September 30, 2024

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Rescheduling of Conclusion of Development and Commercialization Agreement of MultiStem® for ARDS in Japan with Nobelpharma

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 rescheduled the date of conclusion of a development and commercialization agreement ("Agreement") under the letter of intent for a development and marketing alliance in Japan for MultiStem®*1, a somatic stem cell regenerative medicine therapy for the treatment of acute respiratory distress syndrome (ARDS)*2.

Extended deadline for the scheduled date of conclusion of the definitive agreement
Before extension: End of September 2024
After extension: End of January 2025

As announced on September 9 in the press release titled "Agreement with the FDA on Pivotal, Global Phase 3 "REVIVE-ARDS" Clinical Trial", Healios has reached an agreement with the Food and Drug Administration (FDA) in the United States regarding the trial design and is steadily preparing to conduct the global Phase 3 trial. In Japan, based on the positive results of the Phase 2 study (ONE-BRIDGE study) already completed in Japan and the global Phase 3 study as a confirmatory study, we are consulting with the regulatory authorities to submit an application for conditional and time-limited approval.

Healios has decided to reschedule the period of time until the conclusion of this agreement for the treatment of ARDS in Japan in order to continue discussions with Nobelpharma in light of the above-mentioned circumstances which have a significant impact on the direction of development and sales.

Future Outlook
This matter has no impact on our consolidated financial results of the fiscal year ending December 31, 2024 at this time. We will promptly announce any matters that should be disclosed in the future.

Reference:
"Announcement of Letter of Intent with Nobelpharma for the Development and Commercialization of HLCM051 for ARDS in Japan", announced on December 27, 2023.
"Extension of the Term of the Letter of Intent with Nobelpharma for the Development and Commercialization of MultiStem® for ARDS in Japa", announced on June 28, 2024.

*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.

*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