January 10, 2025

Company Name:	HEALIOS K.K.
Representative:	Hardy TS Kagimoto, Chairman & CEO (TSE Growth Code: 4593)
Contact:	Richard Kincaid, Executive Officer CFO (TEL: 03-4590-8009)

Promotion of Contract Manufacturing Business by ProcellCure

HEALIOS K.K. ("Healios") today announces that we have decided to add the CDMO (Contract Development and Manufacturing Organization) function to our wholly-owned subsidiary, ProcellCure, Inc. ("ProcellCure"). With this expansion of ProcellCure's functional remit, we will utilize the know-how we have cultivated to date, and aim to effectively leverage resources as well as strengthen our cash flow through early sales, including contract manufacturing for other companies.

1. Background of the change in ProcellCure's business function

Healios has long developed cell production technologies and know-how through in-house research and development of iPS cells (induced pluripotent stem cells), universal donor cells (UDC) that reduce the risk of immune rejection, and multipotent adult progenitor cells (MAPC). With the aim of developing our group to become one that includes a new contract manufacturing organization business, we have now decided to add the CDMO function to ProcellCure's business description. With the addition of this function, we will 1) optimize the manufacturing process for various cellular pharmaceutical products in the development stage, 2) establish a manufacturing system for use in future commercialization, and 3) strengthen the manufacturing capacity of the entire group.

As announced in the "Healios and Saisei Ventures Enter into a Letter of Intent and Establish Subsidiary for ARDS Treatment Development" on July 6, 2023, Healios originally established ProcellCure, Inc. to promote Phase 3 clinical trials of our product MultiStem®*[1] for acute respiratory distress syndrome (ARDS)*[2] in Japan. Then as further disclosed in our press release "Decision to Apply for Conditional and Time-Limited Approval for ARDS in Japan and ARDS Development Strategy Update" on October 2, 2024, Healios decided that it will submit an application for conditional and time-limited approval in Japan, based on the positive results of the Phase 2 studies already completed in Japan and the U.S. and U.K. (the ONE-BRIDGE and MUST-ARDS studies), and on the premise that we will run as a confirmatory study a pivotal, global Phase 3 trial (REVIVE-ARDS study*[3]) of MultiStem for ARDS that has been agreed with the U.S. Food and Drug Administration (FDA). As a result, the Phase 3 trial in Japan, for which a clinical trial plan notification had been submitted, was also cancelled, and ProcellCure's original purpose of establishment, which was to advance a clinical trial for ARDS in Japan, also became unnecessary.

As announced in the July 6, 2023 press release, Healios concluded basic agreements regarding investment in ProcellCure, primarily for the purpose of contributing to development costs, with Saisei Ventures LLC and Mitsubishi UFJ Capital Co., Ltd. We would also like to announce that we have decided to terminate our discussions on these matters in conjunction with the review of ProcellCure's business activities.

2. Future Outlook

The progress of this plan is not expected to affect our consolidated financial results for the fiscal year ending December 31, 2025 at this time. We will promptly announce any matters that should be disclosed in the future.

*1 MultiStem®

MultiStem (HLCM051) is a somatic stem cell regenerative medicine 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. MultiStem is a proprietary technology wholly owned by Healios. Healios has a long history developing MultiStem. It originally added MultiStem to its pipeline in 2016 through an exclusive license to develop and distribute the product to treat ischemic stroke in Japan. Further, in 2018 Healios expanded its license to include development and distribution to treat ARDS in Japan, and in 2023 it expanded its ARDS license to include global territories. Having acquired the full technology platform in April 2024, Healios is seeking to advance MultiStem on a global basis for ischemic stroke, ARDS, and trauma. In the U.S., MultiStem for the treatment of ischemic stroke and ARDS has received Fast Track and RMAT designation from the FDA, which allows for expedited approval of drugs that meet certain criteria for serious or life-threatening diseases or those for which no treatment is available.

*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 262,000[*c] patients in the United States, 133,000[*d] in Europe, 670,000 in China, and more than 1.1 million people worldwide are affected annually[*e].

(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.

*e song-et-al-2014-acute-respiratory-distress-syndrome-emergingresearch-in-china

*3 REVIVE-ARDS study

A pivotal, global Phase 3 study to demonstrate and confirm the efficacy and safety of MultiStem for ARDS caused by pneumonia, primarily in the United States. We held an End-of-Phase 2 consultation with the FDA (Food and Drug Administration) in September, 2024, as for the study design, we agreed with the FDA on the use of a primary endpoint based on VFD

(Ventilator Free Days: the number of days a patient does not require mechanical ventilation out of 28 days post administration in REVIVE-ARDS study, which is consistent with that utilized in the ONE-BRIDGE study previously completed in Japan). Interim analyses will be conducted at the 300 and 400 patient stages, and the REVIVE-ARDS study can be completed when statistical significance is confirmed. The maximum number of patients is 550. We also confirmed the framework for utilizing 3D investigational product in this study.