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**Execution of Letter of Intent Agreement for Joint Research with the Retina Institute Japan,
K.K.**

Research Development in Transplantation of Retinal Pigment Epithelial Cell,
Derived from Induced Pluripotent Stem Cell,

Shin Nippon Biomedical Laboratories, Ltd. (“SNBL”) today announces the execution of Letter of Intent Agreement on Joint Research with Retina Institute Japan, K.K (“RIJ”) for the development and non-clinical research of transplantation of retinal pigment epithelial (“RPE”) cellsⁱ, derived from induced pluripotent stem (“iPS”) cellsⁱⁱ, for age-related macular degenerationⁱⁱⁱ.

RIJ aim to develop new treatments for age-related macular degeneration by iPS cell derived RPE cell transplantation.

Rodents are a common model in non-clinical research on regenerative medicine of the retina, however, they are not a suitable model to establish the transplantation method of RPE cells due to lack of macula retinae, which is the affected region in age-related macular degeneration, and are also smaller in stature, limiting possibilities of transplantation methods and evaluation.

With this Letter of Intent Agreement, RIJ seeks for opportunities to improve upon current methods of allotransplantation by utilizing transplantation of iPS cell derived RPE cells with non human primates, which possess very similar macular system as humans, with goals of enabling higher survival rate, more stable transplantation method, and reducing of the risk of rejection response. On the basis of extensive experience and expertise in non-clinical researches^{iv} with non-human primates, SNBL will promote this joint research and will fully support RIJ toward successful clinical application of RPE cell transplantation.

At the present time, the effect of this matter on the earnings of SNBL’s current term is minimal.

ⁱ Retinal pigment epithelial cells (RPE cells)

Retinal pigment epithelial cells are single cell layer outside of retina, composed of brown pigments and hexagonal cells, and thus are easily distinguished from other cells. Main functions of RPE cell consist of blood-retinal barrier, phagocytic capacity, and secretion of neurotrophic factors. RPE cell's phagocytic capacity engulfs waste products from adjacent photoreceptor cells. When RPE cell's function of phagocytic capacity goes down, photoreceptor cells are impaired, leading to deterioration of vision. In addition, RPE cells have a function to protect the retina by secreting PEDF and VEGF neurotrophic factors and also to barrier unnecessary blood constituents from entering.

ⁱⁱ Induced pluripotent stem cells (iPS cells)

Induced pluripotent stem cells are established by introducing a small number of genes into ordinary human somatic cells, and these cells can differentiate into any type of cell in the body and proliferate almost indefinitely in culture. iPS cells can be applied for etiological investigation of diseases, development of new drugs, and regenerative treatment such as transplantation.

ⁱⁱⁱ Age-related macular degeneration

Age-related macular degeneration, which is one of the retinal degenerative diseases, is a medical condition that results in a loss of vision in the center of the visual field, due to damage of the retina. Age-related macular degeneration is the leading cause of blindness for adults in Europe and the United States. Cases of age-related macular degeneration have significantly increased during recent years in Japan, due to aging society and altered dietary habits. There are two types of Age-related macular degeneration; "wet (neovascular)" and "dry (non-neovascular)". The wet age-related macular degeneration, which is found more frequently in Japan of the two, is characterized by vascularizing under the RPE. The new vessels under RPE in wet age-related macular degeneration are very delicate and ruptures easily, causing bleeding and damage to surrounding tissue, which results in deterioration of vision. The dry age-related macular degeneration which is found frequently in Europe and the United States is characterized by damaging and atrophying retinal tissue.

^{iv} Non clinical studies

Non clinical studies are conducted to investigate efficacy or side effects of new drugs or remedies using cultured cells or experimental animals, in order to assure safety for subsequent clinical trials.