Medtronic Initiates Study Evaluating Potential of Combination of Pulmonary Vein Isolation and Renal Denervation for Atrial Fibrillation

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Enrollment Underway in the U.S. for Groundbreaking Study Involving Three Medtronic Devices: Arctic Front Advance(TM) Cryoballoon, Symplicity Spyral(TM) & Reveal LINQ(TM) ICM

DUBLIN - April 30, 2015 - Medtronic plc (NYSE: MDT) today announced the start of a clinical study using Medtronic technologies to determine whether paroxysmal and persistent atrial fibrillation (AF) can be treated with a combination of two ablation procedures targeting different anatomical locations - specifically, the pulmonary veins and the renal arteries. Study patients will also receive an implantable cardiac monitor to track their heart rhythm on an automatic and continuous basis. AF is a cardiac rhythm disorder affecting an estimated 2.7 million people in the U.S.

SYMPLICITY AF is a prospective, randomized, multi-center, feasibility clinical study investigating pulmonary vein isolation (PVI) and renal denervation compared to PVI alone, for the treatment of paroxysmal or persistent AF in patients with both AF and hypertension. PVI will be performed with the Arctic Front Advance(TM) Cardiac Cryoablation system, and renal denervation will be performed with the Symplicity Spyral(TM) catheter and Symplicity G3(TM) radiofrequency (RF) generator. The Symplicity Spyral catheter and G3 generator are investigational in the United States.

Patients in both arms of the trial also will receive a Reveal LINQ(TM) Insertable Cardiac Monitor (ICM) to automatically and continuously detect and record the net recurrence of abnormal heart rhythms after therapy randomization. This more comprehensive method of cardiac monitoring will provide greater detail and accuracy about the treatment effect of combination therapy with PVI and renal denervation versus PVI alone. Emile G. Daoud, M.D., at The Ohio State University Wexner Medical Center enrolled the first patient in the trial.

"Hypertension is one of the most prevalent risk factors for developing AF, but we've seen that it is also potentially the most modifiable risk factor for halting the progression of the disease," said principal investigator Larry Chinitz, M.D., director, Heart Rhythm Center, NYU Langone Medical Center in New York. "As we continue to look for ways to prevent AF recurrence and improve outcomes for patients with AF, this trial may reveal a potential new treatment path for patients."

Studies have shown that an overactive sympathetic nervous system (SNS) contributes to the development of both hypertension and AF. Current AF therapies do not specifically address SNS over activity and historically have focused on maintenance and regulation of rate and rhythm as well as anti-coagulation to prevent stroke. Renal denervation has been shown to effectively reduce elevated SNS activity[1], and previous research has signaled that renal denervation combined with PVI may improve patient response to PVI in AF patients.[2]

SYMPLICITY AF will enroll up to 245 patients in up to 12 centers throughout the United States. Seventy of these patients meeting all inclusion but no exclusion criteria and thus determined to be eligible for the trial will then be randomized to either PVI and RDN or PVI alone; all randomized subjects will receive a Reveal LINQ ICM. The primary safety endpoint is comprised of events related to both the PVI and RDN procedures. The primary efficacy endpoint will measure freedom of chronic treatment failure, defined as AF lasting 30 seconds or longer or the requirement for an intervention for atrial fibrillation through a minimum of six months. Heart rhythm data from the Reveal LINQ ICM will be reviewed monthly.

Enrollees in the trial include patients with either paroxysmal or persistent AF, and hypertension defined as office-based systolic blood pressure of >=150 mm Hg, despite treatment with two or more antihypertensive medications at the highest appropriate dose. AF is considered paroxysmal, or occasional, when the upper chambers of the heart beat erratically

during self-terminating episodes lasting from a few minutes to a few days. AF is considered persistent when symptoms persist for more than seven days and medical intervention is needed to terminate the episode.

