease states
- in response to a physiological stimulus
Resistance to several standard of care treatments does not impede sensitivity to BETi
Developing Epigenetic Combination Therapies to Address Resistance & Significantly Increase Revenue of $B Franchises

Current multi $B Markets
- AR antagonists (lead program)
- PD-1/PD-L1Mabs
- CDK 4/6 inh.
- PARPi

DNA Repair
PARPi (Breast, Ovarian, CRPC)

Hormone-Modulation
Androgen (CRPC)
Estrogen (breast cancer)

BRD4

Kinase-Signaling
PI3K (breast, CRPC)
RAF (melanoma)

Immuno-Oncology
Checkpoint Inhibitors (melanoma, NSCLC, etc.)

Increase duration of therapy

Increase patient pool (responders)

Increase IP life

Differentiation

Combination with ZEN-3694 (BETi)

Confidential
Prostate Cancer Rationale Review

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ZEN-3694 Potential in Patients Developing mCRPC Resistance to Enzalutamide

ZEN-3694 works down stream of current therapies

- ZEN-3694 works where resistance to existing lead drugs, like Enzalutamide, has evolved

The combination of ZEN-3694 and enzalutamide shows strong synergy and is expected to reduce the development of resistance

Cell Viability in VCAP P3 + 0.1 nM R1881 Treated with various concentrations of ZEN003694 with Enzalutamide (3 Day)
Potential Resistance Pathways in CRPC in Response to Enzalutamide and/or Abiraterone

**ENZALUTAMIDE/ABIRTERONE THERAPY**

**CRPC**

- **Alterations of AR** (Mutations, amplification, splice-variant)
- **GR up-regulation**
- **Loss of AR**
- **Other mechanisms**
  - MYC/MYCN, BCL-2, FOXA1, ERG, ETS, CHD1, SRC, AKR1C3

**BETi dependent mechanism**

- **Inhibition of AR signaling**
- **Down-regulation of GR**
- **Decrease in NE markers** (activity in AR-cells)
- **BETi downregulates**
  - MYC, ERG, BCL-2, BRD4 interacts with ERG

**ZEN-3694 shows good efficacy in different CRPC models that are resistant to AR antagonists**
Phase 1 Details & Results

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## Zenith’s Principal Investigators

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eric Small, MD</td>
<td>University of California, San Francisco (UCSF)</td>
<td>Developed abiraterone - #2 CRPC drug, owned by J&amp;J.</td>
</tr>
<tr>
<td>Rahul Aggarwal, MD</td>
<td>University of California, San Francisco (UCSF)</td>
<td>Developed enzalutamide - #1 CRPC drug, now owned by Pfizer. Developing ARN-509 for J&amp;J</td>
</tr>
<tr>
<td>Howard Scher, MD</td>
<td>Memorial Sloane Kettering Cancer Center (MSKCC)</td>
<td>Developed enzalutamide - #1 CRPC drug, now owned by Pfizer. Developing ARN-509 for J&amp;J</td>
</tr>
<tr>
<td>Wassim Abida, MD, PhD</td>
<td>Memorial Sloane Kettering Cancer Center (MSKCC)</td>
<td>Developed enzalutamide - #1 CRPC drug, now owned by Pfizer. Developing ARN-509 for J&amp;J</td>
</tr>
<tr>
<td>Joshi Alumkal, MD</td>
<td>Oregon Health Sciences University (OHSU)</td>
<td>Expert in epigenetics in prostate cancer research</td>
</tr>
<tr>
<td>Allan Pantuck, MD</td>
<td>University of California Los Angeles (UCLA)</td>
<td>Involved in enzalutamide and provenge development</td>
</tr>
<tr>
<td>Elizabeth Heath, MD</td>
<td>Karmanos (Wayne State)</td>
<td>Genitourinary oncology specialist</td>
</tr>
<tr>
<td>Mark Fleming, MD</td>
<td>Virginia Oncology Associates</td>
<td>Community site</td>
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</tbody>
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ZEN-3694 Phase 1 Study Endpoints

Primary

• Safety, tolerability, maximum tolerated dose (MTD), and recommended Phase 2 dose (RP2D) of ZEN-3694

