Acucela Inc. (TSE: 4589)  
BioCentury  
NewsMakers in the Biotech Industry  
September 26, 2014

Acucela is a clinical-stage biotechnology company that specializes in discovering and developing novel therapeutics to treat and slow the progression of sight-threatening ophthalmic diseases affecting millions of individuals worldwide.
Disclaimer

This presentation contains forward-looking statements concerning our product development, our technology, our competitors, our intellectual property, our financial condition and our plans for research and development programs that involve risks, uncertainties and assumptions. These statements are based on the current estimates and assumptions of the management of Acucela as of the date of this presentation and are subject to uncertainty and changes in circumstances. Given these uncertainties, you should not place undue reliance upon these forward-looking statements. Such forward-looking statements are subject to risks, uncertainties, assumptions and other factors that may cause the actual results of Acucela to be materially different from those reflected in such forward-looking statements.

Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, those set forth in our reports on file with the Tokyo Securities Exchange and the United States Securities and Exchange Commission. The Company does not undertake any obligation to release publicly any revisions to these forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. All statements contained in this presentation are made only as of the date of this presentation.
Company Overview/Introduction
Company Snapshot

An ophthalmology-focused, science-driven biotechnology company

People and Infrastructure
- Broad-skilled employee base in research, development and operations
- Three Locations: Seattle, WA Global Headquarters; Bothell, WA Research Facility; Tokyo, Japan Office

Partnership
- Long-time partnership with Otsuka Pharmaceutical
- Potential high-reward alliance
- Acucela has rights for lead investigational candidate (emixustat hydrochloride) in Europe, South and Central America and most of Africa

Technology
- Unique mechanism of action in visual cycle modulation (VCM)
- Lead clinical trial program in geographic atrophy (GA) associated with dry age-related macular degeneration (AMD); no treatments currently available
- Over 100 granted patents; almost 200 pending patents

Financials
- Successful IPO; $163M (gross) raised
- Cash, short-term and long-term investments for the three months ended 06/30/14 was approximately $177M ready to deploy
- General and administrative expense for the three months ended 06/30/14 was $2.5M
Corporate Strategy

Three core strengths drive opportunities to expand research and business development

- Leader in VCM research
- Unique and robust partnership with Otsuka Pharmaceutical
- Large potential opportunity with emixustat

Expanded research

Business development
Ryo Kubota, MD, PhD Profile

• Scientific Research and Ophthalmology
  – Performed over 1,000 ocular surgeries to treat cataract, retinal detachment, diabetic retinopathy, glaucoma, strabismus, and other conditions
  – Discovered a glaucoma gene, myocilin; earned the Suda Award
  – Established Acucela in 2002; research helped advance the theory that toxic by-products of the visual cycle could be a causative factor in AMD

• Finance and Business
  – Raised over $40M in venture capital rounds A, B and C
  – Negotiated and signed a co-development and co-commercialization partnership for visual cycle modulation candidates with Otsuka Pharmaceutical
  – Negotiated second partnership for glaucoma with Otsuka Pharmaceutical
  – Led successful IPO in Japan (completed in February 2014)
### Board of Directors

