September 4th, 2024

To Whom It May Concern,

Announcement of First Transplantation in the Domestic Phase II Clinical Trial of the AE101 Regenerative Medicine Cell Product

We are pleased to inform you that the first patient in our domestic Phase II clinical trial of AE101, a regenerative medicine cell product under development by ActualEyes Inc., has successfully received the transplantation. AE101 is designed for the treatment of bullous keratopathy (see Note 1). We are also pleased to report that the necessary safety evaluations have been completed, allowing for the continuation of the trial with subsequent patients.

This study aims to investigate the safety and efficacy of AE101 transplantation in patients with bullous keratopathy. The first transplantation was performed in July 2024, and the patient's post-transplant progress has been favorable. Following a safety review by the independent Efficacy and Safety Evaluation Committee, the trial was approved to proceed with further patient recruitment and treatment.

Please see below for a summary of this clinical trial. We look forward to continuing the evaluation of AE101 and further advancing this promising treatment for bullous keratopathy.

Summary of the phase II clinical trial

Study design	Multicenter, open-label, uncontrolled trial.
Target number of cases	6
Evaluation and observation period	48 weeks after the implantation of the investigational product
Primary endpoint	The number and incidence of adverse events, including those with a non-negligible causal relationship to the investigational product (%)
Secondary endpoints	1. Safety evaluation 1) Observation and evaluation of safety endpoints 2) Number and incidence of serious adverse events (%) 2. Evaluation of effectiveness 1) Improvement in visual acuity at 24 weeks post-implantation of the investigational product. 2) Changes in best-corrected visual acuity over time. 3) Changes in central corneal thickness over time. 4) Changes in corneal endothelial cell density over time.

AE101 is a cryopreserved formulation of cultured human corneal endothelial cells, where human corneal endothelial cells are expanded in vitro and suspended in a cryoprotectant solution containing a Rho kinase inhibitor. The product is injected into the anterior chamber of the eye to promote regeneration of the corneal endothelium.

To expedite the availability of AE101 as a treatment for patients, ActualEyes Inc. will continue to advance this clinical trial, focusing on confirming both its efficacy and safety. D-Western Therapeutics Laboratories Co., Ltd. (see Note 2) is collaborating with us in the development of AE101. Additionally, the production of AE101 for this trial is being outsourced to Japan Tissue Engineering Co., Ltd. (see Note 3), a company with extensive experience in the development, manufacturing, and commercialization of regenerative medicine products.

Terminology
*1 Bullous keratopathy
A condition in which the corneal endothelial cells are damaged, leading to corneal edema, whitening, and cloudiness, resulting in significant vision loss. Causes include Fuchs endothelial corneal dystrophy, cataract surgery, glaucoma, and other ocular surgeries that damage the corneal endothelial cells. The current treatment is corneal transplant surgery using donor corneas.

*2 D-Western Therapeutics Institute, Inc.
For details, please refer to the following website.
De Western Therapeutics Institute (dwti.co.jp)

*3 Japan Tissue Engineering Co., Ltd.
For details, please refer to the following website.
Japan Tissue Engineering Co., Ltd. (jpte.co.jp)