

July 6, 2022

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

Healios Initiates Production of eNK Cells at In-house GMP Facility

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.

[As previously announced](#), Healios has been preparing the establishment of a cell processing center (“CPC”) in the Kobe Center for Medical Innovation. Healios is pleased to announce that the CPC is in operation and it is initiating eNK cell production for clinical trial purposes in this facility.

This GMP grade facility is expected to produce approximately 100 billion eNK cells per production batch using our established 3D perfusion bioreactor system*², enabling efficient and stable mass production of eNK cells.

With the achievement of this important milestone, Healios is positioned well to advance preparations for eNK clinical trials. With the combined strength of the eNK cell therapy technology platform and advanced manufacturing capabilities, we will strive to bring new treatments and greater hope to patients with difficult to treat cancers as quickly as possible.

< Overview of the CPC >

(1) Address:

Minatojima-Minamimachi 6-3-5, Chuo-ku, Kobe-city, Hyogo. Located within the Kobe Center for Medical Innovation (KCMI).

(2) Total floor area: Approximately 240m²

(3) Purpose of use:

Production of investigational iPSC regenerative medicine products that comply with GCTP*³/GMP*⁴ standards



***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 3D perfusion bioreactor system**

After hematopoietic progenitor cells are generated from iPS cells, these progenitor cells are differentiated into eNK cells and cultured in large scale. These processes are performed in a fully closed system with automated medium exchange, enabling efficient and stable eNK cell production of approximately 100 billion cells per batch at a current 2 x 3L scale. Furthermore, we have fully established downstream processes including Healios' proprietary cryopreservation process, which enables eNK cells to be stored frozen while maintaining robust post-thaw cytotoxicity towards cancer.

***3 GCTP**

An acronym for “Good Gene, Cellular, and Tissue-based Products Manufacturing Practice,” GCTP is a set of standards governing the production management and quality control of regenerative medicine products.

***4 GMP**

An acronym for “Good Manufacturing Practice,” GMP is a set of standards governing the production management and quality control of pharmaceutical products.

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 and with [the Hyogo Medical University](#) on cancer immunotherapies for human mesothelioma using eNK cells. 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

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>

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