

October 18, 2022

Company Name: HEALIOS K.K.
Representative: Hardy TS Kagimoto, Chairman & CEO
(TSE Growth Code: 4593)
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Business and Capital Alliance Agreement with SATAKE MultiMix

HEALIOS K.K. (“Healios”) announces the decision reached by the written resolution of our executive officers’ meeting based on the delegation by resolution of our board of directors held on October 18, 2022, to execute a business and capital alliance agreement with SATAKE MultiMix Corporation (“Satake”) to issue new shares to Satake by way of a third-party allotment.

1. Reason for the alliance

Healios is developing next-generation immuno-oncology therapies, with a focus on solid tumors, using NK cells*¹ derived from allogeneic iPSCs (Development Code: HLCN061 “eNK[®] cells”) whose specific functions have been enhanced with gene editing technology. Healios believes that iPSC-based immuno-oncology therapies will change the future of cancer treatment, and we are actively working on the development of new eNK cell-based therapies for solid tumors.

Healios has succeeded in developing eNK cells through its own research. Healios began its research efforts by establishing a fundamental NK cell platform by generating un-edited iPSC derived NK cells that demonstrated robust cytotoxicity towards cancer. Healios built upon this strong foundation by then establishing its eNK cells and confirming their even greater anti-tumor effects both in vitro and in mice engrafted with human lung cancer cells and human liver cancer cells, thereby establishing “animal POC” for the efficacy of eNK cells ([please see page 30 of the FY2022 Q1 Financial Results](#)). Recently, we [disclosed results from testing eNK cells in patient-derived organoids and demonstrated robust anti-tumor killing in models](#) closely resembling the actual clinical situation of patients. We are conducting joint research with the National Cancer Center Japan, Hiroshima University, and the Hyogo Medical University, to further evaluate the effect of eNK cells in various human solid cancers. Through these collaborations and ongoing internal development, Healios is advancing its eNK cells toward the clinic targeting an initial human trial in 2024.

In the cell therapy industry, manufacturing is of paramount importance to the ultimate success of a therapeutic program. By leveraging our deep experience in the production of cell products and with the cooperation of Satake, we have established a proprietary automated, 3D perfusion bioreactor*² based manufacturing system that enables efficient and stable mass production of eNK cells. Healios has [initiated the operations of its in-house Cell Processing Center \(CPC\)](#), a GMP manufacturing facility based on these technologies. The manufacturing process and facility positions us to efficiently supply global clinical trials using eNK cells. In preparation for the start

of these clinical trials, we have [conducted a regenerative medicine product quality consultation](#)^{*3} with the Pharmaceuticals and Medical Devices Agency (PMDA).

Satake is developing its business as a leading manufacturer of agitators and as one of the pioneering companies in environmental testing equipment and refrigeration and air conditioning performance measurement equipment, and is promoting open innovation with domestic research institutes and universities, joint research and collaboration with customers, and is also developing its business in the biotechnology field. At Healios, we have been continuously conducting technical studies with Satake since October 2020 toward establishing an efficient and stable mass production method for eNK cells through 3D perfusion manufacturing. In addition, a portion of the automated 3D perfusion bioreactor system used in our CPC, which went into full operation in July 2022 for the production of investigational drugs, uses the products of Satake.

In order to promote preparations for the start of clinical trials and accelerate our joint activities, Healios and Satake have decided to form an alliance regarding continuous improvement of the perfusion bioreactor system and support services to ensure efficient and stable operations of the system.

As part of the business and capital alliance, Healios has decided that strengthening the relationship with Satake by its holding of Healios shares will contribute to the promotion of the business, and the executive officers, at its meeting held today, has resolved to make this third-party allotment.

