April 13, 2020

Company Name: HEALIOS K.K.
Representative: Hardy TS Kagimoto, Chairman & CEO
(TSE Mothers Code: 4593)
Contact: Richard Kincaid, Executive Officer CFO
(TEL: 03-5777-8308)

# COVID-19 ARDS patients added to Healios ONE-BRIDGE study

HEALIOS K.K. ("Healios") continues to make enrolment progress in its ONE-BRIDGE study, a phase II clinical trial in Japan evaluating the safety and efficacy of HLCM051[*1], a somatic stem cell regenerative medicine therapy, for pneumonia-induced Acute Respiratory Distress Syndrome (ARDS) [*2].

As announced on March 26, 2020, Healios has been in discussions with medical specialists and the Pharmaceuticals and Medical Devices Agency (PMDA) regarding the inclusion of pneumonia-induced ARDS patients infected with the novel coronavirus. We hereby inform you that we have decided to make a protocol change to the ONE-BRIDGE study to include these patients in the ongoing trial.

The ONE-BRIDGE study is designed to confirm the efficacy and safety of HLCM051 for patients with pneumonia-induced ARDS. The trial is conducted under non-blind conditions using standard therapy as a control. Prior to the protocol change, we planned to enroll 30 subjects, but in changing the protocol we will add an additional cohort to be evaluated within the same study and newly recruit an additional approximately five pneumonia-induced ARDS patients with COVID-19 as the causative disease and investigate the safety of the therapy in these patients.

We intend to verify the results of the approximately five newly added COVID-19 ARDS cases separately from the 30 originally planned ONE-BRIDGE patients. The addition of this COVID-19 cohort will have no effect on the progress of the originally planned clinical trial.

The overview of the trial is as follows:

| | Original clinical trial | Newly added cohort |
|---|---|---|
| Objective | Efficacy and safety evaluation | Safety evaluation |
| Subject | Patients with pneumonia-induced ARDS | Patients with pneumonia-induced ARDS caused by COVID-19 |
| Enrolment | 30<br>(HLCM051: 20, Standard therapy: 10) | Approximately 5<br>(HLCM051:5) |

*1 HLCM051
HLCM051 is a somatic stem cell regenerative medicine product. Healios added it to its pipeline by signing an exclusive licensing agreement with the United States based Athersys, Inc. ("Athersys") in January 2016, whereby Healios acquired rights to develop and distribute Athersys' proprietary stem cell product MultiStem® to treat ischemic stroke in Japan. Further, in June 2018 Healios and Athersys expanded their collaboration broadly, and as part of this expansion Healios acquired the development and distribution licenses to use MultiStem to treat ARDS in Japan.

*2 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.

According to the data published on the initial group of cases of the new coronavirus (COVID-19) in Wuhan, 31 to 41.8% of hospitalized patients developed ARDS and ARDS complications were confirmed in 54 to 93% of fatal cases※1※2, indicating that ARDS is a major cause of mortality in COVID-19 patients.

※1 Zhou F, et al. Lancet. 2020 Mar 11. pii: S0140-6736(20)30566-3

※2 Wu C , et al. JAMA Intern Med. 2020 Mar 13. doi: 10.1001

(Note) As the above two reports studied the initial group of patients, the incidence rate and mortality of ARDS patients is expected to fluctuate depending on the current situation in each country.