

## Acucela Announces Top-Line Results from Phase 2b/3 Clinical Trial of Emixustat

*S.E.A.T.T.L.E. study failed to demonstrate a reduction in GA lesion growth rate*

SEATTLE (May 25, 2016) — Acucela Inc. (Tokyo: 4589) (“Acucela”), a clinical-stage ophthalmology company that specializes in identifying and developing novel therapeutics to treat and slow the progression of sight-threatening ophthalmic diseases, announced today top-line results from the Phase 2b/3 clinical trial (S.E.A.T.T.L.E. study) of the investigational visual cycle modulator emixustat hydrochloride (emixustat).

The study enrolled 508 patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD). The study did not meet its primary endpoint with none of the treatment groups showing a significant difference in lesion growth rate from placebo. The lesion growth rates over 24 months for the 10mg, 5mg, 2.5mg and placebo groups were 1.84 mm<sup>2</sup>/year, 1.83 mm<sup>2</sup>/year, 1.69 mm<sup>2</sup>/year, 1.69 mm<sup>2</sup>/year, respectively<sup>1</sup>. There was no significant difference in the mean change of best corrected visual acuity from baseline to month 24 between treatment groups. There was a small numerical treatment difference observed in certain patients with specific genetic profiles in favor of emixustat.

“This is an unfortunate result for patients and physicians who hoped for a treatment for this debilitating disease. We hope to gain important information from this study to better understand this disease and its progression,” said Philip Rosenfeld, MD, Professor of Ophthalmology, Bascom Palmer Eye Institute, University of Miami.

An analysis of the two-year clinical data from the S.E.A.T.T.L.E study showed that adverse events were similar to those seen in earlier trials of emixustat. They include delayed dark adaptation and chromatopsia. There appeared to be no imbalance in serious adverse events between emixustat and the placebo group.

“We are carefully reviewing the data in geographic atrophy before we decide on our next steps with emixustat in this indication. We will continue to advance our in-licensed projects as well as our in-house research,” stated Ryo Kubota, MD, PhD, and Chairman, President and CEO of Acucela.

Further analysis of the clinical data from the S.E.A.T.T.L.E. study will be made in collaboration with Otsuka Pharmaceutical in the ensuing months. Acucela has an ongoing pilot study to explore the benefits of emixustat for the treatment of proliferative diabetic retinopathy. Acucela is also considering the initiation of a study to explore the potential benefits of emixustat in Stargardt Disease.

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<sup>1</sup> Intent-to-Treat data set.

## About Emixustat Hydrochloride

Emixustat hydrochloride (emixustat) is an orally administered small molecule that inhibits RPE65, an enzyme crucial to the visual cycle, the chemical pathway in the retina central to the initiation of visual perception. Emixustat is being developed by Acucela in collaboration with Otsuka Pharmaceutical Co., Ltd. (“Otsuka”). Acucela and Otsuka share commercial rights for emixustat in the USA. Otsuka has exclusive rights in Japan, Asia and other countries, while Acucela has exclusive rights in Europe and other countries.

## About The Safety and Efficacy Assessment Treatment Trials of Emixustat Hydrochloride (the S.E.A.T.T.L.E.) Study

The S.E.A.T.T.L.E study compared the efficacy and safety of emixustat to placebo for the treatment of geographic atrophy (GA) secondary to dry age-related macular degeneration (AMD). A total of 508 subjects were randomized to receive emixustat 2.5 mg, 5 mg, 10 mg, or placebo, administered orally once daily for up to 24 months. The primary efficacy endpoint was the mean rate of change from baseline in the total area of the GA lesion(s) in the study eye as imaged by fundus autofluorescence. Safety and tolerability were assessed on the basis of ocular and non-ocular adverse events, serious adverse events, ophthalmic examination findings, vital signs, physical examination findings, electrocardiogram findings, and laboratory analyses.

## About Geographic Atrophy Secondary to Age-related Macular Degeneration

Geographic atrophy (GA) is a severe and advanced form of age-related macular degeneration (AMD), affecting more than 9 million people worldwide (Market Scope, The Global Retinal Pharmaceuticals & Biologic Market, 2015). In GA, the center of the retina (the macula) responsible for high acuity and color vision becomes atrophic; the atrophic lesion grows over time, eventually leading to irreversible blindness. GA is typically present in both eyes and patients frequently report problems with every day activities such as reading and recognizing faces. GA represents a significant unmet medical need as there are currently no approved treatments for this condition.

## About Acucela Inc.

Acucela Inc. (<http://www.acucela.com/> or <http://www.acucela.jp>) is a clinical-stage ophthalmology company that specializes in identifying and developing novel therapeutics to treat and slow the progression of sight-threatening ophthalmic diseases affecting millions of people worldwide. Acucela’s lead investigational drug candidate, emixustat hydrochloride, is based on Acucela’s proprietary visual cycle modulation technology. Acucela’s pipeline includes additional drug candidates for the treatment of retinitis pigmentosa and cataracts.

## Cautionary Statements

This communication contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995, including statements regarding the Company’s future development plans for emixustat hydrochloride and the Company’s other product candidates and the potential efficacy and commercial potential of the

Company's and its collaborators' product candidates and the progress and potential of ongoing development programs. Such forward-looking statements typically can be identified by the use of words such as "expect," "estimate," "anticipate," "forecast," "intend," "project," "target," "plan," "believe" and similar terms and expressions. Forward-looking statements are based on current expectations and assumptions. Although the Company believes that its expectations and assumptions are reasonable, it can give no assurance that these expectations and assumptions will prove to have been correct, and actual results may vary materially. For example, (1) the Company may be adversely affected by other economic, business, and/or competitive factors; (2) the Company's investigational product candidates may not demonstrate the expected safety and efficacy; (3) the Company's pre-clinical development efforts may not yield additional product candidates; (4) any of the Company's or its collaborators' product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; and (5) new developments in the intensely competitive ophthalmic pharmaceutical market may require changes in the Company's clinical trial plans or limit the potential benefits of its investigational product candidates, as well as the other risks identified in the Company's filings with the Securities and Exchange Commission. The foregoing list of factors is not exhaustive. You should carefully consider the foregoing factors and the other risks and uncertainties that affect the business of the Company described in the "Risk Factors" section of its Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and other documents filed by the Company from time to time with the SEC. All forward-looking statements included in this document are based upon information available to the Company on the date hereof, and the Company does not assume any obligation to update or revise any such forward-looking statements.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, performance or events and circumstances reflected in those statements will be achieved or will occur, and actual results could differ materially from those anticipated or implied in the forward-looking statements. Except as required by law, we do not undertake any obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise. You should read the documents we have filed with the SEC for more complete information about the Company. These documents are available on both the EDGAR section of the SEC's website at [www.sec.gov](http://www.sec.gov) and the Investor Relations section of the Company's website at [ir.acucela.com](http://ir.acucela.com).

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