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Decision to Apply for Conditional and Time-Limited Approval for ARDS in Japan and ARDS Development Strategy Update

HEALIOS K.K. ("Healios") today announces that as disclosed in our press release "Agreement with the FDA on Pivotal, Global Phase 3 "REVIVE-ARDS" Clinical Trial" on September 9, 2024, we have reached an agreement with the FDA (Food and Drug Administration) to conduct a pivotal, global Phase 3 trial (the "REVIVE-ARDS" study) of MultiStem®*1 for acute respiratory distress syndrome (ARDS*2), mainly in the United States, and are preparing for the start of the trial.

In Japan, based on the positive results of the Phase 2 study (ONE-BRIDGE study*3) completed in Japan and the Phase 2 study (MUST-ARDS study) completed in the U.S. and the U.K., and on the premise that the above-described REVIVE-ARDS study will be conducted as a confirmatory study, Healios has decided that it will submit an application for conditional and time-limited approval (hereinafter referred to as the "Application") in Japan. As a result, the previously planned Phase 3 trial in Japan, for which an IND (investigational new drug) plan notification had been submitted, is no longer required and will be cancelled.

Healios will proceed with formal consultations with the regulatory authorities and make preparations for filing the relevant Application as soon as possible. Details will be announced when they are finalized, along with those related to the start of the global Phase 3 trial in the U.S.

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.

*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 ONE-BRIDGE Study
A Phase 2 clinical trial that tested MultiStem for patients with pneumonia-induced ARDS in Japan. In August and November 2021, Healios presented data on the endpoints at 90 and 180 days after treatment with the product, which showed positive results.