<table>
<thead>
<tr>
<th>Name</th>
<th>Title and Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ryo Kubota, MD, PhD</td>
<td>Founder, Chairman and CEO, Acucela Inc.</td>
</tr>
<tr>
<td>Peter Kresel</td>
<td>Sr. Vice President, Global Regulatory Affairs, Allergan (retired)</td>
</tr>
<tr>
<td>Glen Sato, JD</td>
<td>Partner, Cooley LLP</td>
</tr>
<tr>
<td>Michael Schutzler</td>
<td>CEO, The Washington Technology Industry Association</td>
</tr>
<tr>
<td>Brian O’Callaghan</td>
<td>President, Chief Operating Officer and Interim CFO, Acucela Inc.</td>
</tr>
<tr>
<td>Investigational Product Candidate</td>
<td>Potential Indication</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>----------------------</td>
</tr>
</tbody>
</table>
| Emixustat hydrochloride (developed by Acucela) | Dry AMD and other ophthalmic indications | **Joint (50/50)** - North America  
**Acucela** - Europe, South and Central America and most of Africa  
**Otsuka** – Asia-Pacific, some countries in Africa/Middle East | • Otsuka paid $5M cash upfront payment to Acucela  
• Potential milestone payments - $258M total  
• To date (as of 06/30/14) Otsuka has paid approximately $130M for development activities to Acucela (including a $5M milestone payment)  
• Currently Otsuka and Acucela are equally sharing all development expenses; Otsuka loans funds to Acucela for the payment of Acucela’s shares of the development expenses through to product launch |
| OPA-6566 (developed by Otsuka) | Glaucoma and other ophthalmic indications | United States | • Pre-specified condition for Acucela to exercise its right to co-develop and co-promote ("opt-in" right)  
• Otsuka funds all development costs prior to Acucela’s opt-in election  
• If Acucela elects to opt-in, Acucela pays to Otsuka a pre-determined opt-in fee  
• Following the opt-in election, Acucela shares its portion of development expenses, which are capped |
Visual Cycle Modulation (VCM) Technology
The visual cycle is a biological process in which dietary vitamin A is converted to a light-sensitive compound. This process takes place in the photoreceptors and in a specialized tissue called the retinal pigment epithelium (RPE). During exposure to bright light, the visual cycle is extremely active and is thought to produce toxic by-products of vitamin A that cannot be eliminated.
Visual cycle modulators are small molecule compounds which target specific proteins of the visual cycle. The intended effect of VCM compounds is to reduce retinal toxins and preserve the integrity of retinal tissue. Acucela has established a leadership position in this area as a result of our pioneering efforts to research, discover and develop proprietary VCM investigational compounds.
Age-related Macular Degeneration (AMD)
About AMD

• The Disease
  – AMD occurs when the small central portion of the retina, known as the macula, deteriorates
  – AMD exhibits in two forms – dry and wet
    – Dry (non-neovascular) AMD occurs in progressive stages
      – Early Dry AMD can cause blurry vision
      – Geographic Atrophy (GA) is the advanced form of AMD, which can cause permanent vision loss
    – No approved therapies to treat dry AMD at any disease stage are currently available
    – Wet (neovascular) AMD progresses rapidly and may lead to a permanent loss of central vision
      – Approved therapies currently on the market (via injection)
    – The underlying condition of all AMD is the dry form

• Risk Factors
  – Included, but not limited to: genetic factors, lifestyle (diet and smoking), light exposure and hypertension

• Prevalence
  – Aggregate estimates of wet and dry AMD patients in 2012 was 12M (US) and 127M (Global)(1)
  – Dry AMD represents approximately 90% of all AMD cases
    – Approximately 15% of AMD patients develop intermediate or advanced dry AMD (also known as GA)

AMD Disease Progression

- **Normal Retina**
- **Dry AMD**
  - (Drusen)
- **Late-Stage Dry AMD**
  - (Geographic Atrophy or GA)
- **Wet AMD**
  - (Neo-vascularization)
### AMD: Proposed Disease Progression and Potential Targets for Intervention

**Early Pathology**
- Aging, Oxidative Stress, Light Damage, Genetic Factors
  - (lipofuscin, vitamin A toxins, free radicals)
  - (lipid & protein deposits beneath RPE)
  - RPE Dysfunction

**Intermediate Pathology**
- Chronic Inflammation
  - (immune response & complement activation)
  - Damage/Death of RPE

**Late Pathology**
- Photoreceptor Cell Death
  - Geographic Atrophy
  - Choroidal Neovascularization

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**Investigational Approaches**
- Visual Cycle Modulators
- Anti-amyloid β
- Complement Inhibitors
- Stem Cell Transplants

**Approved Therapy**
- Anti-VEGF Medications (CNV)

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Visual Impact of GA Associated with Dry AMD
Autofluorescence is Suggested to be Associated with the Progression of Atrophy*

Emixustat in Clinical Studies for Geographic Atrophy (GA) Associated with Dry Age-Related Macular Degeneration (AMD)
Emixustat Hydrochloride Overview: Lead Investigational Product Candidate

