

June 3, 2022

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

Healios' eNK Cells: Joint Research with Hyogo Medical University for Mesothelioma

HEALIOS K.K. (“Healios”) is developing next-generation cancer immunotherapies for solid tumors using NK cells*¹ derived from allogeneic iPSCs (Development Code: HLCN061 “eNK cells”) whose specific functions have been enhanced with gene editing technology.

Healios is pleased to announce that it has entered into a joint research agreement with the Hyogo Medical University (Located: Nishinomiya City, Hyogo Prefecture), on cancer immunotherapies for mesothelioma*² using eNK cells. In this joint research, we plan to evaluate the anti-tumor effect of eNK cells on mesothelioma *in vitro* and *in vivo* using human mesothelioma cells. The Mesothelioma Center which provides treatment for all thoracic malignancies, including mesothelioma and other asbestos-related diseases, has been established at the affiliated Hyogo Medical University Hospital. Its center is one of the best in Japan in terms of the number of patients treated for malignant pleural mesothelioma and has vast knowledge and experience in the treatment and research of mesothelioma. Mesothelioma is a rare cancer that has high unmet medical needs. We will evaluate the antitumor effects of eNK cells on mesothelioma and will continue to research and develop effective treatments.

Healios has succeeded in developing eNK cells through its own research and has confirmed that eNK cells have anti-tumor effects in mice engrafted with human lung cancer cells and human liver cancer cells. Furthermore, we have established a three-dimensional culture method (three-dimensional perfusion bioreactor system) that enables efficient and stable mass production of eNK cells for the manufacture of investigational products. Healios is planning to start full operations of its Cell Processing Center (CPC), which is based on these technologies, in mid-2022, and further advance preparations for eNK clinical trials.

Even though the advent of molecular targeted drugs and cancer immunotherapy has improved treatment outcomes for some cancer patients, the efficacy of existing treatments for solid tumors remains poor. Healios is committed to its continued research and development of effective treatments for solid cancer patients.

This action has no impact on our company’s consolidated financial results. We will promptly make the necessary announcements if any matter requiring disclosure arises in the future.

***1 Natural killer (NK) cells**

Natural killer (NK) cells are a subset of lymphocytes, a type of white blood cell. NK cells play a central role in a cell mediated defense system that human bodies naturally have, and attack cancer cells and virus-infected cells. The expected efficacy of treatments using NK cells includes life-extension, promotion of healing, relief of symptoms, and improvement of quality of life.

***2 Mesothelioma**

The lungs and abdominal organs are covered by membranes called the pleura, pericardium, and peritoneum. Malignant pleural mesothelioma is a malignant tumor that occurs on the pleura and is known to be caused by asbestos.

About Hyogo Medical University:

Since its founding in 1972, the Hyogo Medical University has been committed to student education, medical research, and the development of advanced medical care. In recent years, the University has been named as one of the top schools in terms of passing the national medical examination for doctors, and its graduates are active in Japan and abroad as good doctors who are responsible for holistic medical care. In April 2022, it was restructured as a medical university with four faculties, including the School of Medicine, by newly establishing the School of Pharmacy, the School of Rehabilitation Science, and the School of Nursing.

In the area of research, we launched the Center for Industry-Government-Academia Collaboration and Research Promotion Division as a centralized organization involved in research following the integration of universities. By actively promoting industry-government-academia collaboration, we aim to contribute to society by contributing to medical care, industry, and welfare by leveraging our research and clinical strengths centered on our headquarters.

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 Growth: 4593). <https://www.healios.co.jp/en>

About Healios' eNK cells:

Healios eNK cells are a gene edited iPSC-NK cell therapy with several functional enhancements achieved through gene-editing including enhanced cytotoxicity towards

cancer, improved capability to migrate and infiltrate solid tumors, and the ability to recruit host immune cells.

Healios has succeeded in developing eNK cells through its own research and has confirmed that eNK cells have anti-tumor effects in mice engrafted with human lung cancer cells and human liver cancer cells. In joint research with [the National Cancer Center Japan](#) (“the NCCJ”) we are evaluating the antitumor effects of eNK cells in a PDX mouse disease model created using the NCCJ’s JPDX samples. Furthermore, Healios is conducting joint research with [Hiroshima University](#) on cancer immunotherapies for hepatocellular carcinoma using eNK cells. Healios is continuing with *in vitro* and animal testing of its eNK cell therapy in preparation for its first clinical trials.

Contact:
Department of Corporate Communications,
HEALIOS K.K. E-mail: ir@healios.jp