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# Acucela Inc.
# FY2015 Q2 Large Meeting

Tokyo August 26, 2015

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.

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# Corporate Overview

# Key areas of strength

## An ophthalmology-focused, science-driven biotechnology company

### People and Strategy

- Executive leadership with experience in health care management, life science administration and technology
- Broad-skilled employee base in research, development and operations
- Strategic plan to develop an innovative portfolio of ophthalmology products

### 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
- 100 granted patents; 175 pending patents (as of 6/30/15)

### 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

### Financials

- Successful IPO; $163M (gross) raised
- Cash, short-term and long-term investments for the three months ended 6/30/15 was $175M ready to invest in ongoing programs, business development and internal research and development

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# FYE2015 Q2 Highlights

# Recent Highlights

| Date | Highlights |
|---|---|
| Mar 31 | Acucela Granted New Patent Covering Method of Use for Emixustat Hydrochloride |
| May 1 | Acucela Shareholders Elect New Board Members at the Special Meeting of Shareholders |
| May 13 | Acucela Announces Publication of Pre-clinical Data for Emixustat Hydrochloride (PLOS ONE) |
| Jun 3 | Acucela Announces Publication of Phase 2a Clinical Trial Results for Emixustat Hydrochloride (June online edition of RETINA) |
| Jun 29 | Acucela Shareholders Elect Board of Directors at the Annual Meeting of Shareholders |
| Jul 2 | Acucela Hires Roger Girard as Chief Strategy Officer |
| Aug 5 | Acucela Hires Dr. Lukas Scheibler as Executive Vice President of Translational Medicine |
| Aug 25 | Acucela Hires Dr. George Lasezkay as Executive Vice President of Legal Affairs |

# New Management Team

## A seasoned management team with significant experience in health care management, life science administration and technology.

**Ryo Kubota, MD, PhD**
Chairman, President and CEO

| John Gebhart, MBA<br>Chief Financial Officer | Steve Tarr, PhD<br>Chief Operating Officer | Ted Danse, MBA<br>Chief Business Officer | Roger Girard*<br>Chief Strategy Officer |
|---|---|---|---|
| Qliance Medical Management, Inc<br>Remote Medical International<br>Ventripoint, PhysioSonics<br>Carena, Clarity Health<br>Nexcura, and DS-IQ | Emeritus Senior Living<br>Santa Clara Valley Health System<br>Scottsdale Lincoln Health Network<br>University of Washington Medicine | Neurotech Pharmaceuticals, Inc.<br>ISTA Pharmaceuticals Inc.<br>Allergan, Coopervision,<br>Bausch & Lomb , Schering-Plough | Xecutive Advisory Partners LLC<br>Terra Vista Software<br>,CareCap, Bellevue,<br>Neuro-ID, IsoRay Medical |

* Effective as of September 1, 2015

# Board of Directors

| Directors | Background |
|---|---|
| Ryo Kubota, MD PhD | Chairman, President and Chief Executive Officer and also founder of Acucela Inc. |
| Shintaro Asako | Chief Executive Officer - DeNA West<br>*Previously, Chief Financial Officer - MediciNova, Inc.* |
| Shiro Mita, PhD | President and Chief Executive Officer - M's Science Corporation<br>*Previously: Executive Director of Drug Discovery, Director - Santen Pharmaceuticals Co., Ltd* |
| Eisaku Nakamura | Director - Koinobori Associates Inc.<br>*Previously: Director and General Manager - Bio Sight Capital Co., Ltd , Chief Executive Officer and President - Berevno Corporation, Board of Directors - CanBas Corporation and Activus Pharma Co. Ltd.* |
| Robert Takeuchi | President - RT Consulting, Inc.<br>*Previously: President - SOFTBANK Finance, America Corporation, Director of International Equity Sales - Credit Suisse First Boston, Board of Directors SBI Investment Co., Ltd. and Quark Pharmaceuticals, Inc.* |