- Non-retinoid small molecule
- Oral administration
- Designed to modulate visual cycle activity and reduce the accumulation of toxins in the retina
- Targets a key rate-limiting enzyme of the visual cycle
- Measureable pharmacologic effect in the retina through ERG (Electroretinography or ERG is an eye test used to detect abnormal function of the retina - the light-detecting portion of the eye)
Drug Development Path: Emixustat for GA Associated with Dry AMD

- 2005
  - Toxicology
  - Proof-of-concept in pre-clinical model
  - Medicinal chemistry

- 2007
  - IND filed
  - First human trial

- 2008
  - Five phase 1 clinical trials completed
  - One phase 2a clinical trial completed (GA subjects)
  - 179 total subjects exposed to emixustat
  - Fast track designation granted

- 2009
  - Phase 2b/3 clinical trial enrollment completed in 508 subjects

- 2012
  - Phase 2b/3 clinical trial top-line results expected

- 2013
  - Fast track designation granted

- 2014
  - Two-year treatment

- 2016
  - Phase 2b/3 clinical trial commences

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Reduction of Rod Photoreceptor Activity and Protection from Light Damage in Mice Treated with Single Dose of Emixustat

Slowing of visual cycle activity:
Dose-dependent reduction of rod photoreceptor activity (ERG following single dose)

Attenuation of A2E Accumulation in abca4-/- Mice Treated Three Months with Emixustat

Reduction of A2E/lipofuscin

- **Wild-type**
- **abcr-/-**
- **abcr-/- (3 mg/kg), 3-month treatment**


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**ED₅₀ = 0.47 mg/kg/day**

**Daily Dosage: log(mg/kg)**

* Data on file.
Emixustat Treatment Reduces Retinal Neovascularization in Mouse Model of Oxygen-Induced Retinopathy

Emixustat Phase 1a Clinical Trial Results: Mean Oral PK Profiles

- Single-ascending dose; phase 1a clinical trial in healthy subjects
- AUC increased approximately proportionally with dose
- Maximal plasma concentration (Cmax) also increased linearly with dose
- Emixustat was readily absorbed from the GI tract

Phase 2a Dose Escalation Study

• Design
  – Multi-center, randomized, double-masked, placebo-controlled, dose-escalation study of the safety, tolerability, pharmacokinetics and pharmacodynamics of emixustat
  – A total of 72 patients with GA associated with dry AMD were enrolled
  – Treatment period for up to three months

• Primary objectives
  – Assess the safety and tolerability of different dose levels of emixustat when administered orally once daily for three months
  – Explore the relationship of biologic activity of emixustat using ERG as biomarker

• Summary of Results (completed in October 2012)
  – Emixustat was generally safe and well tolerated at the doses and duration tested
  – ERG data confirmed dose-dependent pharmacologic activity in the retina
  – Data were presented at The Association for Research in Vision and Ophthalmology (ARVO) 2013 annual meeting in Seattle, Washington

• Next Milestone
  – Podium presentation at the American Association of Ophthalmology (AAO) 2014 annual meeting in Chicago, Illinois
Rod Visual Cycle Suppression with Emixustat in Patients with GA (at Day 14)

- Administration of emixustat to GA subjects resulted in a dose-dependent suppression of mean ERG b-wave rod recovery after photo bleach.
- Mean ERG responses at Days 14, 30 and 60 were comparable, indicating steady-state.
- Within 7 to 14 days after the last dose of emixustat (after photo bleach) mean ERG b-wave responses recovered approximately to baseline.