Secondary

• Pharmacokinetics (PK)
• Preliminary clinical activity
  • PCWG2 Criteria: PSA response rate, Radiographic response rate, PFS
  • Circulating Tumor Cell (CTC) response rate
# ZEN-3694 development in mCRPC- Phase 1 single agent study results

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th></th>
<th>2017</th>
<th></th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1H</td>
<td>2H</td>
<td>1H</td>
<td>2H</td>
</tr>
</tbody>
</table>

- **Single agent dose escalation; enzalutamide and/or abiraterone failures N~12**
- **Single agent expansion at RP2D; same population as dose escalation N=12**

### Key Learnings

- Maximum tolerated dose (MTD) defined ✓
- Dose proportional PK ✓
- Good safety profile, prolonged dosing without dose interruption/reduction is feasible ✓
- Target modulation shown at doses below MTD ✓
- Some single agent anti-tumor activity/disease stabilization observed in multiple patients ✓

### Ongoing activities

- Fully enrolled and dosed,
- Study closeout ongoing, follow on data analysis continues

---

Single agent study key to understanding drug characteristics and supporting combination study
Patient X: Prolonged disease stabilization

Prior Therapy for mCRPC
- Provenge
- Abiraterone: 5/22/2016 – 8/12/2016 – primary resistance

- ZEN-3694: 8/24/2016 – 7/16/2016, 45 weeks

Study Entry

Stable mediastinal nodes over 8 months

32 Weeks
Enzalutamide Combination Trial – Phase 1b

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Epigenetics
Changing the future of medicine.
ZEN-3694 Phase 1b Study Design
Phase 1b, open label, combination, 3x3 dose escalation/confirmation

mCRPC, chemo-naïve, enzalutamide naïve, prior progression on abiraterone

X mg QD ZEN-3694
160 mg QD enzalutamide
N = 3 (planned)

Dose escalation cohorts

MTD / RP2D Confirmation

Seven sites, UCSF and MSKCC leading

MTD: Highest dose with ≤1/6 patients with DLT

Expansion Cohort A
Enza naïve, progression on abiraterone

Expansion Cohort B
Biochemical progression on enzalutamide
ZEN-3694-002 Treatment Duration

Weeks on ZEN-3694-002 Study

Current SOC

Target

ZEN003694 1st Dose C1D1

No lead-in

Anorexia & Fatigue, Nausea

No lead-in

No lead-in

Efficacy at well tolerated doses below MTD

Cohort 4 (72mg QD)
Cohort 3 (60mg QD)
Cohort 2 (48mg QD)
Cohort 1 (36mg QD)

Tumor Assessment
Clinical Progression
Radiographic Progression
Adverse Event
Dose Modification
Withdraw Consent

SOC (2nd line enza/abi)
4-5 months
4-6 months

ZEN-3694 + Enza target
> 8-9 months
> 8-9 months
Two patients progressed on abiraterone in 1 month
Third patient progressed within 4 months on abiraterone
Radiographic and PSA progression

<table>
<thead>
<tr>
<th>PSA50 response</th>
<th>PSA Response duration</th>
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<tbody>
<tr>
<td>SOC (2nd line enza/abi)</td>
<td>15-25%</td>
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<tr>
<td>ZEN-3694 + Enza target</td>
<td>&gt;40%</td>
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</table>
Extensive Translational Medicine Plan for Deciphering MOA and Designing Future Biomarker Driven Trials

Whole blood

- Whole blood
  - CTCs
    - Enumeration, AR-C, AR-N
    - MYC, AR-V7, GR
    - HRD signature
  - Whole blood
    - PD marker assay to measure target modulation
    - Nanostring cancer immune panel
    - AR-V7 target engagement
  - Plasma
    - =>  Immune Tolerance Markers, T cell subtypes, TCR sequencing
  - Buffy Coat
    - =>  Exploratory, Metabolomics/exosomes/protein markers, cytokine panel
  - Erythrocytes
    - =>  Exploratory, Metabolomics/exosomes/protein markers, cytokine panel
  - Erythrocytes
    - =>  Exploratory, Metabolomics/exosomes/protein markers, cytokine panel

Tumor biopsy

- ½ FFPE
  - IHC
    - =>  Expressed mutations
    - Fusions and splice variants
    - Expression profiles and pathway analysis (AR/GR signaling, NFkB, etc.)
    - Immuno-onc markers
  - PD-L1, CD8+ TIL
  - Histology

