

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

## **Academic Paper on the anti-tumor effects of Healios eNK cells against lung cancer in “Cancer Immunology, Immunotherapy”**

HEALIOS K.K. (“Healios”) and Akatsuki Therapeutics, Inc. (“Akatsuki”) are involved in the research of new therapeutic products using eNK cells\*. We are pleased to announce that researchers at Healios have published a recent work revealing the anti-tumor effect of human iPSC-derived NK cells (eNK cells) expressing CCL19, CCR2B, high-affinity CD16, IL-15, and NKG2D-DAP10 complexes by gene-modification on lung cancer. This work has been published in the peer-reviewed journal [”Cancer Immunology, Immunotherapy”](#). This study demonstrates the potential of eNK cells to serve as a groundbreaking “off-the-shelf” allogeneic cell therapy for refractory solid tumors, including lung cancer.

Title: [An innovative treatment for lung cancer using gene-engineered human induced pluripotent stem cell-derived natural killer cells](#)

Journal: [Cancer Immunology, Immunotherapy](#)

DOI : 10.1007/s00262-026-04370-7

Authors: Yuka Sato<sup>1)</sup>, Kumiko Goto<sup>1)\*</sup>, Shigehiro Yagishita<sup>2)</sup>, Kotoko Miyata<sup>1)</sup>, Noriko Uesugi<sup>1)</sup>, Yu-suke Torisawa<sup>1)</sup>, Yoichi Naritomi<sup>1)</sup>, Ryuta Takahashi<sup>1)</sup>, Rumiko Sho<sup>1)</sup>, Yuriko Takeno<sup>1)</sup>, Kenji Kurachi<sup>1)</sup>, Masashi Yamada<sup>1)</sup>, Yasuyuki Higashi<sup>1)</sup>, Hironobu Kimura<sup>1)</sup>, Akinobu Hamada<sup>2)</sup>, Fusako Nishigaki<sup>1)\*</sup> and Kouichi Tamura<sup>1)</sup>

1) Kobe Research Institute, HEALIOS K.K., Kobe, Japan. 2) Division of Molecular Pharmacology, National Cancer Center Research Institute, Tokyo, Japan.

\*: Correspondence Author

### **Abstract:**

Various therapeutic approaches have been developed for lung cancer, including chemotherapy, radiation therapy, and immune checkpoint inhibitors. However, these approaches, including chimeric antigen receptor (CAR)-T cell therapy, have shown limited efficacy against solid tumors, especially in advanced disease.

To enhance the therapeutic effect, we focused on the multiple effects of a new modality of cell therapy and created engineered natural killer (eNK) cells, which are gene-engineered induced pluripotent stem cell (iPSC)-derived NK cells armed with CC motif ligand 19 (CCL19), CC chemokine receptor type 2B (CCR2B), high-affinity cluster of differentiation 16 (CD16), interleukin (IL)-15, and natural killer group 2, member D (NKG2D)-DNAX-activating protein 10 (DAP10) complex. In vitro studies showed that eNK cells exhibit significant long-lasting cytotoxicity and antibody-dependent cell-mediated cytotoxicity (ADCC) against human lung cancer cell lines. In vivo, eNK cells achieved near-complete tumor regression in orthotopic and subcutaneous cell line-derived xenograft (CDX) models. In contrast, in patient-derived xenograft (PDX) models, eNK cells demonstrated modest tumor growth inhibition (28% reduction) as monotherapy and significantly enhanced efficacy (53% inhibition) in combination with

cetuximab via antibody-dependent cellular cytotoxicity. In treated PDX tumors, human CD45-positive cells were detected within the tumor parenchyma, supporting intratumoral presence of administered human cells.

These findings support the potential contribution of the six-gene modifications in enhancing tumor homing, persistence, and cytotoxicity in solid tumor treatment. This study underscores the potential of eNK cells as a novel, "off-the-shelf" allogeneic therapy for refractory solid tumors, including lung cancer.

\* eNK cells

(Development code: AKT-01/HLCN061)

eNK cells are an iPSC-derived NK cell therapy with several functional enhancements achieved through gene-modification 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](#). Akatsuki Therapeutics, Inc. and Healios are collaborating to continue to advance eNK cells 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. Healios is studying cancer immuno-cell therapy using CAR-eNK cells against brain tumors with [Kyushu University](#).

**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 iPSCs. In the somatic stem cell field, Healios is developing HLCM051 (invimestrocel), a proprietary cell product comprised of multipotent adult progenitor cells ("MAPCs") derived from the bone marrow of healthy adult donors. HLCM051 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 HLCM051 on a global basis for ARDS, trauma, and ischemic stroke. In the iPSC regenerative medicine field, Healios has developed HLCN061, a next generation NK cell treatment for solid tumors that has been functionally enhanced through gene-modification. 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 in collaboration with Akatsuki Therapeutics, Inc.. 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>

**About Akatsuki:**

Akatsuki Therapeutics Inc. (Head office: 8-1 Kakuda-cho, Kita-ku, Osaka, Japan; President: Hikaru Saito; a Saisei Ventures portfolio company) is developing innovative cellular immunotherapies with the potential to transform the treatment of cancer and other serious diseases. Its lead program harnesses advanced genetic enhancements, cellular reprogramming, and scalable manufacturing to address the limitations of existing cell therapy approaches. Driven by a mission to create accessible, off-the-shelf solutions, the company aims to deliver life-changing therapies that will improve worldwide patient access and improve the standard of care. At Akatsuki Therapeutics, the company is committed to advancing the next generation of cellular immunotherapies to usher in a new dawn for patients and their families.

**About Saisei Ventures:**

Saisei Ventures is a life science venture capital firm dedicated to building next-generation companies in the healthcare sector. Saisei creates ventures that start from bold ideas and empower dynamic entrepreneurs by providing technical, operational, and financial guidance. The firm's approach combines Western expertise and Japanese innovations to build globally competitive companies that will have the greatest impact on patient lives. With operations in Japan and the United States, Saisei aims to enhance the value of its portfolio by leveraging its unique networks and the institutional advantages of both countries.

<https://www.saiseiventures.com>

Contact:  
IR & PR Division  
HEALIOS K.K.  
E-mail: [ir@healios.jp](mailto:ir@healios.jp)