Developing Epigenetic Combination Therapies: Making Great Drugs Work Better & Longer

Annual General Meeting

October 31, 2019
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
## Corporate Profile and Milestones Leading to Major Collaborations

<table>
<thead>
<tr>
<th>Company</th>
<th>Mid-clinical stage stage Epigenetics, oncology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Programs</td>
<td>Multiple Phase 2 POC combination clinical trials</td>
</tr>
<tr>
<td>Cash Raised</td>
<td>~USD$55M</td>
</tr>
<tr>
<td>Partnerships</td>
<td>Newsoara</td>
</tr>
</tbody>
</table>

- **2013**: Initiated combination study with Enzalutamide in mCRPC patients
- **2016**: Announced issuance of US patent for ZEN-3694
- **2017**: Pfizer clinical trial collaboration announced
- **2018**: Newsoara China Partnership
- **2019**: UCSF initiated clinical study using Keytruda, Enzalutamide and ZEN-3694 for mCRPC

Spun out from Resverlogix Corp. (TSX:RVX)
BET Inhibitors Target Resistance Mechanisms
Re-Sensitizing Tumors to Existing Therapy

- BET (bromodomain and extra-terminal domain) proteins are key regulators of oncogenic transcription factors
- Many of the resistance mechanisms to standard of care treatments involve epigenetic modulation by BET proteins
- BET inhibitors (BETi) inhibition expression of tumor oncogenes by disruption of super-enhancers

Adopted from Clinical Cancer Research 2017, 23(7), 1647-55.
Our Approach: Making Great Drugs Work Better & Longer

Combination therapies with ZEN-3694 represent multi-billion dollar addressable markets

Current markets include:

• AR antagonists
• PD-1/PD-L1 monoclonal antibodies
• CDK 4/6 inhibitors
• PARP inhibitors
Developing multiple epigenetic combination cancer therapies that significantly expand the value of existing standard of care therapeutics.

**ZEN-3694 BETi Programs**

- **Pre-Clin**
  - mCRPC (+ enzalutamide)
    - ARSi resistant
  - TNBC (+ talazoparib),
    - non germline BRCAm
  - AR independent mCRPC
    - (+ pembrolizumab + enzalutamide)
  - ER+ Breast
    - (+ CDK4/6i, + ER modulator)

- **Phase 1**

- **Phase 2**

- **Pivotal**

Newsoara (China)

Pfizer

UCSF
Prostate Cancer (mCRPC) Program Review
Phase 2a completing; Phase 2b/3 Planned

<table>
<thead>
<tr>
<th>Indication</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic Castration-Resistant Prostate Cancer (mCRPC)</td>
<td>Combination expansion ZEN-3694 + enzalutamide; Patients progressed on <em>abiraterone</em> or <em>enzalutamide</em></td>
<td>Planned Phase 2b/3 mCRPC: Patients that progress on ARSi to ZEN-3694 + Enzalutamide vs Enzalutamide single agent</td>
</tr>
</tbody>
</table>

- Prolonged rPFS of 44.6 wks with ZEN-3694 + enzalutamide compared to expected rPFS of 20-24 wks with single agent enzalutamide
- 75/75 patients dosed to date, LPLV 11/19
- Well tolerated, chronic daily dosing
- Very positive FDA feedback for design of registration enabling study

- >$3B* opportunity for ZEN-3694 in mCRPC
  - Will also increase overall market of ARSi to $5B* in mCRPC

* Zenith revenue model
Durable PSA90 responses

In patients with primary resistance to abiraterone

Clinical data and AI platform show that both ZEN-3694 and enzalutamide required for durable PSA response

Three patients with significant and durable PSA response, after poor response to abiraterone

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,¹ Dong-Keun Lee, Theodore Kee, Peter Wang, Sanjay Lakhota, Michael H. Silverman, Colleen Mathis, Alexandra Drakaki, Arie S. Belldegrun, Chih-Ming Ho,² and Dean Ho²
### Leading principal investigators and institutions for CRPC trial