*Data on file.
Clinical Development Progress to Date

- **Completed Clinical Trials to Date**
  - Five phase 1 clinical trials (normal healthy adults)
  - One phase 2a clinical trial (GA subjects)
  - Total of 179 human subjects exposed to emixustat

- **On-going Clinical Trial – Phase 2b/3 “SEATTLE” Study**
  - **Design**
    - Two year, randomized, double-masked, dose-ranging study comparing the safety and efficacy of emixustat with placebo in patients with GA associated with dry AMD
    - A total of 508 patients with GA associated with dry AMD were enrolled
  - **Objectives**
    - Primary: Determine if emixustat reduces lesion growth rate compared to placebo
    - Secondary:
      - Evaluate safety and tolerability
      - Assess changes in best-corrected visual acuity
      - Evaluate the effect on development of wet AMD
  - **Next Milestone**
    - Top-line 2-year trial results anticipated in mid-2016
OPA-6566 - Investigational Compound for Open-angle Glaucoma and/or Ocular Hypertension
OPA-6566 Overview and Status

• **Approach**
  - Adenosine A2a receptor agonist

• **Development Status**
  - IND filed in June 2011
  - US phase 1/2 clinical trial conducted in patients with open-angle glaucoma and/or ocular hypertension

• **Current Status**
  - After a phase 1/2 clinical trial in the United States, it was determined that further pre-clinical evaluations are needed
  - Future development plans for OPA-6566 will be based on the results of such evaluations
  - There are no ongoing or planned clinical studies at this time
Financials
## Condensed Statements of Operations

*(in thousands, except per share data)*

<table>
<thead>
<tr>
<th></th>
<th>Three months ended June 30, 2014</th>
<th>Six months ended June 30, 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenue from collaborations</strong></td>
<td>$9,086</td>
<td>$11,023</td>
</tr>
<tr>
<td><strong>Expenses:</strong></td>
<td></td>
<td></td>
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<tr>
<td>Research and development</td>
<td>6,501</td>
<td>7,845</td>
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<tr>
<td>General and administrative</td>
<td>2,481</td>
<td>3,255</td>
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<tr>
<td><strong>Total expenses</strong></td>
<td>8,982</td>
<td>11,100</td>
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<tr>
<td><strong>Income (loss) from operations</strong></td>
<td>104</td>
<td>(77)</td>
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<tr>
<td><strong>Other income (expense), net:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interest income</td>
<td>120</td>
<td>2</td>
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<tr>
<td>Interest expense</td>
<td>(1)</td>
<td>(30)</td>
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<tr>
<td>Other income, net</td>
<td>39</td>
<td>(76)</td>
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<tr>
<td><strong>Total other income, net</strong></td>
<td>158</td>
<td>48</td>
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<tr>
<td>Income (loss) before income tax</td>
<td>262</td>
<td>(29)</td>
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<tr>
<td>Income tax (expense) benefit</td>
<td>(191)</td>
<td>9</td>
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<tr>
<td><strong>Net income (loss)</strong></td>
<td>71</td>
<td>(20)</td>
</tr>
<tr>
<td><strong>Net income (loss) attributable to participating securities</strong></td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Net income (loss) attributable to common shareholders</strong></td>
<td>$71</td>
<td>$(20)</td>
</tr>
<tr>
<td><strong>Net income (loss) per share attributable to common shareholders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>$-</td>
<td>$-</td>
</tr>
<tr>
<td>Diluted</td>
<td>$-</td>
<td>$-</td>
</tr>
<tr>
<td><strong>Weighted average shares used to compute net income (loss) per share attributable to common shareholders:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>35,641</td>
<td>11,968</td>
</tr>
<tr>
<td>Diluted</td>
<td>35,867</td>
<td>11,968</td>
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</table>
### Condensed Balance Sheets (in thousands)

#### Assets

<table>
<thead>
<tr>
<th> </th>
<th>June 30, 2014</th>
<th>December 31, 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total current assets</strong></td>
<td>128,843</td>
<td>42,281</td>
</tr>
<tr>
<td><strong>Property and equipment, net</strong></td>
<td>861</td>
<td>1,112</td>
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<tr>
<td><strong>Long-term investments</strong></td>
<td>63,229</td>
<td>3,478</td>
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<tr>
<td><strong>Long-term deferred tax asset</strong></td>
<td>1,049</td>
<td>1,280</td>
</tr>
<tr>
<td><strong>Deferred offering costs</strong></td>
<td>-</td>
<td>5,548</td>
</tr>
<tr>
<td><strong>Other assets</strong></td>
<td>344</td>
<td>349</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>$194,326</td>
<td>$54,048</td>
</tr>
</tbody>
</table>