- ½ Frozen
  - RNA-seq
    - =>  Expressed mutations
    - Fusions and splice variants
    - Expression profiles and pathway analysis (AR/GR signaling, NFkB, etc.)
    - Immuno-onc markers

Translational program designed for molecular profiling ARi resistant patients and effect of ZEN-3694 on resistant markers, potential correlation of response to molecular signature
Phase 1: Combination with Enzalutamide

ZEN-3694 combination study with enzalutamide

- Dose escalation progressing
- Dose proportional exposure
- Target modulation shown at well tolerated doses
- Combination well tolerated
Lack of Grade 3-4 Treatment-related Adverse Events (ZEN-3694-002) at Efficacious Doses

<table>
<thead>
<tr>
<th></th>
<th>1.0x mg N=4</th>
<th>1.33x mg N=6</th>
<th>1.66x mg N=3</th>
<th>2.0x mg N=4</th>
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<tbody>
<tr>
<td>Grade</td>
<td>3</td>
<td>4</td>
<td>3</td>
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<tr>
<td>Fatigue</td>
<td>1*</td>
<td></td>
<td></td>
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<tr>
<td>Hypokalemia</td>
<td></td>
<td></td>
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* Patient was suffering from fatigue from enzalutamide before entering Zen-3694 trial, Event occurred after cycle 1 so not a DLT

Very well tolerated in combination with enzalutamide
Zenith’s BETi program is Clinically Differentiated

Other Clinical BETi
- Thrombocytopenia DLT, require 1-2 weeks off
- Poor PK/PD characterization
- Off target tox, CYP liabilities
- Conservative, suboptimal clinical strategy

Zenith’s BETi (ZEN-3694)
- On target tox profile
- Safety profile allows continuous dosing, no thrombocytopenia
- Good clinical exposure with target modulation, no CYP liabilities
- Focused clinical strategy, leader in combination approach

Other companies developing BETi for CRPC
- Gilead – Phase 1b/2a (Single agent and combination)
- GSK – Phase 1, just initiated (combination)
Next Steps

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BET Inhibitors Potential as Combination Agents

**Lymphoma**
- Rituximab (CD20)
- Ibrutinib (BTK)
- CHOP
- Bortezomib
- Everolimus (mTOR)

**Lung cancer**
- Cytarabine
- Idarubicin
- Panobinostat (HDAC)
- Quizartinib (FLT3)

**Lung cancer**
- Trametinib (MEK)
- Crizotinib (ALK)
- Everolimus (mTOR)

**Prostate cancer**
- Abiraterone (CYP17)
- Enzalutamide (AR)

**Breast cancer**
- Tamoxifen (ER)
- Everolimus (mTOR)
- Cisplatin
- Olaparib (PARP)
- Trametinib (MEK)
- Lapatinib (EGFR)
- Olaparib (PARP)

**BRD4 target, is directly involved in the resistance mechanisms of several types of anti-cancer therapies**

**Combination treatment potential with over 20 drugs**

**Melanoma**
- Dabrafenib (BRAF)
- Trametinib (MEK)
ZEN-3694 Synergizes With Several Standard of Care Cancer Drugs
ZEN-3694 is Synergistic With Paclitaxel in Triple-negative Breast Cancer Models

Treatment Groups

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>TGI</th>
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<tbody>
<tr>
<td>EA006 (Vehicle)</td>
<td>0%</td>
</tr>
<tr>
<td>ZEN-3694 50 mg/kg qd</td>
<td>46%</td>
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<tr>
<td>ZEN-3694 100 mg/kg qd</td>
<td>64%</td>
</tr>
<tr>
<td>OTX-015 100 mg/kg qd</td>
<td>54%</td>
</tr>
<tr>
<td>Paclitaxel 15 mg/kg IP</td>
<td>52%</td>
</tr>
<tr>
<td>Paclitaxel 15 mg/kg IP + ZEN-3694 50 mg/kg qd</td>
<td>101%</td>
</tr>
</tbody>
</table>

- Combination regimen is well tolerated
- ZEN-3694 is more potent than OTX at equivalent dose
- ZEN-3694 is synergistic in combo with Paclitaxel (5/12 regressed tumors)