February 3, 2026

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# Start of ARDS Clinical Trial in Japan for the Global Phase 3 REVIVE-ARDS Study

HEALIOS K.K. submitted a clinical trial plan notification to the Pharmaceuticals and Medical Devices Agency (PMDA) on January 20, 2026, for a clinical trial to be conducted in Japan as part of the Global Phase 3 trial (REVIVE-ARDS*[1]) for HLCM051 (invimestrocel) for the treatment of ARDS*[2] (Acute Respiratory Distress Syndrome). We are pleased to announce that after the completion of the 14-day review by the PMDA, the preparation has been completed and the study is being initiated.

**Outline of REVIVE-ARDS Study**

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|---|---|
| Conditions | Placebo-Controlled, Double-Blind, Randomized<br>(IP administered within 48 hours of meeting ARDS diagnosis criteria) |
| Subjects | Patients with pneumonia-induced ARDS |
| Region | US, Japan, APAC, EU |
| Enrollment | Up to 550 (HLCM051 [n=275], placebo [n=275])<br>Interim analyses will be conducted at the 300-case and 400-case milestones. If IP demonstrates statistically significant efficacy at any interim analysis, the trial will be terminated early.<br>*Number of enrolled patients per region undetermined |
| Primary Endpoint | VFD (the number of days out of 28 during which a ventilator was not used for the patient) |
| Secondary Endpoint (examples) | Mortality (90 days after administration) |

Patient enrollment will begin after deliberations, etc. at the Clinical Trial Review Committee established at each investigational medical institution.

**Future Outlook**

This matter has no impact on our consolidated financial results of the fiscal year ending December 31, 2026. We will promptly announce any matters that should be disclosed in the future.

*1 REVIVE-ARDS
REVIVE-ARDS is a pivotal, global Phase 3 study to demonstrate and confirm the efficacy and safety of HLCM051 (invimestrocel) 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 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, 133,000[*d] patients in Europe, 670,000 patients in China[*e] and more than 1.1 million patients worldwide are affected.
(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

**About HEALIOS K.K.:**
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 and owns proprietary, global platforms utilizing both somatic stem cells and iPS cells.

In the somatic stem cell field, Healios is developing invimestrocel (HLCM051), a proprietary cell product comprised of multipotent adult progenitor cells ("MAPCs") derived from the

bone marrow of healthy adult donors. Invimestrocel 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. Healios is seeking to advance invimestrocel on a global basis for ARDS, ischemic stroke, and trauma.

In the iPSC regenerative medicine field, Healios is developing HLCN061, a next generation NK cell treatment for solid tumors that has been functionally enhanced through gene-editing. These cells have demonstrated robust anti-tumor efficacy in animal models, benefit from a scalable 3D bioreactor manufacturing process, and are currently being prepared for initial human testing in collaboration with Akatsuki Therapeutics. The company has also established a proprietary, gene-edited "universal donor" induced pluripotent stem cell line to develop next generation regenerative treatments in immuno-oncology, ophthalmology, liver diseases, and other areas of severe unmet medical need.

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