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HEALIOS K.K. REPORTS TOP-LINE RESULTS FROM TREASURE STUDY FOR ISCHEMIC STROKE

Preliminary results show evidence of therapeutic impact of HLCM051

HEALIOS K.K. ("Healios") has been conducting the TREASURE study to investigate the safety and efficacy of HLCM051[*1] (Multistem®) in patients with ischemic stroke[*2]. The study targeted patients with moderate to moderate-severe stroke (baseline NIHSS score 8-20), with administration of a single dose of HLCM051 intravenously within 18-36 hours from stroke onset. The trial was conducted at 48 sites in Japan and enrolled 206 patients.

Top-line Results

- Global Recovery[*3] (mRS[*4]<=2, NIHSS[*5] improvement>=75% and Barthel Index[*6]>=95) showed a statistically significant difference between the HLCM051 group and the placebo group at 365 days.
- Excellent Outcome[*7] (mRS<=1, NIHSS<=1 and Barthel Index>=95) was not significant at 90 or 365 days.
- There was evidence of improvement in measures of functional "independence" and good outcomes, such as mRS<=2 and Barthel Index >=95, associated with HLCM051 treatment.
- Overall, there was consistent improvement in essentially all measured functional outcomes over time through one year, suggesting long-term impact on and continued improvement in the quality of life of treated patients.
- There were no significant differences in safety outcomes, including mortality and adverse events between the treatment and placebo groups.

Comparison of results between the HLCM051 group and the placebo group at 365 days

	HLCM051	Placebo	p-value*
Global Recovery	27.9%	15.7%	p<0.05
Barthel Index >=95	35.6%	22.5%	P=0.05
Excellent Outcome	15.4%	10.8%	n.s.

Characteristics of TREASURE Patient Population

The TREASURE patient population was substantially older than Athersys' phase 2 "MASTERS-1" study population (and older than expected for the TREASURE study when designed) with moderately greater severity. The median age for TREASURE patients was 78 years old, compared to 63 years old in the MASTERS-1 study.

Due to these differences, compared to the MASTERS-1 population, slower recovery and difficulty to achieve “excellent or ideal” health status post stroke, as measured by Excellent Outcome, would be expected within the TREASURE patient group. At the same time, there would be particular clinical relevance in this population of measures of functional independence and good outcomes, such as mRS<=2 and Barthel Index>=95, and Global Recovery.

Overall, there was good balance between MultiStem and placebo patient groups.

	MultiStem	Placebo
N	104	102
Age, median	79	78
Sex (male)	53.8%	54.9%
Severity		
NIHSS, median	14.0	14.0
Reperfusion Status		
No Prior	46.2%	49.0%
Prior (tPA or MR)	53.8%	51.0%

Based on these top line results, Dr. Kiyohiro Houkin, President, Hokkaido University, the lead investigator in this clinical trial, commented:

“The median age of patients in the TREASURE study was 15 years older than the MASTERS-1 study conducted in the United States prior to this trial, which may explain the inability to clearly demonstrate effect measured by Excellent Outcome. On the other hand, it is important and significant that in the long-term evaluation, the effect of HLCM051 was shown by an index of functional independence using mRS and BI. We anticipate that ongoing analysis may further demonstrate the effectiveness of HLCM051.”

In addition, Dr. Hardy TS Kagimoto, Chairman and CEO of Healios, commented:

“We are delighted to have shown statistically significant benefit to stroke patients, in the largest cell therapy clinical trial ever run in Japan. I would like to express our gratitude to all the people who cooperated in the clinical trial in the midst of the coronavirus epidemic.

In this trial, multiple indicators suggest clinical improvement in the daily lives of stroke patients, and that the therapeutic benefit is maintained and promoted over the course of time. This marks an important milestone in the advancement of this cellular medicine for patients affected by stroke, which is a leading cause of death and disability in Japan. We will take this compelling evidence forward into the regulatory process and work tirelessly towards gaining approval as soon as possible.”

The results are preliminary figures at present, and we will continue to analyze the clinical trial data in detail and proceed with discussions with the regulatory authorities in relation to filing and approval, leveraging the framework of the SAKIGAKE designation system.

This matter has no impact on our business performance for the fiscal year ending December 2022. 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] Global Recovery
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). "Global Recovery" is defined as achieving scores ≤2 on the mRS, NIHSS improvement >=75% and a score ≥95 on the BI. A Global Recovery assessment using multivariate, correlation adjustment, was the primary endpoint in Athersys's Phase 2 MASTERS-1 study run in the United States and Europe, and in this study, Global Recovery was set as a secondary evaluation item.

*[4] 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. In this study, mRS was set as a secondary evaluation item.

*[5] 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. In this study, NIHSS was set as a secondary evaluation item.

*[6] Barthel Index
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. In this study, BI was set as a secondary evaluation item.

*[7] 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. In this study, Excellent Outcome was set as the primary evaluation item.

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

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