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rahul Aggarwal, MD</td>
<td>University of California, San Francisco (UCSF)</td>
<td>National PI for Zenith’s Phase 1b/2a study</td>
</tr>
<tr>
<td>Developmental Therapeutics Specialist, Genitourinary Oncologist</td>
<td></td>
<td>Lead PI of Apalutamide registration study (JNJ), Apalutamide, multiple $B forecast</td>
</tr>
<tr>
<td>Eric Small, MD</td>
<td>University of California, San Francisco (UCSF)</td>
<td>Lead PI of Apalutamide registration study (JNJ), Apalutamide, multiple $B forecast</td>
</tr>
<tr>
<td>Wassim Abida, MD, PhD</td>
<td>Memorial Sloan Kettering Cancer Center (MSKCC)</td>
<td>Experience with BETi and PARPi</td>
</tr>
<tr>
<td>Medical Oncologist</td>
<td></td>
<td>Experience with PARPi</td>
</tr>
<tr>
<td>Joshi Alumkal, MD</td>
<td>University of Michigan</td>
<td>Expert in epigenetics and prostate cancer research</td>
</tr>
<tr>
<td>Leader of the Prostate/Genitourinary Medical Oncology Section and Associate Division Chief for Basic Research in the Hematology-Oncology Division</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tom Beer, MD</td>
<td>Oregon Health Sciences University</td>
<td>Developed enzalutamide - #1 CRPC drug, now owned by Pfizer</td>
</tr>
<tr>
<td>Michael Schweizer, MD</td>
<td>University of Washington</td>
<td>Experience with ARSi</td>
</tr>
<tr>
<td>Oncologist</td>
<td>Fred Hutchinson Cancer Center</td>
<td></td>
</tr>
<tr>
<td>David M. Nanus, MD</td>
<td>Weill Cornell Medicine</td>
<td>Genitourinary oncology specialist</td>
</tr>
</tbody>
</table>
Zenith Epigenetics Announces Clinical Trial Collaboration with Pfizer
November 20, 2018

Collaboration to evaluate ZEN-3694 in combination with Talazoparib in TNBC patients; Phase 1b/2 trial expected to initiate 1Q 2019

CALGARY, Alberta, Nov. 20, 2018 (GLOBE NEWSWIRE) -- Zenith Epigenetics Ltd. ("Zenith" or the "Company"), a wholly-owned subsidiary of Zenith Capital Corp., announced today that it has entered into a clinical trial collaboration with Pfizer Inc. ("Pfizer"; NYSE: PFE) to evaluate the safety and efficacy of a novel anti-cancer combination of Zenith's investigational bromodomain and extra-terminal domain inhibitor ("BETT"), ZEN-3694, and Pfizer’s poly ADP ribose polymerase inhibitor ("PARPi"), talazoparib, in patients with locally advanced or metastatic triple negative breast cancer ("TNBC").

"Zenith is excited to announce this partnership with Pfizer, a leader in oncology," said Don McCaffrey, Chief Executive Officer of Zenith. "The clinical development of BETT and PARPi is expanding the potential treatments for TNBC patients, and this agreement is expected to provide a significant advance in the management of this aggressive form of breast cancer."

Zenith Epigenetics Announces U.S. FDA Clearance of Investigational New Drug Application for ZEN-3694 in TNBC Program
March 18, 2019

Pfizer / Zenith TNBC program collaboration on target to dose first patient in April 2019

Under the terms of the agreement, Zenith Epigenetics and Pfizer will collaborate on a Phase 1b/2 TNBC clinical study. Pfizer will provide talazoparib, Zenith will provide ZEN-3694, and both parties will fund the study. Zenith Epigenetics retains all rights to ZEN-3694.
Supportive Scientific Literature

**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

---

**SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE**

**CANCER**

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

---

**ZEN-3694 and talazoparib synergy in PDX spheres**

---

**Anti-tumor efficacy of ZEN-3694 in combination with talazoparib in MAXFTN 401 PDX (mBRCA)**

Cell Viability

- Talazoparib
- ZEN-3694
- ZEN-3694 + Talazoparib

* adenocarcinoma; M1; lung met; XRT

---

**Anti-tumor efficacy of ZEN-3694 in combination with talazoparib in MAXFTN 1384 PDX**

Cell Viability

- Talazoparib
- ZEN-3694
- ZEN-3694 + Talazoparib

* adenocarcinoma; M1; brain met; XRT
Pfizer / Zenith Clinical Trial Collaboration Summary

<table>
<thead>
<tr>
<th>Indication</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer Collaboration: Triple Negative Breast Cancer (TNBC, non-BRCA 1/2m)</td>
<td></td>
<td>Phase 1b/2: Combination with PARPi (N~50)</td>
</tr>
</tbody>
</table>

- **Objective**: Show safety and activity of ZEN-3694 + talazoparib in TNBC patients, non germline BRCA1/2m
- **Design**: Part 1: Dose escalation, Part 2: Simon 2-stage
- **Patient population**: TNBC: non-germline BRCA1/2 mutations, locally advanced or metastatic
- **Endpoints**: Part 1: Safety, PK/PD, MTD, RP2D; Part 2: Objective response rate (ORR), Duration of response (DOR), rPFS

