Altor BioScience Corporation

Jefferies 2015 Healthcare Conference Presentation

June 2015
Company Highlights

- Focused on discovering and developing novel protein-based immunotherapeutics for cancer
  - Formed in 2002; 28 employees based in Miramar, FL
  - Raised $50M to date excluding $17M in grants from NIH and NCI

- Innovative and disruptive technology platforms in IL-15 based super agonists and STAR™

- Robust pipeline of proprietary product candidates addressing large markets with unmet medical need
  - Initial focus on bladder cancer and hematological cancers
  - Compelling proof-of-concept data for lead clinical candidates ALT-803 and ALT-801; 7 active clinical trials underway
  - Preclinical candidates with unique targeted protein scaffold construct

- Attractive combination opportunities with checkpoint inhibitor, anti-CD20 and other therapeutic mAbs

- Robust IP portfolio with >85 issued and >40 pending patents
Game-changing Technology Platforms

- **IL-15 based Super Agonists**
  - Lead product ALT-803 in Phase 1/2 clinical trials for solid and hematologic tumors
    (funded by MRA, NIH/NCI & CITN)

- **STAR™ (single-chain T-cell receptors)**
  - Lead product ALT-801 completed Phase 2 metastatic bladder cancer and Phase 1/2 metastatic melanoma trials
    (funded by NCI Bridge Grant)
## Altor’s Product Pipeline

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Indication</th>
<th>Preclin.</th>
<th>Ph. 1</th>
<th>Ph. 2</th>
<th>Ph. 3</th>
<th>Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALT-803</strong></td>
<td>w/ BCG for non-muscle invasive bladder cancer (n=6 to date)</td>
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<tr>
<td></td>
<td>Relapse of hematologic malignancy after allogeneic SCT (n=11 to date)</td>
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<td></td>
<td></td>
<td>Data throughout late 2015 – 1H16</td>
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<tr>
<td></td>
<td>Relapsed/Refractory multiple myeloma (n=4 to date)</td>
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<td></td>
<td>Melanoma, renal cell, NSCLC and head &amp; neck cancers (n=6 to date)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>w/ anti-CD20 for relapsed/refractory iNHL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>w/ checkpoint inhibitor</td>
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<td></td>
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<tr>
<td><strong>Targeted T2M</strong></td>
<td>Hematologic cancers (CD20 targeting component)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate Ph. 1 in 2016</td>
</tr>
<tr>
<td></td>
<td>Solid tumors (TCR component)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>ALT-801</strong></td>
<td>Advanced bladder cancer (n=62 to date)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Completed; OS data pending</td>
</tr>
<tr>
<td></td>
<td>BCG failure non-muscle invasive bladder cancer (n=10 to date)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Data throughout late 2015 – 1H16</td>
</tr>
<tr>
<td></td>
<td>w/ checkpoint inhibitor for advanced bladder cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate Ph. 1 in late 2015</td>
</tr>
</tbody>
</table>
ALT-801 is designed to target immunostimulatory activity of IL-2 against tumors that overexpress intracellular p53 protein.

ALT-801 is differentiated from native IL-2 in its pharmacokinetic and biodistribution profiles and immune cell-mediated mechanism of action against orthotopic bladder cancer in mice.

Previous clinical studies with ALT-801 (p53\(^+\) advanced malignancy; Fishman *CCR* 2011;17:7765) and ALT-801 + cisplatin (p53\(^+\) metastatic melanoma; NCT01029873) showed treatment-induced immune responses and anti-tumor activity.
Mechanism of Action of ALT-801

CD4 T\textsubscript{H}1 cells

$\uparrow$ IFN-\gamma

M1

Potent Innate-Type Anti-Tumor Activity

M2

Macrophage Repolarization

CD8 CD44\textsuperscript{Hi} NKG2D\textsuperscript{+} T cells

CD8 CD44\textsuperscript{Hi} T cells

ALT-801

ALT-801

Cytokines

CD4 T\textsubscript{H}1 cells

$\uparrow$ IFN-\gamma

M1

Potent Innate-Type Anti-Tumor Activity

M2

Macrophage Repolarization

CD8 CD44\textsuperscript{Hi} NKG2D\textsuperscript{+} T cells

CD8 CD44\textsuperscript{Hi} T cells

ALT-801

ALT-801
Bladder Cancer Opportunity

- Bladder Cancer Drug Market (Evaluate Ltd.): $22.5B by 2020
- 70-80% of newly diagnosed patients present non-muscle invasive tumors; 20-30% with muscle-invasive BCa
- For non-muscle invasive tumors, ~50% fail SOC (BCG)

