

Company Name: HEALIOS K.K.  
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## **License Agreement with Astellas Pharma Concerning RPE Cell Production Method**

HEALIOS K.K. (“Healios”) today announces that it has entered into a License Agreement with Astellas Institute for Regenerative Medicine (“AIRM”, Location: Westborough, MA; President: Erin Kimbrel, PhD), a subsidiary of Astellas Pharma Inc. (Head Office: Chuo-ku, Tokyo; President and CEO: Naoki Okamura), that investigates novel pluripotent stem cell-derived therapeutic products, concerning the patent on a Retinal Pigment Epithelial (RPE) cells\*<sup>1</sup> production method shared with RIKEN, National Research and Development Agency in Japan, and Osaka University, National University Corporation in Japan, and the patent on a method for purification of RPE cells shared with Osaka University (“Patents”)\*<sup>2</sup>. Healios grants AIRM a non-exclusive license in the countries where the patents are filed outside of Japan.

### **1. Outline of License Agreements**

Healios hereby grants AIRM a non-exclusive right to use the Patents in the countries where the Patents are applied for worldwide except Japan, for AIRM's use in the development, manufacture, and marketing of therapies using pluripotent stem cell-derived RPE cells. Healios will receive an upfront payment of US\$3,000,000 upon execution of this agreement. In addition, Healios may subsequently receive up to US\$8,000,000 in milestone payments from AIRM upon U.S. approval of products developed and manufactured using these patents.

Healios is researching new treatment methods to cure and bring hope to people suffering from intractable diseases with our stem cell technology. By not only conducting our own research and development, but also by providing our iPSC platform technology, experience, and intellectual property to other pharmaceutical companies, Healios will pave the way for the realization of new therapeutic methods and strive to realize our mission through the development of the pharmaceutical industry as a whole.

### **2. Future Outlook**

Upon execution of this License Agreement, Healios expects to recognize an upfront payment of US\$3,000,000 as sales revenue in the second quarter of the fiscal year ending December 31, 2024. We will promptly announce any matters that should be disclosed in the future.

#### **\*1 Retinal Pigment Epithelial (RPE) cells**

RPE cells form the retinal pigment epithelium outside the neural retinal layer. RPE cells come into contact with photoreceptors, and exert physiological functions to maintain and protect the functions of the photoreceptors. Since RPE cells with a single-layer structure do not regenerate, visual functions will be permanently impaired if they are damaged. Therefore, RPE cells have recently attracted attention in the research of regenerative medicine for compensating for a loss or dysfunction due to age-related macular degeneration.

\*2 Patent on a RPE cells production method and Patent on a method for purification of RPE cells

- production method

WO2015053375A1 owned by Osaka University, Healios and RIKEN

The present invention provides a method for purification of retinal pigment epithelial cells that can be obtained in short time by a simple procedure, from a cell group obtained through differentiation induction to retinal pigment epithelial cells from pluripotent stem cells. This purification method includes a step in which a cell group that contains retinal pigment epithelial cells obtained through differentiation induction of pluripotent stem cells on laminin fragments thereof is introduced into a filter, and the cell group that has passed through the filter is obtained.

- method for purification

WO2015053376 owned by Osaka University and Healios

The present invention provides a method for purification of retinal pigment epithelial cells, with which high-purity retinal pigment epithelial cells can be obtained in short time by a simple procedure, from a cell group obtained through differentiation induction to retinal pigment epithelial cells from pluripotent stem cells.

#### **About Astellas:**

Astellas Pharma Inc. is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into VALUE for patients. For more information, please visit our website at <https://www.astellas.com/en/>. For the information about Astellas Institute for Regenerative Medicine, please visit <https://www.astellas.com/en/innovation/astellas-institute-for-regenerative-medicine>.

#### **About Healios:**

HEALIOS K.K. is Japan's leading clinical stage biotechnology company harnessing the potential of stem cells for regenerative medicine. It aims to offer new therapies for patients suffering from diseases without effective treatment options. Healios is a pioneer in the development of regenerative medicines in Japan and owns proprietary, global platforms utilizing both somatic stem cells and iPS cells.

In the somatic stem cell field, Healios is developing MultiStem (HLCM051), a proprietary cell product comprised of multipotent adult progenitor cells ("MAPCs") derived from the bone marrow of healthy adult donors. MultiStem has been shown to exhibit powerful anti-inflammatory and immunomodulatory properties with applicability in a range of disease states, has been tested in hundreds of patients in late stage clinical trials, is manufactured consistently at scale in 3D bioreactors, and has demonstrated both safety and suggested efficacy in hundreds of patients across multiple indications. Healios is seeking to advance MultiStem on a global basis for ischemic stroke, ARDS, and trauma.

In the iPSC regenerative medicine field, Healios' lead candidate, HLCN061, is a next generation NK cell treatment for solid tumors that has been functionally enhanced through gene-editing. These cells have demonstrated robust anti-tumor efficacy in animal models, benefit from a scalable 3D bioreactor manufacturing process, and are currently being prepared for initial human testing. The company has also established a proprietary, gene-edited "universal donor" induced pluripotent stem cell line to develop next generation regenerative treatments in immuno-oncology, ophthalmology, liver diseases, and other areas of severe unmet medical need.

Healios was established in 2011 and has been listed on the Tokyo Stock Exchange since 2015 (TSE Growth: 4593). <https://www.healios.co.jp/en>