December 9, 2025


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| Representative: | Hardy TS Kagimoto, Chairman & CEO (TSE Growth Code: 4593) |
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# Development and Application Policy for HLCM051 (ARDS and Ischemic Stroke Treatment)

In the third quarter of the fiscal year ending December 2025 (announced on November 13, 2025), HEALIOS K.K. ("Healios") provided an update on target milestones related to HLCM051, including the conditional and time-limited approval application for ARDS (Acute Respiratory Distress Syndrome) and Ischemic stroke treatment, as well as the target timeline for initiating the global Phase 3 study for ARDS treatment (REVIVE-ARDS study*[1]). Based on our discussions with regulatory authorities and internal considerations, we have decided to proceed with the development under the policy outlined below.

We will prioritize the development of HLCM051 (invimestrocel) as a treatment for ARDS in the immediate near-term. In Japan, we plan to submit a clinical trial application for the global Phase 3 study in early 2026, and continue to prepare for the application for conditional and time-limited approval, subsequent regulatory approval, and product launch. The enrollment of the first patient in REVIVE-ARDS study is expected to take place in Japan. Following this, we will accelerate patient enrollment globally, with a focus on the United States.

Regarding the conditional and time-limited approval application for the Ischemic stroke treatment under the SAKIGAKE Designation System*[2] (Rolling Submission), we are continuing discussions with regulatory authorities on the details of the confirmatory study. However, considering the current status of discussions with regulatory authorities and the allocation of company resources, we have determined that it will not submit the application documents in a rolling submission format by the end of 2025 or early 2026. We will continue to engage with regulatory authorities and reevaluate our development policy to advance the treatment for acute ischemic stroke. Further details will be announced as decisions are made.

**Future Outlook**

This matter will have no impact on the Company's consolidated results for the fiscal year ending December 2025. We will promptly announce any matters that should be disclosed in the future.

*1 REVIVE-ARDS study

A pivotal, global Phase 3 study to demonstrate and confirm the efficacy and safety of 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 SAKIGAKE Designation System
This system is designed to promote the early practical application in Japan of innovative pharmaceuticals, medical devices, and regenerative medical products that are being developed 3 ahead of the rest of the world and are expected to demonstrate significant efficacy in the early stages of clinical trials. The program aims to accelerate their implementation through various forms of support, including prioritized consultation and review processes for regulatory approval. As part of this system, a rolling submission allows for the phased submission of clinical trial data and documentation as they become available, unlike the conventional one-time submission process. This enables the regulatory review process to proceed concurrently, potentially reducing the time to approval.