- ~$400M* peak revenue for ZEN-3694 with significant upside
  - Movement to neo-adjuvant and 1st line TNBC
  - Expansion to other indications combining ZEN-3694 + PARPi in homologous proficient tumors (Ovarian, CRPC, ER+ breast)

* Zenith revenue model
<table>
<thead>
<tr>
<th>Institution</th>
<th>Investigator</th>
<th>Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSKCC</td>
<td>Mark Robson – Study Lead PI Ayca Gucalp - PI</td>
<td>Led OlympiAD breast cancer registration trial</td>
</tr>
<tr>
<td>MD Anderson</td>
<td>Jennifer Litton</td>
<td>Led EMBRACA breast cancer registration trial</td>
</tr>
<tr>
<td>Jules Bordet, Belgium</td>
<td>Philippe Aftimos</td>
<td>Led Merck and BI BETi trials</td>
</tr>
<tr>
<td>Banner Health</td>
<td>Lida Mina</td>
<td>Investigator on Phase 1, 2 and 3 Talazoparib trials</td>
</tr>
<tr>
<td>University of Kansas</td>
<td>Priyanka Sharma</td>
<td>TNBC specialist</td>
</tr>
<tr>
<td>University of Penn</td>
<td>Payal Shah - PI (Susan Domchek)</td>
<td>Talazoparib investigator, breast cancer specialist</td>
</tr>
<tr>
<td>Sarah Cannon</td>
<td>Erika Hamilton</td>
<td>Breast cancer specialist</td>
</tr>
<tr>
<td>UZ Leuven, Belgium</td>
<td>Kevin Punie</td>
<td>Breast cancer specialist</td>
</tr>
<tr>
<td>VHIO, Spain</td>
<td>Mafalda Oliveira</td>
<td>Investigator on Gilead and GSK ER+ BETi trials</td>
</tr>
<tr>
<td>StartMadrid, Spain</td>
<td>Valentina Boni</td>
<td>Breast cancer specialist</td>
</tr>
</tbody>
</table>
Significant Opportunity in Immuno-Oncology:

- ZEN-3694 works by blocking tumor immune evasion
- Combination potential with checkpoint mAbs
- Triple combination (ZEN-3694 + Keytruda + Enzalutamide) mCRPC
ZEN-3694 BET inhibition Disrupts Tumor Immune Evasion

Chen & Mellman (2013) Immunity

BETi ignites CD8 TIL function by modulating PD-L1, other immune checkpoints, suppressive factors & regulatory cells

Trigger full potential of native CD8 TIL cascade & tumor killing by combining BETi + immune checkpoint drug therapy
Immuno-Oncology Opportunity: Strong Rationale for Checkpoint Combinations


Supportive Scientific Literature

ZEN-3694 enhances anti-PD1 activity in the syngeneic CRC model MC-38
Immuno-Oncology Combination Therapy with a BETi
Prostate Cancer – a cancer where immuno-oncology therapies have been unsuccessful

Functional effects of ZEN-3694 + Keytruda in Keytruda resistant model

#1. ZEN-3694 increases anti-PD1-induced IFN-g expression

ZEN-3694 + Keytruda significantly increases IFN-g compared to controls

** p < 0.01

#2. ZEN-3694 + Keytruda demonstrates lysis of tumor cells

#3. Blood gene expression changes at 4h, mCRPC clinical trial

Clinical Blood Data

TIL and Melanoma Tumor 004
Keytruda-resistant (ImmunAccel)
Objective: Revert primary/secondary resistance to anti PD-1 or PD-L1 inhibitors

Rationale:
• BETi modulate PD-L1, suppressive and regulatory cells, other checkpoints

Study design:
• Dose escalation: ZEN-3694 + checkpoint mAb
• Dose Expansion: ZEN-3694 + checkpoint mAb, n~9 per tumor type (expand to additional 14 patients for tumor type with 1 or more responders)

Patient Population:
• Patients who become resistant to checkpoint inh. therapy (primary or secondary) - potentially select short duration responders

Endpoints:
• ORR, Safety
Zenith is focused on ZEN-3694 combinations with SOC extending and expanding the value of existing therapeutics

Multiple Phase 2 POC clinical trials

- **Prostate Cancer Program**: Promising clinical activity of ZEN-3694 + Enzalutamide in ARi resistant mCRPC patients, Very favorable FDA feedback for registration enabling study

- **Pfizer and Zenith collaboration (TNBC/PARPi)**: Ph. 1b/2 of ZEN-3694 + PARPi in TNBC (non germline-BRCA1/2m) initiated

- **Immuno-oncology Program**: ZEN-3694 + Pembrolizumab + Enzalutamide in AR independent CRPC, Significant potential in other resistant tumors