Innovations in Interventional Cardiology: Next Generation DES, Percutaneous Aortic Valve Replacement and Left Atrial Appendage Closure

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Disclosures

Employee
• Boston Scientific Corporation

Stockholder
• Boston Scientific Corporation
Minimally invasive devices are now being used to treat many cardiovascular conditions previously treated surgically or with chronic pharmacologic therapy.
Agenda

SYNERGY Bioresorbable Polymer Platinum Chromium Stent
LOTUS Transcatheter Aortic Valve
WATCHMAN Left Atrial Appendage Closure Device
Next Generation DES Attributes

- Deliverable, Visible, Trackable, Conformable
- Less Stent Thrombosis
- Shortened DAPT Requirement
- Low TLR, Low Clinical Symptom Recurrence
- Reduced Polymer Load
  - Abluminal Polymer
  - Bioabsorbable Polymer
- Reduced Drug Load
- Stent Delivery System
  - Stent Material
  - Thinner Struts
  - Modified Stent Geometry
SYNERGY design goal: Polymer and drug (Everolimus) gone within 6 months while achieving the same clinical efficacy as PROMUS Element.

- Ultra-thin layer of bioabsorbable polymer (PLGA) and drug are applied only to the abluminal surface of a very thin strut (0.0029”) PtCr Stent.
- Lowest coat weight of any DES currently on the market.
- Design may reduce the risk of ST and minimize the requirement for long-term DAPT.
Relative Drug Coating Weights Across Various DES Platforms

Low coating weight

Initial coat weight is minimized and the polymer resorbs over a period of 4-6 months
### Relative Strut Thickness with Synergy

<table>
<thead>
<tr>
<th>Generation</th>
<th>Stent</th>
<th>Strut Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>Cypher® Stent</td>
<td>0.140 mm (0.0055”)</td>
</tr>
<tr>
<td></td>
<td>TAXUS® Express® Stent</td>
<td>0.132 mm (0.0052”)</td>
</tr>
</tbody>
</table>
| 2nd        | Endeavor® Stent         | 0.091 mm (0.0036”) | Cobalt Chromium
|            | Xience V® Stent         | 0.081 mm (0.0032”) | Cobalt Chromium
|            | TAXUS® Liberté® Stent  | 0.096 mm (0.0038”) | Stainless Steel
|            | Xience Prime® Stent     | 0.081 mm (0.0032”) | Cobalt Chromium
| 3rd        | ION™ Stent              | 0.081 mm (0.0032”) |
|            | PROMUS® Element™ Stent  |                   |
| 4th        | SYNERGY™ Stent          | 0.074 mm (0.0029”) |

Data suggests that thinner strut stents have less inflammation and lower rates of restenosis.
**Study Objective:** To assess the safety and efficacy of the SYNERGY™ Everolimus-Eluting Coronary Stent System compared to the PROMUS® Element™ Stent

**Patient Population:** Symptomatic CAD and 1 or 2 de novo lesions up to 28 mm in length in a native coronary artery 2.25 mm to 3.5 mm in diameter

**Study Design:** Prospective, randomized, single blind, non-inferiority trial

**Primary Safety Endpoint:** TLF (TV-CD, TV-MI, TLR) at 30 days

**Primary Angiographic Endpoint:** In-stent late loss at 6 months

**Number of Patients:**
- SYNERGY Stent: n = 97
- SYNERGY Stent (half dose): n = 97
- PROMUS Element Stent: n = 97

**Number of Sites:** 29 (EU, Australia, New Zealand)

**Enrollment:** July 2010 – Jan 2011

*Anticipate presentation of results at TCT 2011*
Agenda

SYNERGY Bioresorbable Polymer Platinum Chromium Stent
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WATCHMAN Left Atrial Appendage Closure Device
PARTNER Trial
Primary Endpoint Cohorts A and B

- **Cohort A** – High Risk Patients
- Presented by Craig Smith, ACC 2011
- 1:1 TAVR vs surgical AVR
- Showed TAVR non-inferior to surgical AVR for primary endpoint of all-cause mortality at 1 year

- **Cohort B** – Inoperable Patients
- Presented by Marty Leon, TCT 2010
- 1:1 TAVI vs standard therapy
- Showed TAVI to be superior to standard therapy with regards to primary endpoint of all-cause mortality at 1 year
PARTNER Trial
Cohort A (High Risk Patients)