The study will also gather feasibility outcomes data on the use of the Arctic Front Advance Cardiac Cryoablation Catheter for PVI in the persistent AF population. The Arctic Front Advance Cardiac Cryoablation system is not approved in the United States for the treatment of persistent AF; therefore, it is considered investigational in this patient population.

"The SYMPLICITY AF study, investigating three of Medtronic's notable technologies, is a groundbreaking effort and an excellent example of our commitment to driving clinical benefit through innovation," said Michael J. Coyle, executive vice president and president of Medtronic's Cardiac and Vascular Group. "Only Medtronic has the breadth and depth of cardiac-related technology to investigate new treatment and disease management strategies in this unique manner for some of the most difficult-to-treat conditions, such as AF."

About Medtronic Arctic Front Advance CryoAblation Catheter System

Treatment with the Medtronic Arctic Front Advance Cryoballoon System involves a minimally invasive procedure in which the cryoballoon fills with coolant to ablate (freeze) the tissue where the pulmonary veins enter the left atrium, blocking the abnormal electrical signals that trigger erratic heart rhythms. Delivered via a catheter, the cryoballoon technology has been associated with faster procedure times than point-by-point radiofrequency ablation.

In the United States, cryoablation is FDA-approved for patients with drug refractory, recurrent, symptomatic, paroxysmal AF; it is not approved for patients with persistent AF. Cryoablation has been shown to deliver better outcomes in paroxysmal AF patients for whom at least one drug therapy has previously failed. Worldwide, the system has been used to treat more than 120,000 patients in approximately 1,000 centers across 50 countries.

About Medtronic's Symplicity Spyral Catheter and G3 Generator

Medtronic's renal denervation technology consists of the Symplicity Spyral multi-electrode catheter and the Symplicity G3(TM) RF Generator. Treatment involves a minimally invasive endovascular procedure, where the physician inserts the small, flexible Spyral catheter into the femoral artery in the upper thigh and threads it into both renal arteries in turn. Once the catheter is in place within the renal artery, the G3 generator is activated to deliver controlled, low-power radio-frequency (RF) energy, according to a proprietary algorithm aiming to deactivate the surrounding renal nerves for the goal of reducing the increased activity of the sympathetic nervous system. The Spyral catheter uniquely offers physicians control and flexibility with the ability to turn specific electrodes on and off to accommodate different anatomies. The next generation system is based on Medtronic's single-electrode Symplicity renal denervation system, which has an established safety profile.

About Medtronic's Reveal LINQ Insertable Cardiac Monitor (ICM)

Cleared by the Food and Drug Administration (FDA) in 2014, the Reveal LINQ ICM System is the newest generation of ICM and the smallest cardiac monitor available (~1 cc, or one-third the size of a AAA battery). Common uses include monitoring syncope patients for potential episodes of bradycardia/asystole, monitoring cryptogenic stroke (strokes of unknown cause) patients for possible episodes of AF, and monitoring patients suffering from intermittent chest palpitations for potential episodes of atrial or ventricular arrhythmias. The Reveal LINQ ICM is inserted under the skin of the chest (incision less than 1-cm), and its battery allows for up to three years of monitoring. Additionally, the device communicates wirelessly with a patient bedside monitor that uploads device data to the Medtronic CareLink® Network.

In collaboration with leading clinicians, researchers and scientists worldwide, Medtronic offers the broadest range of innovative medical technology for the interventional and surgical treatment of cardiovascular disease and cardiac arrhythmias.

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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[1] Kaltenbach B, Franke J, Bertog SC, Steinberg DH, Hofmann I, Sievert H. Renal sympathetic denervation as second line therapy in mild resistant hypertension - a pilot study. Catheter Cardiovasc Interv. 2013 Feb;81(2):335-9.

[2] Pokushalov E, Romanov A, Corbucci G, et al. A randomized comparison of pulmonary vein isolation with versus without concomitant renal artery denervation in patients with refractory symptomatic atrial fibrillation and resistant hypertension. J Am Coll Cardiol 2012; 60: 1163-1170.

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