Otsuka Medical Devices Co., Ltd.
ReCor Medical, Inc.

Otsuka Medical Devices REQUIRE Trial Results Presented at Japan Society of Hypertension Annual Meeting

REQUIRE trial results published in Hypertension Research journal and simultaneously presented at Japanese Society of Hypertension (JSH) 43rd Annual Meeting

Palo Alto, Calif. – 15 October, 2021 - Otsuka Medical Devices Co., Ltd. (OMD) a subsidiary of Otsuka Holdings, Inc., and its subsidiary, ReCor Medical, Inc. ("ReCor"), today announced that the findings from the REQUIRE trial of ReCor's Paradise™ Ultrasound Renal Denervation System for the treatment of hypertension conducted in Japan and Korea were presented at the Japanese Society of Hypertension (JSH) meeting and published simultaneously in the *Hypertension Research* journal. The trial, "Catheter-based ultrasound renal denervation in patients with resistant hypertension: the randomized, controlled REQUIRE trial," was conducted by OMD and its affiliate.

REQUIRE assessed the change in 24-hour ambulatory systolic blood pressure from baseline to 3 months in renal denervation and sham control groups. REQUIRE did not show a significant difference in blood pressure reduction between the two groups, and therefore did not meet its primary efficacy endpoint. There were no significant differences in adverse events in the renal denervation and sham groups, demonstrating no difference in safety risk.

"The lack of difference in blood pressure reductions between the renal denervation and sham groups, and in particular the blood pressure reduction in the sham group, were not what we expected," said Professor Kazuomi Kario, M.D., REQUIRE principal investigator. "After in-depth analysis, we determined that the lack of effective medication stabilization and adherence control confounded the efficacy signal in both the treatment and sham groups. This, and other important insights from the REQUIRE study are being taken into account as we design a future study of the Paradise System in Japan."

"The REQUIRE results were not in line with the positive results we have observed in other trials with the Paradise System," said Michael Weber, M.D., Professor of Medicine at SUNY Downstate College of Medicine. "As demonstrated in both RADIANCE-HTN SOLO and TRIO – two randomized, sham-controlled studies that met their blood pressure reduction primary endpoints – study design controls that reinforce medication adherence are necessary to reduce the variability of blood pressure results in both treatment and sham groups and are critical to assessing the true treatment effect in these trials. The REQUIRE study design did not standardize medications nor objectively measure adherence, which we believe thus caused the lack of a positive efficacy signal."

"Based on the results from the RADIANCE-HTN SOLO and TRIO trials, the Paradise System has demonstrated a significant and clinically meaningful blood pressure reduction in a range of patients with uncontrolled hypertension," said Andrew M. Weiss, President and CEO, ReCor Medical. "After intense review from our advisors, we understand that inadequate medication control in REQUIRE likely caused the lack of an efficacy signal in that study."

"Otsuka Medical Devices, ReCor and our scientific advisors are working to design a new randomized trial of the Paradise System in Japan," commented Noriko Tojo, President of OMD. "Based on the strong positive results from RADIANCE-HTN SOLO & TRIO, the root cause assessment of the REQUIRE efficacy signals, and the strong REQUIRE safety results, we are working with the Japanese regulatory authorities to plan a new randomized, controlled trial in uncontrolled, 'on-med' hypertension patients."

The Paradise System bears the CE mark in Europe and is an investigational device in the United States. The Paradise System is currently under investigation in the United States and Europe in the on-going FDA IDE pivotal study (RADIANCE-II) in patients with uncontrolled hypertension, with anticipated enrollment completion in 2022.

Hypertension is the leading contributor to disease burden worldwide, leading to increased cardiovascular morbidity and mortality, poorer quality of life, and increased cost to health systems.

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