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# Next Clinical Trial for HLCM051 for ARDS

In developing a treatment for ARDS*[1], HEALIOS K.K. ("Healios") conducted a Phase II efficacy and safety trial for patients with pneumonia induced ARDS (trial name: ONE-BRIDGE) and is continuing discussions with the regulatory authorities to clarify the next steps to advance the program. At the end of February, Healios consulted with the Pharmaceuticals and Medical Devices Agency (hereinafter, "PMDA") regarding an additional trial, and now that we have reached a certain agreement on the outline of the trial necessary for data augmentation, we would like to inform you of the overview as follows:

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| Conditions | Placebo-Controlled, Double-Blind, Randomized |
| Subjects | Patients with pneumonia-induced ARDS<br>*Including Patients with pneumonia-induced ARDS caused by COVID-19 |
| Enrollment | 80 (HLCM051 [n=40], placebo [n=40]) |
| Primary Endpoint | VFD (the number of days out of 28 during which a ventilator was not used for the patient) |
| Secondary Endpoint (examples) | Mortality (180 days after administration) |

The trial protocol will be finalized upon the submission of a future IND.

In August and November 2021, Healios announced results for the evaluation items on the 90th and 180th days after administration of HLCM051 in ONE-BRIDGE, which showed favorable results in terms of efficacy and safety. Subsequently, Healios held a pre-application consultation with the PMDA to obtain guidance and advice on applying for approval. Although a certain level of agreement was reached on the efficacy and safety of the product, Healios received advice that the data package should be reinforced to apply for approval.

Further, in December 2022, Healios announced that it had entered into a Letter of Intent with Mitsubishi UFJ Capital Co., Ltd. (hereinafter, "Mitsubishi UFJ Capital") in relation to joint development being considered between the parties, the result of which would be funding to advance the next phase of ARDS clinical development. Healios and Mitsubishi UFJ Capital continue to work together to finalize the arrangements between the parties.

HLCM051 has been designated as an orphan regenerative medicine product for use in the treatment of ARDS by the Ministry of Health, Labor and Welfare in November 2019.

This matter has no impact on our business performance for the fiscal year ending December 2023 at this time. Healios shall promptly announce all future matters that require disclosure, including any potential impact on expenses associated with launching this clinical trial.

*[1] ARDS

ARDS is a general term for the symptoms of acute respiratory failure suddenly occurring in seriously ill patients. The major causes are severe pneumonia, septicemia, trauma etc. Inflammatory cells are activated in response to these diseases or injuries, causing damage to the tissue of the lungs. As a result, water accumulates in the lungs, leading to acute respiratory failure. According to the ARDS treatment guideline 2016, the mortality rate is approximately 30 to 58%. Artificial respiration using an endotracheal tube or mask is used to treat respiratory failure in an intensive care unit.

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