

April 4, 2022

Company Name: HEALIOS K.K.
Representative: Hardy TS Kagimoto, Chairman & CEO
(TSE Growth Code: 4593)
Contact: Richard Kincaid, Executive Officer CFO
(TEL: 03-5962-9440)

Completion of 365 Days Post-Administration Follow Up for TREASURE Study for Patients with Ischemic Stroke

HEALIOS K.K. (“Healios”) is currently conducting two clinical trials using stem cell product HLCM051^{*1} for ischemic stroke^{*2} (the “TREASURE” study) and acute respiratory distress syndrome (ARDS) patients in Japan. The TREASURE study is a placebo-controlled, double-blind, phase 2/3 trial designed to confirm the efficacy and safety of HLCM051 in treating patients with ischemic stroke. The TREASURE study began enrolling patients in November 2017 and the last patient was dosed in March 2021. As further announced in November 2021, the final patient's 365 day follow up physician’s visit to assess their functional status was anticipated to take place in March 2022. Healios is pleased to report that this event occurred as scheduled. Having completed the collection of this data, the engaged contract research organization can begin its process of preparing for the unblinding of the data, which will take place in May 2022. In the same month, Healios plans to announce top-line results.

In the TREASURE study, patients were randomized 1:1 to receive either a single intravenous infusion of HLCM051 or placebo within 18–36 hours of the onset of stroke. The primary efficacy endpoint is the proportion of subjects achieving an Excellent Outcome^{*3} at day 90. In addition, several secondary endpoints, such as the proportion of subjects achieving an Excellent Outcome at day 365, have also been set.

(Overview of the TREASURE study)

Trial	Placebo-controlled, double-blind, phase 2/3 efficacy and safety trial of HLCM051 (MultiStem [®]) in patients with ischemic stroke
Subjects	Ischemic stroke within 18 to 36 hours
Conditions	Placebo-controlled, double-blind

Enrollment	220 (HLCM051 [n=110], placebo [n=110], randomized)
Primary Endpoint	Proportion of subjects with an Excellent Outcome defined by functional assessments [Day 90]
Secondary Endpoints (examples)	Proportion of subjects with an Excellent Outcome defined by functional assessments [Day 365] Proportion of subjects exhibiting functional outcome throughout the range of mRS scores by shift analysis [Days 90 and 365]

This matter has no impact on our business performance for the fiscal year ending December 2022 at this time. Healios shall promptly announce all future matters that require disclosure.

^{*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} Ischemic Stroke

Ischemic stroke, which represents the most common form of stroke (70-75% of cases in Japan), is caused by a blockage of blood flow in the brain that cuts off the supply of oxygen and nutrients, resulting in tissue loss. In Japan, it affects approximately 230,000 to 330,000 patients per annum and is one of the leading causes of death and disability, with an estimated 37.9% of bedridden patients and 21.7% of persons who were in need of care being affected by ischemic stroke. Current approved treatments are limited to TPA, a clot dissolving agent, and mechanical reperfusion therapy, which are only available for use during a limited time frame post stroke onset.

^{*3} Excellent Outcome

Functional and neurological deficit and recovery following ischemic stroke are evaluated using three standard methods: the modified Rankin scale (mRS), the NIH stroke scale (NIHSS), and the Barthel Index (BI). “Excellent Outcome” is defined as achieving scores ≤ 1 on the mRS and on the NIHSS and a score ≥ 95 on the BI.

mRS

The mRS measures the degree of disability or dependence in the activities of daily living of people who have had a stroke or have a neurological disability due to other reasons. It is used to categorize the level of functional independence with reference to pre-stroke activities. The scale includes scores from 0 to 6, ranging from perfect health without symptoms of disability (i.e., a score of 0) to death (a score of 6). A lower score indicates a lower degree of disability.

NIHSS

The NIHSS is a systematic assessment tool that provides a quantitative measure of stroke-related neurologic deficit in the following areas: level of consciousness, facial paralysis, visual acuity and function, arm and leg motor function, limb coordination, language and speech, sensory loss, and other parameters. A higher score on the NIHSS indicates a higher degree of neurological impairment in a stroke patient. The score for each function ranges from 0 to 4, with 0 indicating normal function (i.e., no deficit) and 4 indicating complete impairment (Note that some functional assessments use a scale of 0–2, or 0–3). The total NIHSS score of the patient is calculated by adding the score for each element on the scale, based on the individual assessments; 42 is the highest possible score, which reflects the maximum disability of the patient in each category.

BI

The BI is a 100-point scale that is used to assess the ability of the patient to independently perform activities of daily living and to evaluate a range of different functions. These include the ability of the patient to walk, dress, feed, bathe, climb stairs, use a toilet, self-groom, and certain other metrics. The patient is evaluated for each activity to assess for independence, partial dependence, or complete dependence, and then, a score between 0 and 10 is assigned (10 points = independence, 5 points = partially dependent, and 0 points = completely dependent). The BI score ranges from 0 to 100; a score of 100 indicates no dependence on any activity, and a lower score indicates a greater need for assistance.

(Source) Prepared by Healios on the basis of materials provided by The Japan Stroke Society.