# RETINA June 2015:

## *Analysis of Change in Lesion Size from Baseline at Day 90*

Table 4. Lesion Size Change From Baseline at Day 90

| | Mean (SD) Change From Baseline for Study Eye | | | |
|---|---|---|---|---|
| | | Emixustat* | | |
| | Placebo (N = 18) | 2 mg qAM (N = 12) | 5 mg qAM (N = 12) | 5 mg qPM (N = 12) |
| CP | | | | |
| Total area, $mm^2$ | 0.4 (0.7) | 0.2 (0.5) | 0.3 (0.5) | 0.1 (0.5) |
| n | 9 | 11 | 10 | 8 |
| FAF | | | | |
| Total area, $mm^2$ | 0.2 (0.4) | −0.1 (1.4) | 0.0 (0.2) | 0.0 (1.0) |
| n | 8 | 11 | 4 | 8 |
| FA | | | | |
| Total area, $mm^2$ | 0.4 (0.5) | 0.2 (0.6) | 0.5 (0.5) | 0.2 (0.6) |
| n | 12 | 12 | 10 | 9 |

*Lesion data were not analyzed for the 7 mg qAM and 10 mg qAM cohorts.
CP, color photography; FAF, fundus autofluorescence photography.

Source: Dugel P, Novack R, Csaky K, Richmond P, Birch D, Kubota R. Phase II, randomized, placebo-controlled, 90-day study of emixustat hydrochloride in geographic atrophy associated with dry age-related macular degeneration. *RETINA*. June 2015; 35(6): 1173–1183

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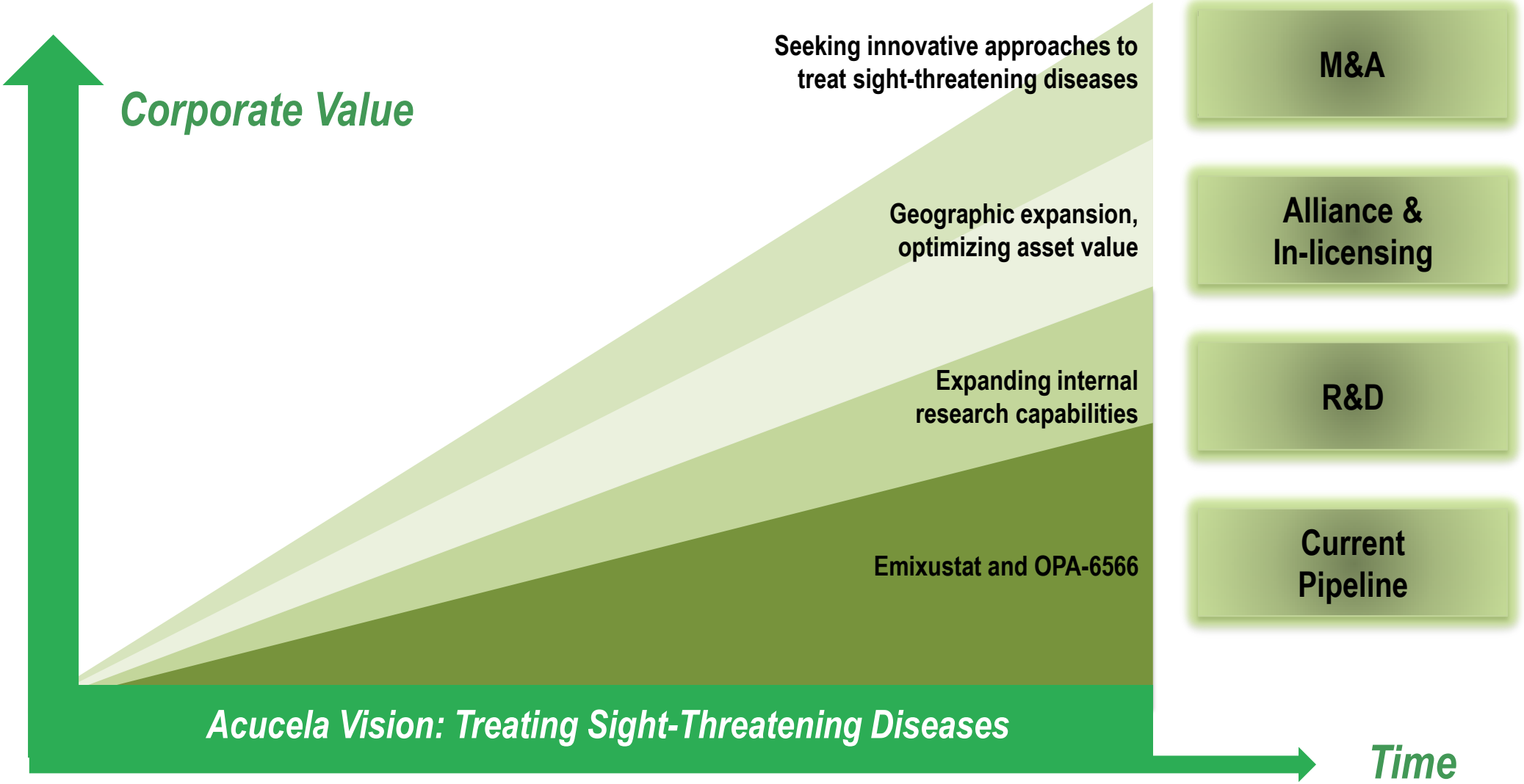
# Corporate Strategy

