Corporate Update – September 12, 2018
Annual Meeting of Shareholders

Link to webcast archive: http://services.choruscall.ca/links/zenithagm20180912.html
1. Corporate Profile

2. Epigenetic Mechanism Review

3. Prostate Cancer Rationale Review

4. Phase 1 Details & Early Results

5. Enzalutamide Combination Trial – Phase 2a

6. Next Steps

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Suite 300, 4820 Richard Road S.W. Calgary, AB, Canada T3E 6L1
Tel: (403) 254-9252, Fax:(403) 256-8495, http://www.zenithepigenetics.com
| **Founded** | Corporate spin out from Resverlogix in June 2013 |
| **Status** | Private company, full reporting issuer |
| **Cash Raised 2014-2018** | US$50MM @ US$1.00 & US$2.00 per share (all pre-clinical results based) |
| **Enterprise Value est.** | US$325MM (US$2.50 per share) est. |
| **Shares Outstanding** | 129.6MM |
|  | 142.0MM fully diluted |
| **Cash Burn** | $2MM per quarter - Current |
Epigenetics Mechanism

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Epigenetics, the Mechanism Behind Our Approach

- Early Epigenetic Approach
- Advanced Epigenetic Approach
Resistance to several standard of care treatments does not impede sensitivity to BETi.
Epigenetic Combination Therapies - Addressing Resistance & Increasing Revenue of $B Franchises

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

Increase duration of therapy
Increase patient pool (responders)
Differentiation
Increase IP life

Combination with ZEN-3694 (BETi)
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

CRPC

ENZALUTAMIDE/ABIRATERONE THERAPY

Alterations of AR
(Mutations, amplification, splice-variant)

GR up-regulation

Loss of AR

Other mechanisms
MYC/MYC, BCL-2, FOXA1, ERG, ETS, CHD1, SRC, AKR1C3

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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<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Comments</th>
</tr>
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<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>
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<tr>
<td>Rahul Aggarwal, MD</td>
<td>University of California, San Francisco (UCSF)</td>
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<tr>
<td>Howard Scher, MD</td>
<td>Memorial Sloane Kettering Cancer Center (MSKCC)</td>
<td>Developed enzalutamide - #1 CRPC drug, now owned by Pfizer.</td>
</tr>
<tr>
<td>Wassim Abida, MD, PhD</td>
<td>Memorial Sloane Kettering Cancer Center (MSKCC)</td>
<td>Developing ARN-509 for J&amp;J</td>
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<tr>
<td>Joshi Alumkal, MD</td>
<td>Oregon Health Sciences University (OHSU)</td>
<td>Expert in epigenetics in prostate cancer research</td>
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<tr>
<td>Allan Pantuck, MD</td>
<td>University of California Los Angeles (UCLA)</td>
<td>Involved in enzalutamide and provenge development</td>
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<tr>
<td>Elizabeth Heath, MD</td>
<td>Karmanos (Wayne State)</td>
<td>Genitourinary oncology specialist</td>
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<tr>
<td>Michael Schweizer, MD</td>
<td>University of Washington</td>
<td>Genitourinary oncology specialist</td>
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<tr>
<td>David M. Nanus, MD</td>
<td>Weill Cornell Medicine</td>
<td>Genitourinary oncology specialist</td>
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ZEN-3694 Development in mCRPC- Phase 1 Single Agent Study Results

<table>
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<tr>
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<th>2016</th>
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<td>1H</td>
<td>2H</td>
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**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 ✓

Single agent study key to understanding drug characteristics and supporting combination study
Prior Therapy for mCRPC

- Provenge
- Abiraterone: 5/22/2016 – 8/12/2016 – primary resistance

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

Stable mediastinal nodes over 8 months
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Efficacy at well tolerated doses below MTD
Strong PSA Response with ZEN-3694 + Enzalutamide in Patients with Poor Prior Response to Abiraterone

PSA profile of 3 patients with significant and durable PSA response

PSA profile of 5 patients with poor prior response to abi.

Prior abiraterone
ZEN-3694 + enzalutamide

Prior abiraterone
ZEN-3694 + enzalutamide

PSA Percent Change from Baseline

Prior Abiraterone PSA Response at 12 weeks
ZEN-3694 PSA Response at 12 Weeks

Cohort 3 (Abi)
Cohort 1 (Abi)
Cohort 2 (Abi)
Cohort 2 (Abi)
Cohort 2 (Abi)
Modulating BET Bromodomain Inhibitor ZEN-3694 and Enzalutamide Combination Dosing in a Metastatic Prostate Cancer Patient Using CURATE.AI, an Artificial Intelligence Platform

Allan J. Pantuck,* Dong-Keun Lee, Theodore Kee, Peter Wang, Sanjay Lakhotia, Michael H. Silverman, Colleen Mathis, Alexandra Drakaki, Arie S. Beldegrun, Chih-Ming Ho,* and Dean Ho*  

Combination chemotherapy is a cornerstone of cancer treatment. Optimizing its effectiveness requires dose- and time-dependent regulation of drug synergy. In this report, CURATE.AI, an artificial intelligence platform, is used to prospectively guide the dosing of a bromodomain inhibitor (ZEN-3694) and enzalutamide administered in combination to a patient with metastatic castration-resistant prostate cancer to reduce serum prostate-specific antigen (PSA) levels. CURATE.AI successfully identifies substantial ZEN-3694 and enzalutamide dose adjustments, increasing both treatment efficacy and tolerance. CURATE.AI analysis also confirms that the patient’s durable response is mediated by ZEN-3694 inclusion in the regimen. Due to CURATE.AI-enhanced efficacy and safety, the patient was able to continue with the combination regimen, resulting in a durable response and no disease progression based on CURATE.AI-sustained control over PSA levels and reduced lesion size.

1. Introduction

Conventional chemotherapy simultaneously addresses multiple aberrant disease pathways to potentially improve treatment outcomes. Drug doses are typically determined using dose escalation to reach a maximum tolerated dose (MTD) or via dose expansion to identify suitable regimen administration guidelines.1,2 These combinations are subsequently administered at fixed doses. While the administration of combination therapy using these approaches has served as a clinical standard for clinical care, the patient’s response to therapy evolves during the course of treatment due to the time-dependent, dose-dependent, and patient-specific nature of drug synergy and resulting efficacy and
UCLA Artificial Intelligence Program Confirmation
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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)
ZEN-3694 Synergizes With Several Standard of Care Cancer Drugs

Synergy

CL Values

<table>
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<tr>
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<td>H2228 (ALK)</td>
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<td>OCI-AML2 (DNMT3A/MLL)</td>
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<td>OCI-AML3 (DNMT3A/NPM1)</td>
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Repression of BET activity sensitizes homologous recombination-proficient cancers to PARP inhibition

Cancer Cell
BRD4 Inhibition Is Synthetic Lethal with PARP Inhibitors through the Induction of Homologous Recombination Deficiency

Cell Reports
BET Bromodomain Inhibition Synergizes with PARP Inhibitor in Epithelial Ovarian Cancer