ACUCELA

Press Release

Acucela Results to be Presented at ARVO 2019 Annual Meeting in Vancouver, BC

Dr. Chirag Jhaveri will present "Positive Diabetic Retinopathy Outcomes with Emixustat in a Pilot Study"

SEATTLE (April 17, 2019) — Acucela Inc. ("Acucela"), a clinical-stage ophthalmology company and wholly-owned subsidiary of Kubota Pharmaceutical Holdings Co., Ltd. (Tokyo 4596), announced today that Dr. Chirag Jhaveri, Clinical Assistant Professor of Ophthalmology at the Dell Medical School, the University of Texas at Austin, will present Acucela clinical trial results at The Association for Research in Vision and Ophthalmology (ARVO) 2019 Annual Meeting being held April 28 – May 2, 2019 in Vancouver, BC.

ARVO is the largest and most respected eye and vision research organization in the world. Their members include nearly 12,000 researchers from over 75 countries. Dr. Jhaveri will present "Positive Diabetic Retinopathy Outcomes with Emixustat in a Pilot Study" at the Vancouver Convention Centre.

Acucela conducted a phase 2 clinical trial exploring the effect of oral emixustat in a proliferative diabetic retinopathy (DR) population with and without macular edema. The 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 to investigate the effects of emixustat in DR. The presentation will cover the findings from the phase 2 study.

"We are pleased to see the positive outcomes for the phase 2 study of emixustat in proliferative DR and thrilled to have the opportunity to present the results at the ARVO Annual Meeting 2019," stated Dr. Ryo Kubota, MD, PhD, and Chairman, President and CEO of Acucela.

About Diabetic Retinopathy and Diabetic Macular Edema

Nearly 415 million people in the world have diabetes[(1)], 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[(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.

(1) IDF Diabetes Atlas. 7th ed. Brussels: International Diabetes Federation; 2015.
(2) Market Scope, The Global Retinal Pharmaceuticals & Biologic Market, 2015.

About Emixustat Hydrochloride

The visual cycle is the process by which vitamin A is recycled in the eye; vitamin A is crucial to the visual process. Emixustat modulates the visual cycle by inhibiting a critical enzyme of this pathway, retinal pigment epithelium protein 65 (RPE65). Slowing the visual cycle reduces the availability of vitamin A derivatives (11-cis-retinal) to bind opsin, a protein responsible for the initiation of visual signaling. Increased levels of unbound opsin decrease retinal metabolism and oxygen consumption, reducing retinal hypoxia, a significant pathogenic factor in DR progression. In animal models, emixustat was found to reduce retinal metabolism and hypoxia and reduce hypoxia-driven retinal neovascularization. Emixustat when delivered orally was found to be generally well tolerated in human clinical studies with delayed dark adaptation being the most common ocular adverse event.

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).

Media and Investor Relations Contact :

Hiroki Maekawa
Chief Financial Officer
Phone: +81-3-6550-8928
Email: hmaekawa@acucela.com

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