# Acucela's Four Strategic Initiatives



# Achievements in 1st Half of FY2015

## Continuous development in the current pipeline and increase in business development activities to expand the portfolio.

**Current Pipeline**

**Emixustat for GA associated with dry AMD**

- 50% of our enrolled patients have now completed the 24 months Ph2b/3 trial as of August 2015
- No safety issues have been reported as of today
- Approaching European regulatory bodies for possible expansion into the territory

**Emixustat for DR/DME**

- Evaluating the potential to develop emixustat for additional indications such as diabetic retinopathy (DR) or diabetic macular edema (DME)

**R&D**

- Hiring of new Executive VP of Translational Medicine
- Increase in budgeting for internal R&D resources to seek new indication for VCM
- Funding more internal research

**Alliance & In-licensing**

- Conducting multiple due diligence in the focusing on ophthalmology led by Ted Danse

**M&A**

- Expanding our business strategy to include broad range of business focused on ophthalmology

# Partnership with Otsuka Pharmaceutical

## Unchanged stable relationship with Otsuka Pharmaceutical

| Investigational Product Candidate | Potential Indication | License Territory | Financial Terms |
|---|---|---|---|
| Emixustat hydrochloride (developed by Acucela) | Dry AMD and other ophthalmic indications | Joint (50/50) - North America<br><br>Acucela - Europe, South and Central America and most of Africa<br><br>Otsuka – Asia-Pacific, some countries in Africa/Middle East | • Otsuka paid $5M cash upfront payment to Acucela<br>• Potential milestone payments: $258M total<br>• Currently Otsuka and Acucela are equally sharing all development expenses; Otsuka loans funds to Acucela for the payment of Acucela's share of the development expenses through to product launch |
| OPA-6566 (developed by Otsuka) | Glaucoma and other ophthalmic indications | United States | • Currently evaluating next steps for the program |

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# FY2015 Q2 Financial Summary

