December 9, 2024


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| Company Name: | HEALIOS K.K. |
| Representative: | Hardy TS Kagimoto, Chairman & CEO (TSE Growth Code: 4593) |
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# Healios Selected for the AMED "Project to Promote the Industrialization of Regenerative/Cell Medicine and Gene Therapy"

HEALIOS K.K. ("Healios") announces that our ongoing research and development of eNK* cells has been selected as a research project supported by AMED (Japan Agency for Medical Research and Development) for the fiscal year 2024 "Development of Basic Technologies for Industrialization of Regenerative Medicine and Gene Therapy (Project to Promote the Industrialization of Regenerative/Cell Medicine and Gene Therapy) (Development Support Project)" (hereinafter referred to as "the Project").

**Publicly disclosed information: Development Support Project**

Development of Basic Technologies for Industrialization of Regenerative Medicine and Gene Therapy (Project to Promote the Industrialization of Regenerative/Cell Medicine and Gene Therapy)

**Title:**

Research and Development of HLCN061 (transgenic iPS cell-derived NK cells = eNK cells) for the treatment of Malignant Pleural Mesothelioma

**Max. subsidy amount: 59,900,000 yen per year**

(Maximum of 180 million yen over the three years from the decision to grant to the end of FY2026)

Our research and development has been selected as a project under the "Support for R&D to Promote Industrialization of Drug Discovery Seeds Aimed at Regenerative Medicine Products" program. For details of the subsidy amount, please refer to the AMED website (in Japanese).

In the Project, Healios will conduct research and development with the goal of starting clinical trials for malignant pleural mesothelioma, a rare disease with a very poor prognosis and limited treatment options, with the aim of developing a breakthrough therapeutic drug of a new modality with a completely different mechanism of action from existing treatments.

Note: In the adopted research plan, we will validate our NK cell mass culture method and complete GLP and non-GLP non-clinical safety studies and pharmacokinetic studies in accordance with pharmaceutical regulations using the manufactured HLCN061 to confirm its potential for clinical application. Furthermore, we will establish administration methods and cell preparation methods for clinical administration that are useful in collaborative research with clinicians. After the completion of this research, we aim to start clinical trials as soon as possible.

Through this project, AMED will support companies, including venture companies that will be the main developers, to conduct non-clinical trials, establish manufacturing methods, and develop evaluation indices in accordance with pharmaceutical regulations in order to advance to clinical development of seeds of regenerative medicine products with a view to industrialization. In order to develop evaluation indicators, we will work with CMO/CDMOs and CROs to establish a development system with an awareness of regulatory requirements and provide support to increase the value of the seeds owned by the company. Through this research and development, we aim to increase the value of the seeds of regenerative medicine products and promote not only clinical development such as corporate clinical trials, but also future fundraising from venture capitalists and other sources and out-licensing to other pharmaceutical companies.

**Future Outlook:**
This matter has no impact on our consolidated financial results of the fiscal year ending December 31, 2024 at this time. We will promptly announce any matters that should be disclosed in the future

*** eNK cells**
(Development code: HLCN061)
Healios' eNK cells are an iPSC-derived NK cell therapy with several functional enhancements achieved through gene-editing including enhanced recognition of and cytotoxicity towards cancer, improved persistence, increased capability to migrate to 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 the anti-tumor effect of eNK cells in mice engrafted with human lung cancer cells and human liver cancer cells. In joint research with the National Cancer Center Japan ("the NCCJ") Healios confirmed the antitumor effect of eNK cells in a PDX mouse disease model created using the NCCJ's JPDX samples. Healios is also conducting joint research using eNK cells for hepatocellular carcinoma with Hiroshima University and for mesothelioma with Hyogo Medical University. Healios is continuing with in vitro and in vivo testing of its eNK cell therapy in preparation for its first clinical trials. In addition to advancing eNK cells as a monotherapy and in combination with existing drugs, Healios is developing a dual CAR-eNK cell product, in which chimeric antigen receptors (CARs) that specifically recognize cancer antigens are introduced into the eNK to facilitate enhanced targeting of certain solid cancers.

**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