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Healios and Saisei Ventures Enter into a Letter of Intent and Establish Subsidiary for eNK Research and Development

HEALIOS K.K. (“Healios”) is developing next-generation immuno-oncology therapies, with a focus on solid tumors, using NK cells derived from allogeneic iPSCs and whose specific functions have been enhanced with gene editing technology (development code: HLCN061 “eNK cells”). Healios is executing on its strategy to advance its therapeutic programs while leveraging efficient external funding sources involving investments from third parties including project finance, grants and partnerships. Today, consistent with its strategy, Healios is pleased to announce that it has decided to establish a subsidiary to promote the development of its eNK pipeline and has concluded an additional letter of intent with Saisei Ventures LLC (hereinafter referred to as "Saisei"), whereby Saisei will seek to commit invested capital of at least 1 billion yen and up to 2 billion yen to the subsidiary in the future from Saisei managed funds. The initial goal of the subsidiary is to run a Phase 1 trial for the generation of first-in-human data for eNK cells.

1. Outline of letter of intent with Saisei Ventures

Cancer remains a disease area marked by low therapeutic efficacy, although the advent of molecular-targeted drugs and cancer immunotherapy has improved treatment outcomes. Healios believes that immuno-oncology therapies using iPS cells as a starting material will change the future of cancer treatment, and we are actively working to develop novel therapeutics using eNK cells. Healios is not only targeting multiple cancer types with eNK cells as a monotherapy and in combination with other drugs, but is also developing eNK cells as a platform to create multiple products over the long term such as dual CAR-eNK cells. Healios is promoting the commercialization of eNK cells by leveraging our R&D capabilities, manufacturing technologies, and experience in conducting clinical trials in the field of regenerative medicine, centered on our core capabilities of developing high quality iPS cell derived products that we have built over many years.

With the aim of accelerating the research and development of eNK cells as a therapeutic medicine, Healios and Saisei Ventures have agreed that, upon entering into a definitive agreement, Saisei would make commitments to invest in the subsidiary described further in 2. below from Saisei managed funds and would provide support to the subsidiary with respect to activities to obtain non-dilutive grant funding, towards the goal of running a Phase 1 trial and generating first-in-human data for eNK cells. It is anticipated that at least 1 billion yen and up to 2 billion yen in total invested capital would be committed to the subsidiary from Saisei funds.

Regarding the sources of funds for investment, in addition to Saisei’s flagship fund, Saisei Bioventures L.P., it is anticipated that a new Saisei launched fund, the Saisei Special

Opportunities Fund, L.P., a fund being established to make investments in certain promising therapeutics opportunities in Japan, would also commit capital to this opportunity.

Saisei Ventures is a venture capital firm that aims to nurture next-generation companies in the healthcare field. As announced [on Feb 6, 2023](#), Japan Investment Corporation committed \$30 million of capital to Saisei Ventures' flagship fund. In addition, as further [announced on May 17, 2023](#), Saisei Ventures was selected as one of nine certified venture capital firms in the fiscal year 2023 "Strengthening Program for Pharmaceutical Startup Ecosystem (Approval of Venture Capital)" (2nd round), by the Japan Agency for Medical Research and Development ("AMED"), allowing for Saisei backed companies to apply for certain AMED grant funding opportunities.

2. Establishment of subsidiary

The subsidiary to be established will initially be wholly owned by Healios and is scheduled to be established in August 2023, with the business of research, development, manufacturing and marketing of pharmaceutical products. The name of the subsidiary, its location, the name and title of representative director and capital stock will be decided later.

There is no confirmed impact of this matter on the business results for the fiscal year ending December 31, 2023 at this time. We will promptly announce any matters that should be disclosed in the future.

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, mice engrafted with human mesothelioma cell 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 on cancer immunotherapies using eNK cells for hepatocellular carcinoma with [Hiroshima University](#) and for mesothelioma with [Hyogo Medical University](#). Healios is continuing with in vitro and animal testing of its eNK cell therapy in preparation for its first clinical trials. In addition, we are working on the development of a dual CAR-eNK cell product, in which chimeric antigen receptors (CAR) that specifically recognize cancer antigens are introduced into the eNK, with the aim of expanding the application of eNK cells to other solid tumors.

About Saisei Ventures:

Saisei Ventures is a leading venture capital firm dedicated to building next-generation companies in the healthcare sector. It aims to partner with passionate bio-entrepreneurs to develop and implement business strategies that will generate strong proof of concept, clinical validation, and market value. With operations in Japan and the United States, Saisei aims to enhance the value of its portfolio companies by leveraging its unique networks in and the institutional advantages of both countries. Saisei's first fund, Saisei Bioventures L.P., is focused on building revolutionary cell and gene therapy and regenerative medicine companies from foundational technologies originating from Japan. For more information, visit <https://www.saiseiventures.com>

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 has been 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>