January 7, 2025

Company Name: HEALIOS K.K.
Representative: Hardy TS Kagimoto, Chairman & CEO
(TSE Growth Code: 4593)

Appointment of D.J. Skelton as an Advisor to Healios

HEALIOS K.K. ("Healios") announce that D.J. Skelton, former Special Assistant to the Assistant Secretary of Defense for Health Affairs of the U.S. Department of Defense, has been appointed Advisor to Healios, effective January 5, 2025.

1. Reason for Appointment

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*1) of MultiStem®*2 for acute respiratory distress syndrome (ARDS*3), mainly in the United States, and are preparing for the start of the trial. We are also working to promote the development of somatic stem cell regenerative medicines and iPSC regenerative medicines for the global launch of these products through collaborations, venture capital investments and government grants, etc. in the U.S.

D.J. Skelton graduated from United States Military Academy at West Point, and served in Afghanistan, where he was wounded but survived. Later, he served in the U.S. Army as a company commander and as a foreign area officer (China), and then as Military Advisor to Deputy Secretary of Defense and Special Assistant to the Assistant Secretary of Defense for Health Affairs. Mr. Skelton, who himself suffered from ARDS as well as near-fatal trauma (Phase 2 trial, MATRICS-1 study*4, is underway in the U.S.) after being attacked, understands firsthand the need for MultiStem, which is being developed by Healios.

Healios has invited Mr. Skelton, who has such a background and relationships, to join us as an advisor and he will help us promote our global drug development activities, especially in discussions with the U.S. government and in promoting cooperation with medical facilities conducting clinical trials.

2. Personal Record

Name	Record
D.J. Skelton	After graduating from United States Military Academy at West Point, he was dispatched to Afghanistan and attacked and hit by 13 bullets while serving, losing his left eye but surviving. He later served in the U.S. Army as a company commander and foreign area officer (China), and then as Military Advisor to Deputy Secretary of Defense and Special Assistant to the Assistant Secretary of Defense for Health and Human Services.

*1 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.

*2 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.

*3 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

*4 MATRICS-1 study
The 156-patient randomized, double-blind, placebo-controlled Phase 2 trial of MultiStem for

multiple organ failure/systemic inflammatory response syndrome (SIRS) due to trauma. Currently underway at the University of Texas Health Science Center at Houston (UTH) and Memorial Hermann Texas Medical Center, one of the top trauma centers in the United States, and funded almost entirely by the U.S. Department of Defense and the Memorial Hermann Foundation. The trauma being treated in this study is that which results from car accidents, industrial accidents, gunshot wounds, etc., and is the leading cause of death for people under the age of 45 and the leading cause of quality-of-life years lost. The use of MultiStem in the treatment of trauma also has meaningful potential US military applicability.

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