Medtronic Announces New SPYRAL HTN Global Clinical Trial Program for Renal Denervation

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DUBLIN - April 1, 2015 - Medtronic plc (NYSE:MDT) today announced the initiation of the SPYRAL HTN Global Clinical Trial Program, a unique, phased clinical program studying renal denervation in uncontrolled hypertension. This announcement follows investigational device exemption (IDE) approval by the U.S. Food and Drug Administration (FDA). The program will begin with two global studies designed to address the confounding factors encountered in the SYMPLICITY HTN-3 clinical trial, including medication, patient population and procedural variability, to ensure the clinical potential of the therapy is evaluated.

Physicians in both studies will perform renal denervation with Medtronic's next-generation renal denervation technology, composed of the highly flexible 6 Fr compatible, multi-electrode Symplicity Spyral(TM) catheter and Symplicity G3(TM) radiofrequency (RF) generator. The Symplicity Spyral catheter and G3 generator are investigational in the United States and Japan.

"Medtronic believes the underlying science behind renal denervation is strong and that there is a clear unmet need for people with uncontrolled hypertension. Therefore, we remain committed to exploring the clinical potential of renal denervation in this population," said Jason Weidman, vice president and general manager, Medtronic Coronary and Renal Denervation, within Medtronic's Coronary and Structural Heart business. "To get to this point, we've performed extensive analyses and conducted additional pre-clinical testing following the SYMPLICITY HTN-3 trial. We've also consulted with the FDA and reimbursement bodies, and partnered with renowned thought-leaders worldwide to develop this novel clinical trial protocol."

The principal investigators for the initial two global studies represent some of the most experienced renal denervation specialists, including: Michael Böhm, M.D., Ph.D., chairman, Department of Internal Medicine, University of Saarland in Homburg/Saar, Germany; David Kandzari, M.D., director and chief scientific officer, Piedmont Heart Institute in Atlanta, Ga.; Kazuomi Kario, M.D., chairman, Department of Cardiovascular Medicine, Jichi Medical University School of Medicine in Tochigi, Japan; and Raymond Townsend, M.D., director of the hypertension program, University of Pennsylvania.

The SPYRAL HTN Global Clinical Trial Program includes two global, prospective, randomized, sham-controlled trials conducted simultaneously by experienced proceduralists to investigate the impact of renal denervation both in the absence of and in the presence of antihypertensive medications. The SPYRAL HTN-OFF MED and SPYRAL HTN-ON MED studies will each include approximately 100 patients with moderate- to high-risk hypertension, as opposed to the severe, treatment resistant population studied in the SYMPLCITY HTN-3 trial. These studies will be conducted at approximately 20 centers in the U.S. and other global geographies.

The SPYRAL HTN-OFF MED study is designed to isolate the effect of renal denervation on blood pressure reduction. Similar to the traditional design of antihypertensive pharmaceutical clinical trials, this approach was recommended by both the FDA and the global clinical community.

Separately, the SPYRAL HTN-ON MED study will evaluate the effect of renal denervation on blood pressure in the presence of antihypertensive medication. Unlike the SYMPLICITY HTN-3 trial, which enrolled patients with very high blood pressure that was not controlled despite an average of five antihypertensive medications at maximum tolerated dosages, the SPYRAL HTN-ON MED study requires patients who, despite use of drugs from three of the most common classes of medications prescribed for hypertension, do not achieve adequate blood pressure control. These drugs are not required to be prescribed at maximum tolerated medication dosages, a factor which may have contributed to variability in patient adherence and the large number of medication changes during the SYMPLICITY HTN-3 trial. Additionally, patient

medication adherence will be closely monitored and there will be a focus on ambulatory blood pressure monitoring (ABPM) to ensure consistency between both arms of the on- and off-medication studies.

"Studying patients both on and off medication in a less severe and more homogenous population than we saw in the SYMPLICITY HTN-3 trial is critical to gaining clarity on the true effect of this therapy," said Dr. Townsend. "By specifying medication classes and not requiring maximum tolerated doses, we can expect medication variability to be reduced, which will allow for a more controlled assessment of the impact of renal denervation in the presence of medication."

Based on the outcomes of these two initial studies of the SPYRAL HTN Global Clinical Trial Program, Medtronic will evaluate next steps for a pivotal study to support a pre-market application (PMA) submission to the FDA and Shonin submission in Japan.

"With this clinical program, Medtronic continues to make significant contributions to the field of renal denervation," Prof. Böhm added. "Not only will these data add to the scientific basis for renal denervation at large, but if we see positive outcomes, it will help reinforce what many physicians have experienced in their practice, and will provide even more confidence to support continued use of the therapy in geographies where the technology is currently available."

In collaboration with leading clinicians, researchers and scientists, Medtronic offers the broadest range of innovative medical technology for the interventional and surgical treatment of cardiovascular diseases and cardiac arrhythmias. The company strives to offer products and services that deliver clinical and economic value to healthcare consumers and providers worldwide.

About Medtronic

Medtronic plc (www.medtronic.com), headquartered in Dublin, Ireland, is the global leader in medical technology - alleviating pain, restoring health, and extending life for millions of people around the world.

Any forward-looking statements are subject to risks and uncertainties such as those described in Medtronic's periodic reports on file with the Securities and Exchange Commission. Actual results may differ materially from anticipated results.

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