ACUCELA

Press Release

Acucela Receives Orphan Designation from the EMA for Emixustat for the Treatment of Stargardt Disease

SEATTLE (June 9, 2019) — Acucela Inc. ("Acucela"), a clinical-stage ophthalmology company and wholly-owned subsidiary of Kubota Pharmaceutical Holdings Co., Ltd. (Tokyo 4596), announced today that the European Medicines Agency (EMA) granted orphan designation to Acucela's leading drug candidate emixustat hydrochloride ("emixustat") for the treatment of Stargardt disease. The orphan designation does not apply to other indications for which emixustat is being developed.

To receive an orphan designation from the EMA, the medicine has to be developed for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition that affects no more than five in 10,000 within the European Union. Upon receiving the orphan designation, the sponsor will qualify for multiple development incentives which include ten years of market exclusivity after product approval, fee reductions of regulatory activities, access to the centralized marketing authorization procedure, and protocol assistance that provides scientific advice for the orphan designated medicines.

In January 2017, Acucela also received orphan drug designation for emixustat for the treatment of Stargardt disease by FDA (U.S. Food and Drug Administration). According to the FDA's Center for Drug Evaluation and Research's annual report, the number of approved orphan drugs has been increasing year by year, and 58% of the drugs approved by the FDA in 2018 were orphan drugs. Many of them are expected to have peak sales of over US$1 billion.

About Stargardt Disease

Stargardt disease is a rare, genetically inherited disease that directly affects the retina of the eye, often resulting in the slow progression of vision loss in children. It may also be referred to as Stargardt macular dystrophy or juvenile macular degeneration and affects approximately 1 in 8,000 - 10,000 individuals worldwide[(1)]. The most common form of the disease is caused by a genetic mutation of the ABCA4 gene leading to the accumulation of toxic vitamin A byproducts (primarily A2E) in the retina, which results in the gradual deterioration of photoreceptors and vision. Symptoms of Stargardt disease typically appear during childhood or adolescence, but in some cases difficulty with eyesight and vision loss may not be identified until later in life.

Stargardt disease affects less than 150,000 patients in total in U.S., Europe and Japan where it is recognized as an orphan disease. Currently, there are no known therapies that exist to slow the advance of the disease, and it is recognized as a serious unmet medical need.

[(1)] Facts About Stargardt Disease, National Eye Institute. https://nei.nih.gov/health/stargardt/star_facts, accessed on 14 September 2018.

About Emixustat Hydrochloride

Emixustat modulates the visual cycle by inhibiting a critical enzyme of this pathway, retinal pigment epithelium protein 65 (RPE65). The visual cycle is the process by which vitamin A is recycled in the eye; vitamin A is crucial to the visual process. Slowing the visual cycle reduces the availability of vitamin A derivatives (11-cis- and all-trans-retinal) to form precursors of A2E and related compounds. In animal models of Stargardt disease and retinal degeneration, emixustat was found to stop and reverse the accumulation of A2E and to preserve the integrity of the retina. 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. Acucela is planning to explore emixustat's potential to stop or slow the progression of vision loss in patients diagnosed with Stargardt disease in ongoing and future clinical studies.

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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