

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

**Notice of Joint Research Agreement with Kyushu University at the Graduate School of Medical Sciences on Immuno-Cell Therapy for Brain Tumors Using Healios' Gene-Edited CAR-eNK Cells**

HEALIOS K.K. ("Healios") has been advancing research on cancer immune cell therapy using allogeneic iPS cell-derived NK cells<sup>\*1</sup>(hereinafter referred to as "eNK cells"<sup>\*2</sup>) which are genetically modified to enhance specific functions, within the field of iPSC regenerative medicine. Development in this area is being led by our partner company, Akatsuki Therapeutics. Concurrently, Healios has been conducting basic research on next-generation eNK cells, which involve the introduction of chimeric antigen receptors (CAR) into eNK cells (hereinafter referred to as "CAR-eNK cells"<sup>\*3</sup>).

We are pleased to announce that we have entered into a joint research agreement with the Department of Neurosurgery, Graduate School of Medical Sciences, Kyushu University (Professor Koji Yoshimoto), to study cancer immuno-cell therapy using CAR-eNK cells against brain tumors. In this joint research, the antitumor effects of CAR-eNK cells on brain tumors will be evaluated in vitro and in vivo.

The Department of Neurosurgery at the Graduate School of Medical Sciences(<https://www.ns.med.kyushu-u.ac.jp/>), Kyushu University, has been actively engaged in advanced cancer treatment research and clinical applications targeting central nervous system diseases, including brain tumors. In particular, in the field of malignant brain tumors, the department is focused on developing novel therapies, incorporating advanced medical technologies such as genome-informed personalized treatments, awake surgeries, and endoscopic procedures.

Although the advent of molecular-targeted therapies and cancer immunotherapies has improved clinical outcomes in oncology, many diseases remain with unsatisfactory treatment responses. Healios will continue to advance the research and development of effective therapies for solid tumors.

This matter will have no impact on the Company's consolidated financial results for the current fiscal year. We will promptly disclose any information requiring public announcement as it arises.

\*1 Natural killer (NK) cells

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 eNK cells

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. 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.

### \*3 CAR-eNK cells

CAR-eNK cells are next-generation cancer immuno-cells developed from our eNK platform by introducing a chimeric antigen receptor (CAR) that recognizes molecules specifically expressed on cancer cells. CAR-eNK cells exhibit strong selectivity and powerful cytotoxic activity against target cancer cells. Thus, in addition to the innate immune activity of conventional NK cells, they possess acquired immunity-like specificity for particular cancer antigens. These features make CAR-eNK cells a promising new therapeutic approach to enhance antitumor activity against diverse cancers and overcome challenges such as therapeutic resistance and immune evasion due to antigen loss.

### 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 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-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 in collaboration with Akatsuki Therapeutics. 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>

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