# Overview of FY2015 Q2: P/L

(US$ and JPY in thousands)

| | FY2014Q2 | FY2015Q2 | | FY2014Q2 | FY2015Q2 | Reasons for change |
|---|---|---|---|---|---|---|
| P/L Statement | USD | USD | | JPY | JPY | |
| **Revenues from collaboration** | 19,632 | 14,396 | | 2,403,938 | 1,762,790 | Due to fewer billable activities related to Exmixustat program in 2015 |
| **Expenses** | | | | | | |
| R&D | 14,471 | 11,509 | | 1,771,974 | 1,409,277 | |
| Emixustat | 13,943 | 10,753 | | 1,707,320 | 1,316,705 | Due to fewer billable activities related to emixustat in 2015 |
| In-licensed(1) | 22 | - | | 2,694 | - | |
| Internal research(2) | 506 | 756 | | 61,960 | 92,572 | Increase in R&D for VCM technology and new compounds |
| General and administrative | 4,842 | 17,050 | | 592,903 | 2,087,773 | |
| General and administrative | 4,842 | 8,004 | | 592,903 | 980,090 | Increased compliance and IR costs, and expanded management staff |
| May 1st Special Shareholder Meeting and management change | - | 9,046 | | - | 1,107,683 | Consisting of severance cost (cash and stock compensation) of USD6.4M, legal and consulting fees of 2.2M and others including retention costs and executive hiring costs |
| **Income (loss) from operations** | 319 | (14,163) | | 39,061 | (1,734,260) | |
| **Net income** | 125 | (13,678) | | 15,306 | (1,674,872) | |

(1) In-Licensed: includes Rebamipide (program under the terminated Rebamipide Agreement) and OPA-6566 (program under the Glaucoma Agreement)
(2) Internal Research: includes costs and expenses associated with our discovery research activities related primarily to our VCM compounds
Note: 1 USD = 122.45 as of June 30, 2015

# Overview of FY2015 Q2: Cash Flow

(US$ and JPY in thousands)

| | FY2014Q2 | FY2015Q2 | | FY2014Q2 | FY2015Q2 | Reasons for change |
|---|---|---|---|---|---|---|
| Cash flow Statement | USD | USD | | JPY | JPY | |
| **Cash flows from operating activities** | (1,827) | (10,589) | | (223,699) | (1,296,622) | Cash outflow was primarily the result of a net loss of $13.7 million (¥1.7 billion), and a decrease in deferred revenue from collaborations of $4.4 million (¥536.1 million). |
| **Cash flows from investing activities** | (126,849) | 717 | | (15,532,674) | 87,785 | Changes were primarily the result of net purchases of marketable securities. |
| **Cash flows from financing activities** | 147,661 | (1,099) | | 18,081,088 | (134,573) | Net cash used primarily for repurchase of restricted stock units for employee tax withholdings. |
| | | | | | | |
| **Cash, cash equivalents and short and long-term investments - end of period** | 177,282 | 174,508 | | 21,708,181 | 21,368,505 | |

- **Cash from operations and our existing cash and investment balances will be sufficient to fund our ongoing operating activities, working capital, capital expenditures and other capital requirements for at least the next 12 months**
- **Our future capital requirements will depend on many factors, including our rate of revenue growth, the expansion of our research and development activities, the timing and extent of our elections to co-promote product candidates under our collaboration agreements with Otsuka, and the timing of achievement of milestones under our collaboration agreements with Otsuka**

Note: 1 USD = 122.45 as of June 30, 2015

# Overview of FY2015 Q2: Balance Sheet

(US$ and JPY in thousands)

