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Chairman & CEO
(TSE Mothers Code: 4593)

Secondary Analysis from Athersys' Acute Respiratory Distress Syndrome Clinical Trial (MUST-ARDS)

HEALIOS K.K. ("Healios") is developing a new treatment for Acute Respiratory Distress Syndrome (ARDS) [*1] and Ischemic Stroke in Japan using the stem cell product HLCM051 (MultiStem®) [*2], for which the patent and licensing rights are held by Athersys, Inc ("Athersys").

In January 2019, Athersys announced positive results from its exploratory Phase 1/2 clinical study, named the MUST-ARDS study, investigating the use of MultiStem for patients suffering from ARDS. Dr. Geoff Bellingan, a principal investigator of the MUST-ARDS study, subsequently presented at the American Thoracic Society International Conference held in May 2019 and showed that subjects who had received MultiStem treatment exhibited different biomarker results in terms of inflammatory markers/cytokines from subjects who had not, which provided deeper insights into the consistent immunomodulatory effects of MultiStem.

<The results of MUST-ARDS study>

	MultiStem	Placebo
Mortality	25%	40%
Ventilator-free days (VFD)	12.9	9.2
ICU-free days	10.3	8.1

<In more severe ARDS patients>

	MultiStem	Placebo
Mortality	25%	50%
Ventilator-free days (VFD)	14.6	8.0
ICU-free days	11.4	5.9

Healios is conducting the ONE-BRIDGE study in Japan using MultiStem for patients suffering from pneumonia-induced ARDS, and its primary endpoint is the number of ventilator-free days (VFD) within a 28-day post-administration period.

Healios has performed a secondary analysis using the results of the MUST-ARDS study conducted by Athersys including only subjects who are as similar as possible to the subjects we are enrolling in the ONE-BRIDGE study. As detailed below, the analysis shows an even greater difference in the mortality rate and VFD between the subjects treated with MultiStem and subjects in the placebo-controlled group.

<Post-hoc analysis of patients in severe condition and pneumonia-induced ARDS>

	MultiStem	Placebo
Mortality	**20%**	50%
Ventilator-free days (VFD)	**14.8**	7.5
ICU-free days	**12.0**	5.0

Hardy TS Kagimoto, MD, CEO of Healios, commented as below:

"From the initial analysis of the MUST-ARDS study, with respect to the primary endpoint of VFD employed in the ONE-BRIDGE study that Healios is currently conducting, as well as mortality rate (which is not the primary endpoint), it has been announced that the group of subjects treated with MultiStem tends to exhibit more favorable outcomes, with the effect more pronounced in cases of patients with serious conditions. Moreover, our secondary analysis has shown that for pneumonia-induced ARDS patients, who are similar to the subjects we are enrolling in Healios' clinical trial, the difference in the favorability of outcomes is even more significant – a finding that increases our confidence in the ONE-BRIDGE study in Japan."

"ARDS still has no effective treatment today, despite the fact that severe cases of ARDS can quickly kill nearly half the patients afflicted with this condition. Our mission is 'To foster a Life Explosion that enriches the lives of people around the world.' Bolstered by this encouraging data, we will work even harder to deliver this treatment to many patients as soon as possible," concluded Dr. Kagimoto.

*1. Acute Respiratory Distress Syndrome (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. However, it is known that prolonged use of a ventilator worsens a patient's prognosis. There is demand for a new treatment for ARDS that will lead to improvement in patients' symptoms and prognosis.

*2. 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 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.

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