Favorable regulatory pathway for BCG failure non-muscle invasive BCa
- Single-armed pivotal study in 80 – 100 patients with approvable endpoints

For muscle invasive BCa, there has been no new FDA-approved drug in the last 20 years
- Gemcitabine + Cisplatin is standard-of-care 1st line treatment; 14 month median OS
- No standard 2nd line therapy
Phase Ib/II study of an IL-2/T-cell receptor fusion protein in combination with gemcitabine and cisplatin in advanced/metastatic chemo-refractory urothelial cancer

**Mayer N. Fishman**, Daniel A. Vaena², Parminder Singh³, Joel Picus⁴, Ulka N. Vaishampayan⁵, Joel Slaton⁶, John Francis Mahoney⁷, Sanjiv S. Agarwala⁸, Charles Joel Rosser⁹, Danny Landau¹⁰, Julio Hajdenberg¹⁰, Peter J. Van Veldhuizen¹¹, Rahul Atul Parikh¹², Sarah Alter¹³, Liza Hernandez¹³, Peter Rhode¹³, Hing C. Wong¹³

¹Moffitt Cancer Center, Tampa, FL; ²University of Iowa and Iowa City VAMC, Iowa City, IA; ³University of Arizona Cancer Center, Tucson, AZ; ⁴Division of Oncology, Washington University, St. Louis, MO; ⁵Karmanos Cancer Institute, Wayne State University, Detroit, MI; ⁶University of Oklahoma, Oklahoma City, OK; ⁷Carolinas Hematology-Oncology Associates, Charlotte, NC; ⁸St. Luke's Hospital and Health Network, Bethlehem, PA; ⁹University of Hawaii Cancer Center, Honolulu, HI; ¹⁰UF Health Cancer Center at Orlando Health, Orlando, FL; ¹¹University of Kansas Medical Center, Westwood, KS; ¹²University of Pittsburgh Medical Center, Pittsburgh, PA; ¹³Altor BioScience Corp., Miramar, FL, USA

This study is supported by NIH-NCI SBIR Phase 2 Bridge grant CA097550 (Wong) and Altor BioScience Corp.
## Summary of Responses in Evaluable Patients with ALT-801 plus GC

<table>
<thead>
<tr>
<th>Response, n (%)</th>
<th>Group 1 n=17&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 2 n=17&lt;sup&gt;b&lt;/sup&gt;</th>
<th>All n=34</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR&lt;sup&gt;c&lt;/sup&gt;</td>
<td>7 (41%) (18%-67%)</td>
<td>5 (29%) (10%-56%)</td>
<td>12 (35%) (16%-59%)</td>
</tr>
<tr>
<td>CR</td>
<td>2 (12%)</td>
<td>1 (6%)</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>PR</td>
<td>5 (29%)</td>
<td>4 (24%)</td>
<td>9 (26%)</td>
</tr>
<tr>
<td>SD</td>
<td>5 (29%)</td>
<td>2 (12%)</td>
<td>7 (17%)</td>
</tr>
<tr>
<td>PD</td>
<td>4 (24%)</td>
<td>8 (47%)</td>
<td>12 (35%)</td>
</tr>
</tbody>
</table>

- **CR**: complete response, **ORR**: objective response rate, **PD**: progressive disease, **PR**: partial response, **SD**: stable disease
- <sup>a</sup> 1 patient was unevaluable or missing
- <sup>b</sup> 2 patients were unevaluable or missing
- <sup>c</sup> Investigator assessed best overall response per RECIST v1.1

- **39% ORR of evaluated patients (n=31) vs. 19% anticipated per baseline prognostic factor model of Pond et al. (BJU Int 2014; 113: E137)**
Waterfall Plot of Best Response in ALT-801 Study

Maximum change in sumed target lesion size from baseline (%)

- CR
- PR
- SD
- PR - symptomatic progression (*)
or new lesions (**)
Summary of Progression-Free Survival and Overall Survival in Evaluable Patients