#### Liabilities and shareholders’ equity

<table>
<thead>
<tr>
<th> </th>
<th>June 30, 2014</th>
<th>December 31, 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total current liabilities</strong></td>
<td>8,672</td>
<td>22,869</td>
</tr>
<tr>
<td><strong>Commitments (Note 4)</strong></td>
<td>7</td>
<td>55</td>
</tr>
<tr>
<td><strong>Long-term deferred rent, lease incentives, and others</strong></td>
<td>7</td>
<td>55</td>
</tr>
<tr>
<td><strong>Total long-term liabilities</strong></td>
<td>7</td>
<td>55</td>
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<tr>
<td><strong>Shareholders’ equity:</strong></td>
<td> </td>
<td> </td>
</tr>
<tr>
<td>Convertible preferred stock</td>
<td>-</td>
<td>28,209</td>
</tr>
<tr>
<td>Common stock, no par value, 100,000 shares authorized as of June 30, 2014 and 60,000 shares authorized as of December 31, 2013; issued and outstanding, 35,641 shares as of June 30, 2014 and 11,971 shares as of December 31, 2013</td>
<td> </td>
<td> </td>
</tr>
<tr>
<td>Additional paid-in capital</td>
<td>3,111</td>
<td>2,728</td>
</tr>
<tr>
<td>Accumulated other comprehensive loss</td>
<td>(105)</td>
<td>(7)</td>
</tr>
<tr>
<td>Accumulated deficit</td>
<td>(335)</td>
<td>(3,460)</td>
</tr>
<tr>
<td><strong>Total shareholders’ equity</strong></td>
<td>185,647</td>
<td>31,124</td>
</tr>
<tr>
<td><strong>Total liabilities and shareholders’ equity</strong></td>
<td>$194,326</td>
<td>$54,048</td>
</tr>
</tbody>
</table>
Financial Overview

(US$ in thousands)

**Revenues from Collaboration**

<table>
<thead>
<tr>
<th>Year</th>
<th>FY09</th>
<th>FY10</th>
<th>FY11</th>
<th>FY12</th>
<th>FY13</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27,019</td>
<td>36,457</td>
<td>34,226</td>
<td>46,424</td>
<td>52,947</td>
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</table>

CAGR 18.3%

**R&D**

<table>
<thead>
<tr>
<th>Year</th>
<th>FY09</th>
<th>FY10</th>
<th>FY11</th>
<th>FY12</th>
<th>FY13</th>
<th>FY14Q2</th>
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<tbody>
<tr>
<td></td>
<td>23,638</td>
<td>34,809</td>
<td>41,495</td>
<td>47,024</td>
<td>54,048</td>
<td>194,326</td>
</tr>
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</table>

CAGR 18.8%

**Total assets**

<table>
<thead>
<tr>
<th>Year</th>
<th>FY09</th>
<th>FY10</th>
<th>FY11</th>
<th>FY12</th>
<th>FY13</th>
<th>FY14Q2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4,209</td>
<td>14,101</td>
<td>20,840</td>
<td>25,607</td>
<td>31,124</td>
<td>185,647</td>
</tr>
</tbody>
</table>

**Total shareholders’ equity**

<table>
<thead>
<tr>
<th>Year</th>
<th>FY09</th>
<th>FY10</th>
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<td>46,424</td>
<td>52,947</td>
<td>194,326</td>
</tr>
</tbody>
</table>

Note: FY09 and FY10 are unaudited figures.
Investor Rationale

• Significant unmet medical need (GA associated with dry AMD)
  – No approved therapy currently on the market

• Differentiated product candidate (emixustat)
  – Oral administration
  – Unique mechanism of action
  – Ongoing phase 2b/3 clinical trial (ClinicalTrials.gov identifier: NCT01802866)

• Competitive and defensible IP position (as of July 31, 2014)
  – 111 granted patents; 167 pending patent applications

• Healthy balance sheet
  – $163M IPO (gross proceeds)
  – Financially beneficial collaboration agreement with Otsuka Pharmaceutical
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