THE MEDTRONIC HARMONY™ TRANSCATHETER PULMONARY VALVE (TPV) CLINICAL STUDY

Clinical Protocol Summary

This material is provided strictly for physician use for potential participation in the Medtronic Harmony™ Transcatheter Pulmonary Valve Study.

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<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>The Medtronic Harmony™ Transcatheter Pulmonary Valve Clinical Study</th>
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<tbody>
<tr>
<td><strong>Design</strong></td>
<td>Multi-center, prospective, non-randomized, interventional, pre-market</td>
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<td><strong>Purpose</strong></td>
<td>To evaluate the safety and effectiveness of the Harmony™ TPV system</td>
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<td><strong>Number of Subjects</strong></td>
<td>Up to 40 subjects implanted at up to 15 study centers</td>
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<td><strong>Subject Population</strong></td>
<td>Patients who have congenital heart disease and are clinically indicated for pulmonary valve replacement</td>
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<td><strong>Primary Safety Endpoint</strong></td>
<td>Freedom from procedure- or device-related mortality at 30 days</td>
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**Primary Effectiveness Endpoint**

- Percentage of subjects with acceptable hemodynamic function composite at 6 months as defined by:
  - Mean RVOT gradient as measured by continuous-wave Doppler $\leq 40$ mmHg
  - Pulmonary regurgitant fraction as measured by magnetic resonance imaging $<20\%$

**Additional Outcome Measures**

- Technical success at exit from catheterization lab/operating room
- Device success out to 5 years
- Procedural success at 30 days
- Freedom from TPV dysfunction out to 5 years
- Assessment of safety
- Characterize quality of life scores over time
- Characterize right ventricle remodeling following TPV implant
Protocol Summary

Subject Evaluation
- Clinical assessment at pre- and post-implant, 1 month, 6 months, 1 year, and annually through 5 years
- Echocardiography at pre- and post-implant, 1 month, 6 months, 1 year, and annually through 5 years
- Cardiac magnetic resonance (CMR) at pre-implant, 6 months, 2 years, and 5 years
- CT cardiac angiography at pre-implant
- Fluoroscopy at implant, 1 month, 6 months, 1 year, and 5 years
- SF-36 at pre-implant, 1 month, 6 months, 1 year, and annually through 5 years

Inclusion Criteria
- Subject has pulmonary regurgitation as per one or more of the following criteria:
  - Severe pulmonary regurgitation as measured by Doppler echocardiography, or
  - Pulmonary regurgitant fraction ≥ 30% as measured by cardiac magnetic resonance imaging
- Clinical indication for surgical placement of a RV-PA conduit or prosthetic pulmonary valve per one or more of the following criteria:
  - Subject is symptomatic secondary to pulmonary insufficiency (e.g., exercise intolerance, fluid overload) as classified by the investigator, or
  - Right ventricular end diastolic volume index (RVEDVi) ≥ 150 mL/m², or
  - Subject has RVEDV: LVEDV Ratio ≥ 2.0
- Subject is willing to consent to participate in the study and will commit to completion of all follow-up requirements

Exclusion Criteria
- Anatomy unable to accommodate a 25 Fr delivery system
- Obstruction of the central veins
- Clinical or biological signs of infection including active endocarditis
- Planned concomitant procedure at time of implant
- Positive pregnancy test at baseline (prior to CT angiography and again prior to implant procedure) in female subjects of child bearing potential
- Patients with right ventricular outflow tract obstruction (RVOTO) lesions surgically treated with an RV-PA conduit implant
- A major or progressive non-cardiac disease (e.g., liver failure, renal failure, cancer) that results in a life expectancy of less than one year
- Planned implantation of the Harmony™ TPV in the left heart
- RVOT anatomy or morphology that is unfavorable for device anchoring
- Known allergy to aspirin, heparin, or nickel
- Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
- Pre-existing prosthetic heart valve or prosthetic ring in any position
The figures below depict general guidance for device sizing based on CMR. Dimensions should be representative of the entire cardiac cycle. Final valve sizing will utilize CT imaging with tighter dimensional limits.

**Sizing**

- Distal MPA Perimeter: 63 - 110 mm, Average Diameter: 20 - 35 mm
- Mid MPA Perimeter: < 63 mm, Average Diameter: > 20 mm
- RVOT Perimeter: 63 - 126 mm, Average Diameter: 20 - 40 mm

**RVOT/MPA Short-Axis**
- Maximum Diameter
- Minimum Diameter
- Perimeter

**RVOT/MPA Long-Axis**
- RVOT/MPA Length: > 15 mm

**RVOT/MPA Length**
- RVOT Perimeter: 63 - 126 mm, Average Diameter: 20 - 40 mm

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**Clinical Study Sites**

- **Nationwide Children's Hospital**
  - 700 Children's Drive
  - Columbus, OH 43205
  - John Cheatham, MD
  - jcheatham@nationwidechildrens.org

- **Yale New Haven Hospital**
  - 12 York St.
  - Room LCI 302
  - New Haven, CT 06610
  - Jeremy Arnes, MD
  - jeremy.arnes@yale.edu

- **Mayo Clinic (Rochester MN)**
  - 200 First Street SW
  - Rochester, MN 55905
  - Allison Cateska, MD
  - cateska.allison@mayo.edu

- **The Children's Hospital of Philadelphia**
  - 3031 Civic Blvd.
  - CTBS 3111
  - Philadelphia, PA 19104
  - Matthew Gilliespie, MD
  - gilliespie@email.chop.edu

- **Primary Children's Hospital**
  - 81 N. Maria Capocchi Drive
  - Salt Lake City, UT 84113
  - Robert Gray, MD
  - robert.gray@utah.edu

- **Seattle Children's Hospital**
  - MS RC 2.820
  - PO Box 1221
  - Seattle, WA 98104
  - Tom Jones, MD
  - thomajones@seattlechildrens.org

- **Texas Children's Hospital**
  - 6621 Fannin Street
  - MC:19345-C
  - Houston, TX 77030
  - Horri Justin, MD
  - hjustin@texaschildrens.org

- **Ronald Reagan UCLA Medical Center**
  - 100 Medical Plaza
  - Santa Monica East
  - Los Angeles, CA 90026
  - Daniel Lew, MD
  - dlew@mednet.ucla.edu

- **Stanford Hospital & Clinics**
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  - Suite C2132
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