***1 Natural killer (NK) cells**

Natural killer (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 3D perfusion bioreactor system**

After hematopoietic progenitor cells are generated from iPS cells, these progenitor cells are differentiated into eNK cells and cultured at a large scale. These processes are performed in a fully closed system with automated medium exchange, enabling efficient and stable eNK cell production of approximately 100 billion cells per batch at a current 2 x 3L scale. Furthermore, we have fully established downstream processes including Healios' proprietary cryopreservation process, which enables eNK cells to be stored frozen while maintaining robust post-thaw cytotoxicity towards cancer.

***3 Regenerative medicine product quality consultation**

Guidance and advice are provided as a specialized consultation on matters related to the quality of processed cells, etc. and regenerative medicine products, such as specifications, test methods, stability, and manufacturing methods.

2. Overview of the alliance

(1) Overview of the business alliance

The purpose of this alliance is to study the improvement of Satake's perfusion equipment for use in the manufacture of regenerative medicine products using eNK cells, which will be developed by Healios. In order to achieve this objective, Satake will be responsible for overall customization of production and perfusion equipment and related support services, and Healios will be responsible for providing information on production and perfusion conditions of eNK cells and for perfusion evaluation. The business alliance is currently scheduled to continue until September 30, 2023.

(2) Overview of the capital alliance

In connection with this business and capital alliance, Healios will allot shares of its common stock equivalent to approximately 100 million yen to Satake by the method of the third-party allocation.

3. Overview of the alliance partner

(1) Name	SATAKE MultiMix Corporation https://www.satake.co.jp/en/	
(2) Location	66, Nizo, Toda-city, Saitama 335-0021, Japan	
(3) Post and Name of Representative	President Mitsutoshi Nishioka	
(4) Outline of Business	Manufacture and sale of industrial machinery	
(5) Capital	90 million Japanese Yen	
(6) Date of Establishment	February 28, 1938	
(7) Number of shares outstanding	1,800,000 shares	
(8) Accounting period	August	
(9) Number of Employees	179 employees	
(10) Major Shareholders and Shareholding Ratio	Mitsutoshi Nishioka: 29.33%	
(11) Relationship between Healios and the partner	Capital	There is no corresponding matter.
	Personal	There is no corresponding matter.
	Business	Technical support of perfusion-related equipment and materials
	Status of relationship with related parties	There is no corresponding matter.
(12) Consolidated operating results and consolidated financial condition over the last three years		

Accounting period	FY2019/8	FY2020/8	FY2021/8
Total net assets	7,940	7,797	7,790
Total liabilities and net assets	5,638	5,863	6,027
Net assets per share of common stock (Yen)	3,132	3,257	3,348
Net sales	5,433	4,542	4,152
Operating income	475	166	70
Ordinary income	410	237	182
Net income attributable to shareholders	410	237	182
Net income per share of common stock (Yen)	228	132	101
Dividend per share (Second quarter ended) (Yen)	7 (-)	10 (-)	10(-)

As of October 17, 2022 (Unit: million yen. Except what is specified.)

4. Schedule

(1) Board of executives' resolution date	October 18, 2022
(2) Contract date	October 18, 2022
(3) Starting date of Business alliance	November 7, 2022 (Planned)

5. Future outlook

This agreement has a material impact to our consolidated financial results for the current fiscal year. Healios shall promptly announce all future matters that require disclosure.

About Pharmaceuticals and Medical Devices Agency (PMDA):

PMDA is a Japanese regulatory agency, working together with Ministry of Health, Labour and Welfare. Its obligation is to protect the public health by assuring safety, efficacy and quality of pharmaceuticals and medical devices. It conducts scientific reviews of marketing authorization application of pharmaceuticals and medical devices, monitoring of their postmarketing safety. It is also responsible for providing relief compensation for sufferers from adverse drug reaction and infections by pharmaceuticals or biological products. In response to applications from sponsors, etc., we provide guidance and advice on clinical trials for pharmaceuticals, medical devices, regenerative medicine products, etc., as well as on clinical trials for reevaluation and reassessment.

<https://www.pmda.go.jp/english/review-services/consultations/0002.html>

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 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 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 immunology, 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>