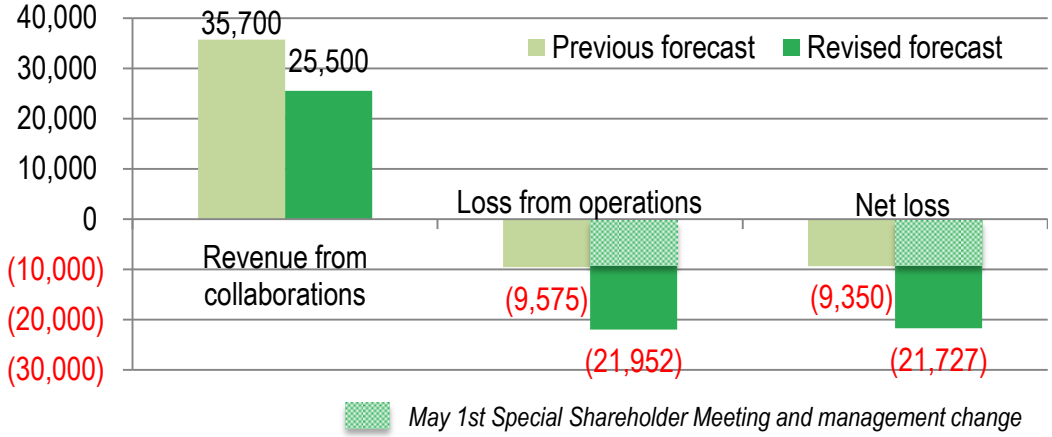
| | 12/31/2014 | 6/30/2015 | | 12/31/2014 | 6/30/2015 | Reasons for change |
|---|---|---|---|---|---|---|
| **Balance sheet statement** | USD | USD | | JPY | JPY | |
| **Current Assets** | 111,714 | 101,392 | | 13,679,378 | 12,415,439 | |
| Cash, cash equivalents and short-term investments | 103,786 | 92,690 | | 12,708,595 | 11,349,879 | |
| **Non-current Assets** | 85,252 | 83,146 | | 10,439,105 | 10,181,227 | |
| Long-term investments | 84,033 | 81,818 | | 10,289,840 | 10,018,614 | |
| **Total Assets** | 196,966 | 184,538 | | 24,118,483 | 22,596,666 | |
| **Current Liabilities** | 12,556 | 8,183 | | 1,537,478 | 1,001,977 | |
| **Long-term Liabilities** | 47 | 1,175 | | 5,755 | 143,879 | Deferred rent related to lease expansion |
| **Shareholders' Equity** | 184,363 | 175,180 | | 22,575,250 | 21,450,810 | |

Note: 1 USD = 122.45 as of June 30, 2015

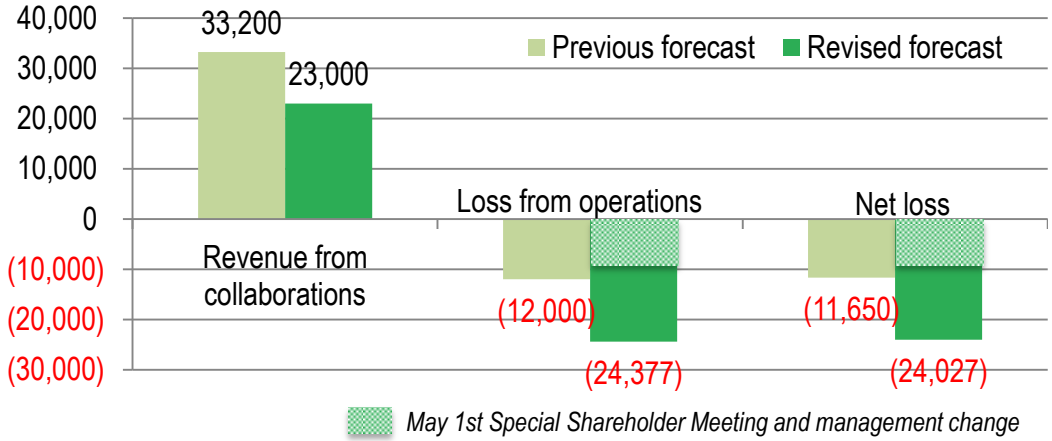
# FY2015 Revised Forecast

(US$ in thousands)

