New Acucela Data on the Effect of Emixustat Hydrochloride on Retinal Thickness in Diabetic Retinopathy

SEATTLE (June 21, 2018) — Acucela Inc. (“Acucela”), a clinical-stage ophthalmology company and wholly-owned subsidiary of Kubota Pharmaceutical Holdings Co., Ltd. (Tokyo 4596), announced today new data on the effect of emixustat hydrochloride on retinal thickness in diabetic retinopathy (DR).

The study (Protocol 4429-203) is a randomized, placebo-controlled, phase 2 clinical trial exploring the effect of oral emixustat hydrochloride in a proliferative diabetic retinopathy (PDR) population with and without macular edema. Twenty-four subjects were enrolled in the study, in which subjects in the emixustat group were titrated to their maximum tolerated dose of up to 40 mg per day. Beyond the initial assessment of the primary endpoint, a key secondary objective was to evaluate the effects of emixustat on the change in central subfield (retinal) thickness as assessed by spectral domain optical coherence tomography (SD-OCT) from baseline to Day 85.

The study results indicate that the emixustat group experienced a reduction in central subfield thickness when compared to placebo at a statistical significant level (difference in means of 48.1 microns favoring emixustat, p=0.0764; statistical significance pre-specified at p<0.1). Additionally, the emixustat group experienced a reduction in total macular volume in the study eye compared to placebo that also met statistical significance (difference in means of 0.361 mm³ favoring emixustat, p=0.0263). Both pre-specified analyses included nine patients in the emixustat group and eleven patients in the placebo group.

These results illustrate the potential for emixustat to decrease retinal thickness in patients with DR. From these phase 2 findings, Acucela is preparing to advance the clinical program and is actively discussing research partnerships prior to the planned regulatory approval studies.

Dr. Ryo Kubota, MD, PhD, Chairman, President and CEO of Acucela stated, “We are thrilled to see these results for emixustat in the diabetic retinopathy population and are excited to advance the program. This proof of concept is exciting as it not only addresses an important unmet need but does so through oral administration, a first for the industry. We are now focused on securing the right strategic partner as we finalize our plans to advance our clinical program”

About Diabetic Retinopathy and Diabetic Macular Edema

Nearly 415 million people in the world have diabetes¹, a chronic condition that affects the function of insulin, a hormone that regulates blood sugar. Diabetics are at an increased risk of developing serious eye conditions, including diabetic retinopathy (DR). DR is a very common complication of diabetes and a leading cause of vision loss in adults. Loss of vision from DR is often characterized by blurred central vision with some dark patches. DR is a progressive condition in which there is damage to the tiny blood vessels, or capillaries, of the retina; this vascular damage results in a chronic decrease in oxygen supply to retinal cells.
DR is a progressive condition that can be broadly classified into: non-proliferative and proliferative diabetic retinopathy (PDR), depending on the progression of the disease. Diabetic macular edema (DME) is a manifestation of non-proliferative diabetic retinopathy and can develop at any stage of diabetic retinopathy. DME is caused by leaky blood vessels in the retina that result in blurred vision, loss of contrast, and overall vision loss, and is the most common cause of vision loss in diabetic patients. PDR occurs when chronic retinal hypoxia causes proliferation of new, fragile vessels that tend to leak fluid and blood. This is the most advanced stage of diabetic eye disease and can result in permanent vision loss. PDR affects over 19 million people worldwide today, and this number is expected to grow to almost 22 million by 2020\(^\text{(2)}\).

The most important risk factors for DR are increased blood sugar levels, raised blood pressure, and longer duration of diabetes. All people with Type 1 or Type 2 diabetes are at risk for DR and DME. The risk of developing DR or DME increases significantly the longer a person has diabetes. The American Academy of Ophthalmology estimates that nearly 80% of patients with Type 1 diabetes will have developed DR after living with diabetes for 15 years. Early treatment of DR or DME can slow the progression of the disease, but there are currently no treatments that can reverse advanced vision loss.


About Acucela Inc.

Acucela Inc. is a wholly-owned subsidiary of Kubota Pharmaceutical Holdings Co., Ltd. (Tokyo 4596) committed to translating innovation into a diverse portfolio of drugs and devices to preserve and restore vision for millions of people worldwide. Acucela’s development pipeline include drug candidates for the treatment of diabetic retinopathy, diabetic macular edema, Stargardt disease, age-related macular degeneration, cataracts and presbyopia, and, optogenetics-based gene therapy for the treatment of retinitis pigmentosa. The company is also developing a handheld OCT device for the monitoring of neovascular retinal diseases, to be used directly by patients. http://www.acucela.com;  http://www.kubotaholdings.co.jp/en/

Cautionary Statements

Certain statements contained in this press release are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include statements regarding our expectations related to our development plans and ability to
successfully develop and commercialize our product candidates and the potential efficacy, future development plans and commercial potential of our product candidates. These statements are based on current assumptions that involve risks, uncertainties and other factors that could cause the actual results, events or developments to differ materially from those expressed or implied by such forward-looking statements. These risks and uncertainties, many of which are beyond our control, include, but are not limited to: our investigational product candidates may not demonstrate the expected safety and efficacy; our pre-clinical development efforts may not yield additional product candidates; any of our or our 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; our clinical trials could be delayed; new developments in the intensely competitive ophthalmic pharmaceutical market may require changes in our clinical trial plans or limit the potential benefits of our investigational product candidates; the impact of expanded product development and clinical activities on operating expenses; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in our filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and we assume no obligation to update these forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements. For a detailed discussion of the foregoing risks and other risk factors, please refer to our filings with the Securities and Exchange Commission, which are available on Kubota Pharmaceutical Holdings (Acucela’s parent company) investor relations website (http://www.kubotaholdings.co.jp/en/ir/) and on the SEC’s website (http://www.sec.gov).

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