- Median PFS = 3.2 months (95% CI, 2.6-5.3 months)
- Median OS = 11.7 months (n=34, 95% CI, 6.5-15.3 months), Group 1 median OS = 12.3 months, Group 2 median OS = 8.1 months
- 67% 6-month survival rate (n=33) vs. 54% anticipated per baseline prognostic factor model of Pond et al. (BJU Int 2014; 113: E137)
IL-15-based Superagonist Complex

ALT-803

“ALT-803 Ranked as #1 Immunotherapeutic Agent for Cancer”

-Mac Cheever, Head of CITN, at the 2013 Annual Society for Immunotherapy of Cancer Conference
ALT-803: A Superagonist Fusion Complex

Human IL-15N72D:IL-15RαSu/Fc Complex
Biodistribution of ALT-803 versus IL-15
Quantitative PETscan Imaging/Organ Biodistribution

$^{64}$Cu-ALT-803

$^{64}$Cu-IL-15

Cai, W., Univ. of Wisconsin

Altor BioScience Corporation
ALT-803: A Superagonist Fusion Complex

Human IL-15RαSu/Fc Complex: Superior vs. Recombinant IL-15

IL-15N72D

IL-15Rα

IgG1 Fc

ALT-803

- Improved IL-15Rβγ binding activity through N72D mutation and IL-15Rα
  - 30x more active vs. IL-15 in vivo

- Induces IFN-γ and NK and CD8+ T-cell proliferation

- Increased serum half-life
  - 25hrs in vivo vs. <40min for IL-15

- Longer residence time in lymphoid tissue for lymphocyte stimulation
ALT-803 Mechanism of Action against Myeloma

1. ALT-803 promotes rapid expansion of memory CD8⁺ T cells but not naïve CD8⁺ T lymphocytes in myeloma-bearing mice.
2. The memory CD8⁺ T cells secrete IFN-γ and upregulate innate type receptors on their surfaces.
3. ALT-803-activated cells mediate nonspecific cytotoxicity against myeloma and other tumor cells.
4. Short-term ALT-803 treatment also provides tumor-bearing mice with protective immunity against a subsequent tumor challenge.

Potential Synergistic Effect of ALT-803 and Checkpoint Blockers for Immunotherapy

Rubinstein, M., MUSC
Efficacy of ALT-803 + anti-PD-L1 in 5T33 Myeloma Model

A

Survival Curve (5T33P)

B

Study Day

Percent survival

PBS

ALT-803 (0.05 mg/kg)

ALT-803 (0.2 mg/kg)

αPD-L1 (5 µg)

αPD-L1 (25 µg)

αPD-L1 (100 µg)

n = 5

P ≤ 0.048
Antitumor efficacy of ALT-803 + rituximab against human Daudi B lymphoma in SCID mice

A. SCID mice (NK cell competent) (N=3/group) bearing Daudi cell tumors (1x10^7 injected iv two weeks prior to treatment) were treated with PBS, ALT-803 (0.2 mg/kg), rituximab (10 mg/kg) or ALT-803+rituximab on 15 and 18 days post tumor inoculation. Daudi cell percentages in bone marrow were determined 4 days after the second treatment. B. Effect of ALT-803 dose titration in combination with rituximab on Daudi cell burden in tumor-bearing SCID mice (N=6-7/group).
1. Relapse of Hematologic Malignancy after Allogeneic Stem Cell Transplantation
2. Advanced Solid Tumors (melanoma, renal cell, non-small cell lung, head & neck cancers)
3. Non-Muscle Invasive Bladder Cancer
4. Refractory Multiple Myeloma
5. Indolent non Hodgkin’s B cell lymphoma
ALT-803 Hematologic Malignancy Study
Serum Cytokine Levels

IFNγ

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Predose</th>
<th>30 min</th>
<th>2 hr</th>
<th>4 hr</th>
<th>6 hr</th>
<th>8 hr</th>
<th>24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ug/kg</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3 ug/kg</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6 ug/kg</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</table>

IL6

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Predose</th>
<th>30 min</th>
<th>2 hr</th>
<th>4 hr</th>
<th>6 hr</th>
<th>8 hr</th>
<th>24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ug/kg</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3 ug/kg</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6 ug/kg</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
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</table>
ALT-803 Hematologic Malignancy Study
Lymphocyte Proliferation in 3 µg/kg Patient with ALT-803 Treatment