**FY 2015 - High Case Scenario**




**FY 2015 - Low Case Scenario**



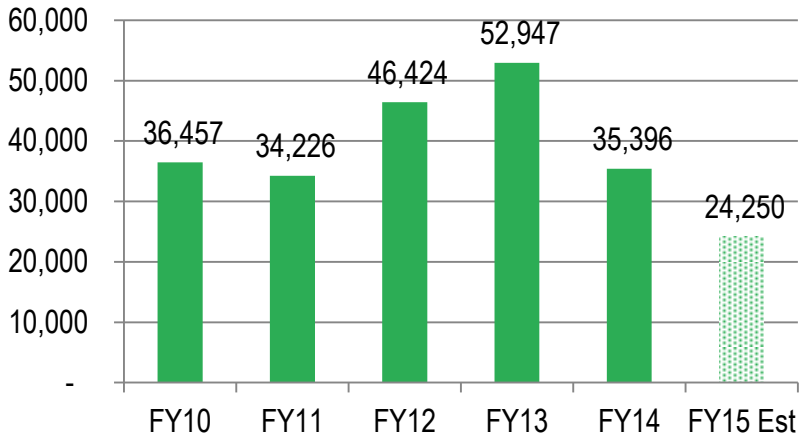

Note: 1 USD = 122.45 as of June 30, 2015

- **Revenue from collaborations**
  - Revisions are due to lower than expected reimbursable expenses.
- **Loss from operations**
  - Revisions are due to an increased allocation of company personnel to internal research, which is not reimbursed, and expenses associated with the May 1, 2015 Special Shareholders' meeting, related management change expenses consisting of legal and consulting fees, severance costs, and recruiting and retention costs.
- **Net loss**
  - Revisions are due to the same factors outlined in the operating loss

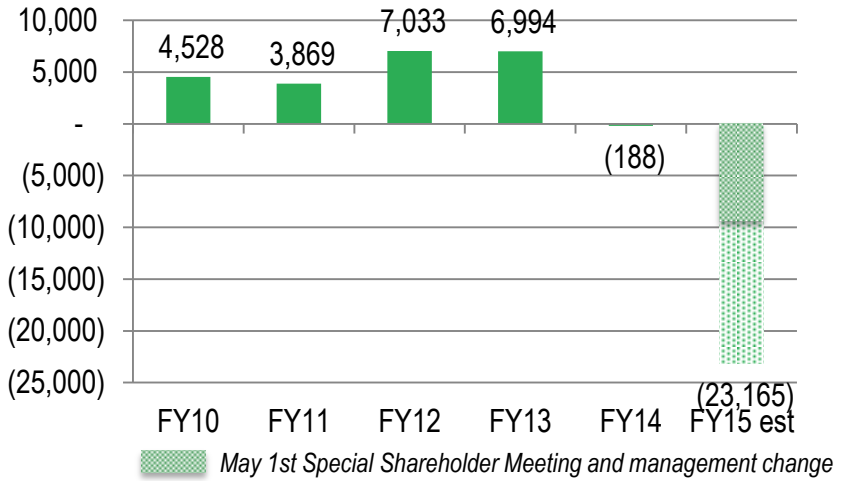
# Financial Overview

(US$ in thousands)

