

April 1st, 2022

Company Name: HEALIOS K.K.
Representative: Hardy TS Kagimoto,
Chairman & CEO
(TSE Mothers Code: 4593)

Joint Research with the Division of Regenerative Medicine, the Institute of Medical Science for Developing a Mass Production Method of UDC Liver Buds

HEALIOS K.K. (“Healios”) is currently developing a regenerative medicine treatment whereby liver organ buds created from iPS cells are injected into the liver and grown into functioning liver tissue, with the aim of improving or restoring the function of a damaged liver (development code: HLCL041). This treatment could potentially replace the need for an organ transplant for certain patients. Liver buds are created by co-culturing liver progenitor cells, which can differentiate into hepatocytes; MSCs, which have the ability to develop into various types of connective-tissues; and vascular endothelial cells, which form blood vessels. Healios has pursued research and generated data on functional assessments and quality standards for these component cells and the liver buds created from them, and it is also proceeding with the development of mass culturing and manufacturing methods.

In addition, [as announced on October 20th, 2020](#), Healios established Universal Donor Cells (“UDCs”)*, which are next-generation iPS cells created with gene-editing technology that have a reduced risk of immune rejection regardless of a patient’s HLA type, and its proprietary clinical-grade UDC line. We are currently conducting research both internally and through joint collaborations with several institutions on new treatments for diseases for which there is no existing cure.

As part of these efforts, Healios is pleased to announce that it has entered into a joint research agreement with the Division of Regenerative Medicine (Prof. Hideki Taniguchi) of the Institute of Medical Science at the University of Tokyo, to advance HLCL041 utilizing UDCs. In this joint research, we plan to establish a new method for inducing differentiation of liver buds using UDCs and to develop a highly efficient and scalable cell culturing and mass manufacturing system.

For many diseases where the only effective treatment is an organ transplant, Healios believes that organ buds created from iPSCs, which have the potential to restore organ function, hold significant promise as an alternative to organ transplants and as a means to address the perennial shortage of organ donors.

This agreement does not have a material impact on our consolidated financial results for the current fiscal year. We will promptly make an announcement on any matter that requires disclosure in the future.

■ Outline of the Collaboration Partner

- Name of the Collaborator: Division of Regenerative Medicine, The Institute of Medical Science
- Address: 4-6-1 Shirokanedai Minato-ku, Tokyo, 108-8639, Japan
- Representative: Professor Taniguchi Hideki

* UDCs

UDCs are iPS cells created using gene-editing technology that allows them to avoid and / or reduce the body's immune rejection response. The production of Healios' UDCs involve the removal of certain HLA genes that elicit a rejection response, the introduction of an immunosuppression gene to improve immune evasion, and the addition of a suicide gene serving as a safety mechanism, each in an allogeneic iPS cell. This next-generation technology platform allows for the creation of regenerative medicine products with enhanced safety and a lower risk of immune rejection, while preserving the inherent ability of iPS cells to replicate themselves continuously and their pluripotency in differentiating into various other kinds of cells.

About the Division of Regenerative Medicine, The Institute of Medical Science:

Regenerative medicine is a challenging scientific field that is going to convert the pioneering knowledge of developmental biology and stem cell biology to clinical application. For patients with end-stage organ failure, organ transplantation is the only effective treatment; however, the paucity of transplantable organs hinders the application of this treatment for most patients. Recently, regenerative medicine with transplantable organs has attracted attention. Our laboratory is developing a novel therapeutic strategy to substitute organ transplantation. We have established novel organoid culture technologies to reconstruct human organs from stem cells, including human induced pluripotent stem cells (iPSCs), and we are going to realize transplantation of human liver primordia (liver buds [LBs]) generated from iPSCs for the treatment of liver diseases. <https://stemcell-imsut.org/laboratory/?id=en#labo1>

About Healios:

Healios 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, where it has established a proprietary, gene-edited "universal donor" induced pluripotent stem cell (iPSC) line to develop next generation regenerative treatments in immuno-oncology, ophthalmology, liver diseases, and other areas of severe unmet medical need. Healios' lead iPSC-derived cell therapy candidate, HLCN061, is a next generation NK cell treatment for solid tumors that has been functionally enhanced through gene-editing. Its near-term pipeline includes the somatic stem cell product HLCM051, which is currently being evaluated in Japan in Phase 2/3 and Phase 2 trials in ischemic stroke and acute respiratory distress syndrome (ARDS), respectively. Healios was established in 2011 and has been listed on the Tokyo Stock Exchange since 2015 (TSE Mothers: 4593). <https://www.healios.co.jp/en> .

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