NK Cells

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4⁺</td>
<td>7.83%</td>
<td>48.5%</td>
<td>76.5%</td>
<td>8.76%</td>
</tr>
<tr>
<td>CD8⁺</td>
<td>12.8%</td>
<td>22.2%</td>
<td>29.3%</td>
<td>19.6%</td>
</tr>
<tr>
<td>Ki67</td>
<td>4%</td>
<td>17.5%</td>
<td>40%</td>
<td>7.85%</td>
</tr>
</tbody>
</table>

CD4⁺

CD8⁺
# Summary of ALT-803 vs. rIL-15

<table>
<thead>
<tr>
<th>ALT-803</th>
<th>rIL-15¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing Regimen:</strong></td>
<td><strong>Dosing Regimen:</strong></td>
</tr>
<tr>
<td>• Once-a-week IV dosing for 4 weeks</td>
<td>• IV daily dosing for 12 consecutive days</td>
</tr>
<tr>
<td><strong>Less Toxicity Observed:</strong></td>
<td><strong>Less Toxicity Observed:</strong></td>
</tr>
<tr>
<td>• ≥ 6 µg/kg; MTD not yet defined</td>
<td>• MTD at 0.3 µg/kg</td>
</tr>
<tr>
<td>• Transient fever and chills/rigor</td>
<td>• Transient fever and chills/rigor</td>
</tr>
<tr>
<td>• Out-patient treatment</td>
<td>• Hypotension, thrombocytopenia and elevations of liver enzymes ALT and AST at DLT levels</td>
</tr>
<tr>
<td></td>
<td>• In-patient treatment</td>
</tr>
<tr>
<td><strong>Cytokine Induction:</strong></td>
<td><strong>Cytokine Induction:</strong></td>
</tr>
<tr>
<td>• IFN-γ and IL-6</td>
<td>• IFN-γ, IL-6, IL-8, TNF-α and IL-1β</td>
</tr>
<tr>
<td>• No TNF-α, IL-4, IL-10 and IL-2</td>
<td></td>
</tr>
<tr>
<td><strong>Increased Immune Cell Proliferation:</strong></td>
<td><strong>Increased Immune Cell Proliferation:</strong></td>
</tr>
<tr>
<td>• Promotes NK, CD8⁺ and CD4⁺ cell proliferation after a single dose</td>
<td>• Promotes NK, CD8⁺ and CD4⁺ cell proliferation after multiple rounds of dosing</td>
</tr>
<tr>
<td>• Induces long lasting cell proliferation; supports a weekly dosing regimen</td>
<td></td>
</tr>
</tbody>
</table>

¹ Conlon, KC et al. (2015) J Clinical Oncology
IL-15 Based Technology Platform

Human IL-15N72D: IL-15RαSu/Fc complex (ALT-803)

Functional scaffold for multi-specific molecules (T2M)

IL-15N72D

IL-15RαSu

IgG1 Fc

Cancer or infected cell

Target antigen (e.g., CD20)

Targeting domain

NK / T cell / Macrophage

IL-15βγ receptor

Low affinity Fcγ receptor

NK cell / Macrophage
STAR™ Technology Platform

Validated Tumor or Viral Targets

Sources of TCRs

In Vitro Mutagenesis

Affinity Improvement

TCR

HLA/peptide

Functional Fusions

Cytokine

scTCR

IgG

scAb

Toxin/Drug

Testing

HLA-tg Mice

Xenograft Tumor & Viral Models

huTCR-tg Mouse
Corporate Development Strategies

- Advance ALT-801 for bladder cancer
  - Combination with checkpoint inhibitors (N=40 pilot study) for refractory metastatic bladder cancer
  - Registration trial for BCG failure non-muscle invasive bladder cancer (N=100, single-arm)

- Complete ALT-803 Phase 1 clinical development
  - Establish therapeutic index of ALT-803
  - Move forward on combination trials with immune checkpoint inhibitors/therapeutic antibodies
  - Execute strategic collaborations with major pharma at appropriate value inflection point

- Leverage T-cell receptor platform in the cell therapy space through partnership (discussions/negotiations ongoing)

- Expand targeted T2M platform and advance clinical development of anti-CD20T2M for proof-of-principle objective