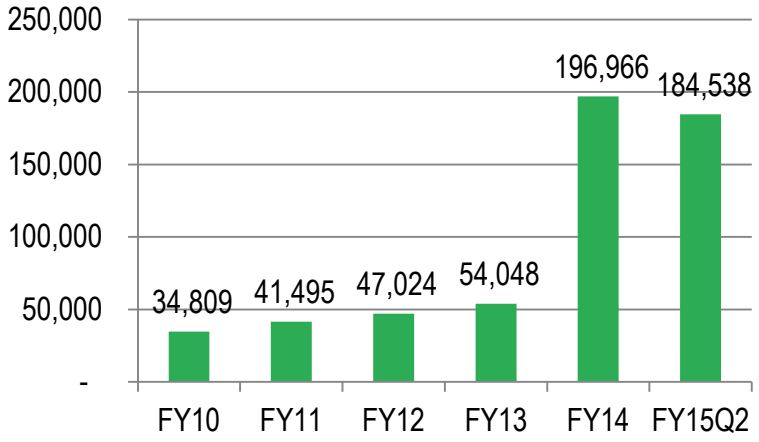
**Revenues from collaboration**



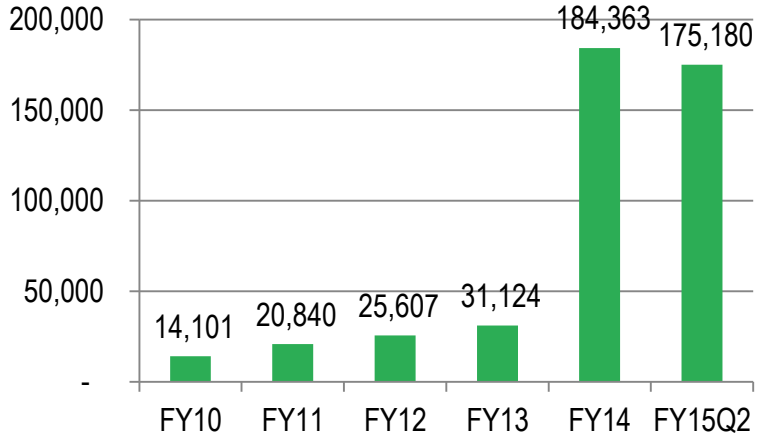

**Operating profit (loss)**




**Total assets**




**Total shareholders' equity**




Note: FY10 is unaudited figure, FY15 forecast indicates the average of the low and high range

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# IR Activities

# Recent IR Activities

| Date | IR Activities |
|---|---|
| May 13 | Acucela Announces Publication of Pre-clinical Data for Emixustat Hydrochloride (*PLOS ONE*) |
| May 20 | Analyst Meeting |
| Jun 3 | Acucela Announces Publication of Phase 2a Clinical Trial Results for Emixustat Hydrochloride (June online edition of *RETINA*) |
| Jun 11 | Renewal of English IR site |
| Jun 16 | IR movie: CEO Interview with Morning Star on New Management Team and Business Strategy |
| Jul 1 | Annual Shareholder Event<br>– 93% of the shareholders answered either to increase or hold Acucela shares[1] |
| Jul 2 | R&D meeting |
| Aug 26 | FY2015Q2 Analyst Meeting |
| Aug 28-29 | Nikkei IR Fair |

*Photos of the 2015 Annual Shareholder Event

[1] Total of 81 shareholders who have answered the questionnaire: 22 shareholders said they would increase the holdings and 55 said they will hold on to the shares

# Planned Investor Relations Activities for 2nd Half of FY2015

## Maximizing shareholder return is a core element of our business. We will continue to place further investor relations effort going forward.

- **Institutional Investor focused activities: increase holdings by mid to long term investors**
  - One-on-one meetings with institutional investors and analysts
  - Quarterly analyst meetings
  - Overseas investor meetings and non-deal roadshows (North America planned in October and Europe planned in November)
  - Presentation at Global Healthcare Conferences
- **Retail Investor focused activities: increase awareness and understanding and create loyal shareholders**
  - Retail investor IR site renewal
  - Retail investor events (e.g.2015 Nikkei IR Fair)
  - Retail investor conferences in Tokyo and local areas
  - Increase press coverage

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# Appendix

# Drug Development Path

## Emixustat for GA associated with dry AMD: Investigational compound based on Acucela's proprietary VCM

**2005**
- Toxicology
- Proof-of-concept in preclinical model
- Medicinal chemistry

**2007**

**2008**
- IND filed
- First human trial

**2009**
- Five phase 1 clinical trials completed
- One phase 2a clinical trial completed (GA subjects)
- 179 total subjects exposed to emixustat
- Fast track designation granted

