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

## **Healios eNK Cells: Regenerative Medicine Product Quality Consultation with the PMDA for Planned Clinical Trials**

HEALIOS K.K. (“Healios”) is developing next-generation cancer immunotherapies for solid tumors using NK cells\*<sup>1</sup> derived from allogeneic iPSCs (Development Code: HLCN061 “eNK cells”) whose specific functions have been enhanced with gene editing technology. In preparation for the start of clinical trials using eNK cells, we have conducted a regenerative medicine product quality consultation\*<sup>2</sup> (face-to-face advice) with the Pharmaceuticals and Medical Devices Agency (PMDA).

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. We are conducting joint research with the National Cancer Center Japan, Hiroshima University, and the Hyogo Medical University, to evaluate the effect of eNK cells in various human solid cancers. Furthermore, we have established an automated, 3D perfusion bioreactor based manufacturing system that enables efficient and stable mass production of eNK cells for the manufacture of investigational product. Healios initiated the operations of its Cell Processing Center (CPC), a GMP manufacturing facility based on these technologies, and is advancing preparations for eNK clinical trials.

As part of these preparations, we have begun consultations with the PMDA through a formal regenerative medicine product quality consultation process. In an initial face-to-face consultation meeting, we have discussed with the authorities genome analysis and evaluation of transgenic iPS cells for the purpose of assessing the quality of HLCN061, among other matters. We will continue with consultations with the PMDA as we work towards the submission of an investigational new drug application and the start a clinical trial in FY2024.

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.

### **\*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 Regenerative medicine product quality consultation

Guidance and advice are provided as a specialized consultation on matters related to the quality of processed cells, etc. and regenerative medicine products, such as specifications, test methods, stability, and manufacturing methods.

**About Pharmaceuticals and Medical Devices Agency (PMDA):**

PMDA is Japanese regulatory agency, working together with Ministry of Health, Labour and Welfare. Its obligation is to protect the public health by assuring safety, efficacy and quality of pharmaceuticals and medical devices. It conducts scientific reviews of marketing authorization application of pharmaceuticals and medical devices, monitoring of their post-marketing safety. It is also responsible for providing relief compensation for sufferers from adverse drug reaction and infections by pharmaceuticals or biological products.

In response to applications from sponsors, etc., we provide guidance and advice on clinical trials for pharmaceuticals, medical devices, regenerative medicine products, etc., as well as on clinical trials for reevaluation and reassessment.

<https://www.pmda.go.jp/english/review-services/consultations/0002.html>

**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 on cancer immunotherapies using eNK cells for hepatocellular carcinoma with [Hiroshima University](#) and for mesothelioma with [Hyogo Medical University](#). Healios is continuing with in vitro and animal testing of its eNK cell therapy in preparation for its first clinical trials.

**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 immunoncology, 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 has been 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>

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