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Company:	CYBERDYNE Inc.
Name of Representative:	Yoshiyuki Sankai, President and CEO
Code:	7779 (Mothers Section of the Tokyo Stock Exchange)
Contact:	Shinji Uga, Director and CFO (Tel. +81-29-869-9981)

【News】 Preliminary results of Medical HAL Lower Limb Type stroke clinical trial

CYBERDYNE Inc. (Tsukuba, Ibaraki, Japan, CEO Yoshiyuki Sankai, from now on referred to as "the Company") announces its assessment on the results of the analysis of the investigator-initiated clinical trial (from now on referred to as "the Trial") on its product HAL for Medical Use Lower Limb Type (Single-leg model). The Trial's objective was to obtain clinical data necessary for medical device approval as a product intended to improve the walking ability and other movements of hemiplegic stroke patients.

The Trial was a multicenter, randomized, open-label, controlled trial from May 2016 to December 2020. It included 52 patients with hemiplegia due to stroke. The Trial was designed as an investigator-initiated clinical trial to examine the efficacy and safety of a gait training program with HAL (single-leg type) to improve lower limb and trunk motor skills and ultimately enable the patient to walk without the device at the end of the program.

In the investigators' additional in-depth analyses of the results in which the study population excluded subjects who experienced adverse events that could significantly affect the results of their endpoint measurements, the changes from pre-treatment to post-treatment in the 6-minute walking distance, which is an important outcome measure to evaluate improvements in walking ability, showed a statistically significant difference favoring the efficacy of HAL (single leg type) Treatment over conventional gait rehabilitation.

The 10-meter maximum walking speed, which was the primary outcome measure planned for this trial, was discovered to have concerns about bias effects (*) that may have affected the results, and was deemed to be an inappropriate efficacy index to evaluate the efficacy of treatment with HAL on improving gait function. Since the 6-minute walking distance, a secondary endpoint, was less affected by these bias effects, it was considered more suitable for this trial's objective of comparative evaluation of the impact of treatment with HAL to that of conventional gait rehabilitation on improving gait function.

Since the clinical trial also verified sufficient safety of HAL, the Company will consult with the regulatory authorities (PMDA) and prepare an application for manufacturing and marketing approval of HAL as a medical device for stroke patients in Japan. The Company also believes that the results of this clinical trial are useful for applications for medical insurance in other countries.

*Explanation of bias effects in this study

During this clinical trial, a situation occurred raising concern of bias effects on the primary endpoint, which was the 10m maximum walking speed. This concern was not foreseen at the planning phase, and became clear during the post-analysis report. In the statistical analysis of the two groups in the 10m maximum walking speed, it was discovered that there was large variance in the change in speed from pre-treatment to post-treatment within the assigned groups, and it was thought to be important to consider possible bias effects that could lead to such a large variance. One of the factors that may have contributed to this effect was the selection criteria for secondary enrollment in this study. Enrollments were limited to patients with a 10-meter maximum walking speed in the range of 30-60 m/min at the last measurement in the previous observation period, so the same evaluation test was used for the selection method and the primary endpoint. As such, selection bias and assessment bias may have occurred simultaneously, and therefore the 10-meter maximum walking test in this study is thought to be inadequate for evaluating the effect of improving gait function. The results for this outcome measure showed greater improvements in the HAL group than the conventional gait rehabilitation group, but with this bias effect of high variance, the difference was not sufficient to show statistical significance. On the other hand, since the investigator did not include the 6-minute walking distance measurement in the criteria for secondary enrollment, it was less prone to selection bias and evaluation bias as an endpoint and was therefore more appropriate for evaluating the effect of improving walking function in hemiplegic patients.