**2012**
- Phase 2b/3 clinical trial commences
- Two-year treatment

**2013**
- Phase 2b/3 clinical trial enrollment completed in 508 subjects

**2014**

**2016**
- Phase 2b/3 clinical trial top line results expected

# Current Status and Upcoming Events in Relation to Emixustat

## Acucela will continue to focus on conducting its Phase 2b/3 “SEATTLE” study as originally planned

- **Current status of the “SEATTLE” study**
  - Completed enrollment in the phase 2b/3 “SEATTLE” study ahead of schedule
  - The study will be carried out through the original 24-month treatment
  - Depending on the results of the study, which are anticipated to be announced in mid-2016, Acucela will conduct at least one additional confirmatory phase 3 clinical trial in patients with GA associated with dry AMD
- **Anticipated disclosures and events related to the emixustat program**
  - Pre-clinical and phase 2a data publications in peer reviewed journals
  - Continue to build patent estate with important patents disclosures

# Acucela's Intellectual Property Position in VCM and Emixustat

## Acucela intends to aggressively protect and defend its intellectual property position in emixustat and VCM

| (June 30, 2015) | Emixustat related patents | | VCM related patents | | Other patents | Total patents |
|---|---|---|---|---|---|---|
| Region | *US* | *Non-US* | *US* | *Non-US* | | |
| Granted patents | 3 | 13 | 13 | 44 | 27 | 100 |
| Pending patents | 2 | 52 | 13 | 90 | 18 | 175 |
| Expiry year | 2029 | 2028-2033 | 2028-2034 | 2028-2034 | | |

- Strong patent portfolio is critical to our success
- Patents cover compositions of matter and methods of using the compositions

# Major press coverage (Japanese)

- **日経デジタルヘルス (Nikkei Digital Health)**
  起業家の条件、Acucela社の窪田氏が語る　（2015年8月12日掲載）
- **日刊工業新聞 (Nikkan Kogyo Newspaper)**
  創薬専業から脱皮　眼科領域で共同開発加速　（2015年7月9日掲載）
- **BSスカパー「Newsザップ！」(BS SkyPerfect TV)**
  加齢黄斑変性、世界で初めての失明を防ぐ飲み薬開発、米国で起業した理由をテーマにゲスト出演　（2015年6月1日放送）
- **日経バイオテク (Nikkei Bio-tech)**
  米Acucela社窪田氏、「企業買収や導入でパイプラインの拡充図る」　（2015年5月21日掲載）
- **週刊東洋経済・東洋経済Online　(Tokyo Keizai Magazine, Toky Keizai Online)**
  バイオのアキュセラが米国で起業したワケ　（2014年5月16日掲載）
- **朝日新聞 (Asahi Newspaper)**
  （あの人とこんな話）　成長には痛みが伴うが筋トレ同様、鍛えられる　（2014年4月15日掲載）
- **日経新聞 (Nikkei Newspaper)**
  「重い目の病に飲み薬」東証単独上場初の米企業に　（2014年3月25日掲載）
- **週刊ダイヤモンド (Diamond Magazine)**
  米国で起業しマザーズ上場　目のアルツハイマーを治す　（2014年2月24日掲載）
- **TBS「夢の扉+」ドキュメンタリー (TBS Documentary)**
  世界の1億2000万人を“失明の危機”から救え！　日本人トップイノベーターが挑む　“不治の病”の治療薬開発　(2013年10月27日放送)
- **ウォール・ストリート・ジャーナル (Wall Street Journal)**
  世界を変える日本人–シアトルで起業した窪田良氏が挑む難病治療薬（2013年3月29日掲載）
- **PRESIDENT Online (President Online)**
  ＜経営者の言葉：アキュセラCEO・窪田 良＞開眼！「朝令暮改」仕事術　（連載中）

***Please see the website for other press coverage: wwww.acucela.jp***

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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.