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## **Joint Research Agreement with the National Cancer Center Japan**

HEALIOS K.K. (“Healios”) has signed an agreement with the National Cancer Center Japan ( “the NCCJ”) to jointly research Healios’ allogeneic iPS cell-derived gene-edited NK cells (development code: HLCN061) as an immune cell therapy for cancer.

Recent reports highlight the potential of cancer immune cell therapies using gene-edited T cells and NK cells\*<sup>1</sup>. For hematological cancers, autologous CAR-T cell therapy involving the extraction of T cells from the patient, enhancement of the attacking power on the target cancer cells by gene editing, followed by the return of the enhanced cells back into the body, has been approved in Japan. On the other hand, there is no approved immune cell therapy for solid tumors. Solid tumors account for the majority of cancer diseases and represent a tremendous unmet medical need on a global basis.

HLCN061 is an off-the-shelf NK cell therapy that has been enhanced by gene editing to promote various antitumor functions. We are aiming to produce an NK cell treatment that is effective against a wide range of cancer diseases and not limited to specific cancer antigens.

In our joint research with the NCCJ, we will test whether several types of molecules are recognized by HLCN061 in the NCCJ PDX model\*<sup>2</sup>, with the aim of examining the expression status and clarifying the characteristics of solid tumors in which HLCN061 exerts an antitumor effect. Based on the results, we will consider further evaluation of the antitumor effect of HLCN061 in PDX models in the future.

Through this joint research, we will clarify the characteristics of patients who can take advantage of HLCN061 and aim to advance the development of a product that is expected to be highly effective for those patients.

Future outlook:

The anticipated period of this joint research is approximately one year. In the future, we will promptly inform the market of any matters that need to be disclosed.

About National Cancer Center Japan:

Founded in 1962 as a national institution to serve as a base for cancer treatment and research in Japan, it is a cancer-based hospital that has been a strong leader in cancer treatment and research in Japan. The NCCJ was incorporated into an independent administrative agency in 2010, designated as a national research and development corporation in 2015, and has a central hospital (Tsukiji Campus) and east hospital (Kashiwa Campus) designated as core clinical research hospitals under the Medical Law. It has played and is expected to continue to play a central role in international standard clinical research and doctor-initiated clinical trials, and aims to create world-class research results and maximize R&D outcomes.

\*<sup>1</sup> NK cells

NK (natural killer) cells are a natural defense mechanism of the human body and are a type of white blood cell that attacks cancer cells and virus-infected cells. In addition, NK cells are classified as lymphocytes in the classification of white blood cells. The efficacy of treatment using NK cells is expected to include prolonging life, alleviating symptoms, improving quality of life, and curing disease.

\*<sup>2</sup> PDX model

PDX (Patient-Derived Xenograft) model is a patient tumor tissue transplant model in which a tumor tissue piece derived from a patient is transplanted into an immunodeficient mouse to reproduce a tumor. It is used in preclinical drug discovery research because it reproduces a condition close to that observed in a clinical setting. The cancer cell lines used in conventional experiments may not be able to predict the exact therapeutic effect of an anticancer drug because the original cancer tissue characteristics have been lost. The PDX model retains the characteristics of the cancer tissue and can bring high accuracy in predicting the therapeutic effect of an anticancer drug.