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Company Name:	HEALIOS K.K.
Representative:	Hardy TS Kagimoto, Chairman & CEO (TSE Growth Code: 4593)
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Announcement of Letter of Intent with Nobelpharma for the Development and Commercialization of HLCM051 for ARDS in Japan

HEALIOS K.K. ("Healios") today announces that Healios, its wholly owned subsidiary ProcellCure Inc. ("ProcellCure") and Nobelpharma Co., Ltd. ("Nobelpharma" https://www.nobelpharma.co.jp/en/) have entered into a letter of intent ("LOI") for a development and marketing alliance in Japan for HLCM051[*1], a somatic stem cell regenerative medicine therapy for the treatment of acute respiratory distress syndrome (ARDS)[*2].

1. Outline of the Agreement

The purpose of this LOI is to confirm the understanding between the parties with respect to the development and marketing alliance of HLCM051 for ARDS in Japan. Under the terms of a definitive agreement, the further details for which will be finalized and executed in the future, ProcellCure is expected to receive approximately 25 billion yen based on projected sales as of the date of the LOI, through milestone payments based on obtaining regulatory approval and sales. It is also agreed that ProcellCure will develop and supply the drug product to Nobelpharma and would receive revenue from product supply. Nobelpharma will support the development and application for approval that is agreed in the future, in addition to marketing the product. The three companies will continue negotiations to conclude the final terms and conditions based on this LOI.

2. About the development of HLCM051 for ARDS and ProcellCure, Inc.

In 2018, Healios obtained a license to develop and market HLCM051 for ARDS in Japan and started a phase II study (clinical study name: ONE-BRIDGE study) to evaluate the efficacy and safety of HLCM051 in patients with pneumonia-induced ARDS. In 2021, we signed an agreement with Athersys to expand our comprehensive collaboration for commercialization and obtained licensing rights for the commercial manufacture of the product. In August and November 2021, we released topline data on the endpoints at 90 and 180 days after administration of HLCM051 in the ONE-BRIDGE study, showing favorable efficacy and safety results. In consultation with the Pharmaceuticals and Medical Devices Agency (PMDA), we agreed on the outline of the registrational clinical trial to be conducted in the future, as announced on March 2, 2023. In addition, we announced the plan to use investigational product manufactured by a 3D bioreactor-based manufacturing method, which enables mass production, and it is expected that we will be able to supply drug product in larger quantities and more stably than the conventional 2D culture method. Under these circumstances, Healios established a new subsidiary, ProcellCure, Inc., to proactively promote this clinical trial and is currently preparing for the start of a clinical trial in Japan.

Tadahisa Kagimoto, MD, Chairman and CEO of Healios, made the following comment:

“Nobelpharma has received approval for 16 drug products and is a leader in the field in Japan, especially in the area of orphan drugs. They have also obtained approvals in the United States. By magnifying our efforts with their experience and support, we are delighted to steadily advance HLCM051 towards an approval for ARDS in the Japanese market.”

3. Future Outlook

This matter has no impact on our consolidated financial results at this time. We will promptly announce any matters that should be disclosed in the future.

*1 HLCM051

HLCM051 is a somatic stem cell regenerative medicine product. Healios added it to its pipeline by signing an exclusive licensing agreement with the United States based Athersys, Inc. (“Athersys”) in January 2016, whereby Healios acquired rights to develop and distribute Athersys’ proprietary stem cell product MultiStem® to treat ischemic stroke in Japan. Further, in June 2018 Healios and Athersys expanded their collaboration broadly, and as part of this expansion Healios acquired the development and distribution licenses to use MultiStem® to treat ARDS in Japan and in October 2023, we agreed to expand our license for ARDS to cover all territories globally.

*2 Acute Respiratory Distress Syndrome (ARDS) ARDS is a general term for respiratory failure that occurs suddenly in a variety of critically ill patients. Although there are many causes of ARDS, approximately one-third of ARDS cases are caused by pneumonia, and it has been confirmed that ARDS also occurs in critically ill patients with COVID-19. There is currently no approved drug therapy that can directly improve the prognosis of patients with ARDS, and respiratory failure is treated with mechanical ventilation. The mortality rate after the onset of ARDS is 30~58%[*a], and there is a need for new therapies that can improve the prognosis of patients with ARDS. Currently, the number of patients in Japan is estimated to be approximately 28,000[*b] per year, and ARDS is designated as a rare disease. However, it is estimated that between 213,000 and 262,000[*c] patients in the United States and 133,000[*d] patients in Europe are affected annually.

(Source)

*a ARDS Diagnostic Guidelines 2016

*b Healios Estimates Based on the Incidence Rate of Epidemiological Data and the Total Population of Japan by Demography

*c Diamond M et al. 2023 Feb 6. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: Estimates for our company based on 28613773 Data and US Population Based on the Ministry of Foreign Affairs Basic Data

*d Community Research and Development Information Service (CORDIS) 2020 7-9.

About Nobelparma:

Since its establishment in 2003, Nobelpharma Co., Ltd. (Head Office: Chuo-ku, Tokyo; President: Hitoshi Shiomura) has been striving to promptly introduce and deliver to patients pharmaceuticals and medical devices for which there is a strong need from patients and which other companies do not offer, under the mission of "Contribute to society by providing critical but neglected pharmaceuticals and medical devices". Over the past 20 years, the company has received numerous approvals for 16 new drugs, 6 additional indications, and 1 new medical device, as well as 15 orphan drug and medical device designations and 2 SAKIGAKE, Japanese accelerated approval, designations.

https://www.nobelpharma.co.jp/en/

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, 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, and is currently being advanced globally by Healios in ARDS. 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 ProcellCure:
ProcellCure Inc. was established in July 2023 as a wholly-owned subsidiary of Healios to proactively promote the development of HLCM051, a somatic stem cell regenerative medicine for acute respiratory distress syndrome (ARDS). Its location is Chuo-ku, Kobe, Hyogo Prefecture.