Procedural Outcomes - TAVR vs AVR

<table>
<thead>
<tr>
<th></th>
<th>AVR</th>
<th>TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternal wound infection - no. (%)</td>
<td>7 (2.0)</td>
<td>Access site infection - no. (%)</td>
</tr>
<tr>
<td>Total cross clamp time - min</td>
<td>74</td>
<td>Fluoroscopy time - min</td>
</tr>
<tr>
<td>Pump time - min</td>
<td>105</td>
<td>Converted to AVR - no. (%)</td>
</tr>
<tr>
<td>Multiple (≥2) valves - no. (%)</td>
<td></td>
<td>Multiple (≥2) valves - no. (%)</td>
</tr>
<tr>
<td>Valve embolization - no. (%)</td>
<td></td>
<td>Valve embolization - no. (%)</td>
</tr>
</tbody>
</table>

Rates of stroke and vascular complications higher with TAVR
Technically challenging procedure with relatively high rates of valve embolization (2.6%) and placement of multiple valves (2.0%)
Limitations of Current Devices

Provide patients with another option for AS treatment

• Difficult to position precisely
  – Too deep in the ventricle
    • Impingement of mitral valve
    • Damage to the conducting system
  – Too high in the aorta
    • Coronary occlusion

• Limited or no ability to reposition
• Cannot be recaptured and redeployed
• Perivalvular regurgitation is common
Background and Company Status

• Since 2007, Boston Scientific Corp. has been a strategic investor in Sadra Medical, Inc.

• Nov 19, 2010 - Boston Scientific entered into a definitive merger agreement with Sadra Medical

• Jan 4, 2011 – Boston Scientific completed acquisition of Sadra Medical.
Lotus Valve Components

Locking Mechanism (1 of 3)
Braided Nitinol Frame
Bovine Pericardium
Adaptive Seal
Lotus™ Valve Concept

Braided nitinol stent structure

• Radial expansion as it shortens
  ▪ Enables a more flexible delivery system
  ▪ Enables device repositioning or retrieval
  ▪ Provides significant radial strength
Advantages of the Lotus Valve System

Ease of Use
- System is pre-packaged on delivery system
- Two handle controls
  - 1 - deploy / retrieve and 2 - release
Advantages of the Lotus Valve System

- **Ease of Use**
- **Controlled Positioning**
  - Predictable, reversible deployment
  - Recapturable and retrievable at any point prior to release
  - Fully repositionable, both toward the ventricle or back into the aorta as needed
Advantages of the Lotus Valve System

• Ease of Use
• Controlled Positioning
• Accurate Placement
  – Center marker facilitates alignment with native valve
  – Valve leaflet function begins early during deployment
    • Hemodynamic stability
    • Enhances precision positioning
Advantages of the Lotus Valve System

• Ease of Use
• Controlled Positioning
• Accurate Placement
• Minimal perivalvular leakage
  – Adaptive™ Seal fills gaps between native valve and implant
Advantages of the Lotus Valve System

• Ease of Use
• Controlled Positioning
• Accurate Placement
• Minimal perivalvular leakage
• Percutaneous delivery
  – Proprietary Lotus Introducer Sheath provides access to \( \geq 6.0\text{mm} \) femoral vessels - equivalent to Cook 18F introducer
LOTUS Valve Clinical Program

• FIM (n=10) and Feasibility (n=12) studies already conducted using earlier iterations of the Sadra device
• CE Mark study
• US pivotal trial
Agenda

SYNERGY Bioresorbable Polymer Platinum Chromium Stent
LOTUS Transcatheter Aortic Valve
WATCHMAN Left Atrial Appendage Closure Device
**WATCHMAN® LAA Closure System Implanted Device**

**Frame:** Nitinol structure
- Available sizes:
  - 21, 24, 27, 30, 33 mm (diameter)
  - 10 Fixation barbs around device perimeter engage LAA tissue
  - Contour shape accommodates most LAA anatomy

**Fabric Cap:** (PET) Fabric Polyethyl terephthalate
- Prevents harmful emboli from exiting during the healing process
- 160 micron filter

Watchman device is deployed in the left atrial appendage, endothelializes over time and excludes the LAA from the circulation.

Hypothesis is that LAA closure with Watchman will reduce the incidence of thromboembolism in patients with AF.
Watchman Deployment
WATCHMAN Positioning
## Clinical Studies

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PATIENTS</th>
<th>SITES</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot</td>
<td>66</td>
<td>8</td>
<td>• 318 patient years of follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 30 patients with 5+ years of follow-up</td>
</tr>
<tr>
<td>PROTECT AF</td>
<td>800</td>
<td>59</td>
<td>• 1,500 patient years of follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 27 months average follow-up per patient</td>
</tr>
<tr>
<td>Continued Access Registry (CAP)</td>
<td>567</td>
<td>26</td>
<td>• Significantly improved safety results</td>
</tr>
<tr>
<td>ASAP</td>
<td>106</td>
<td>4</td>
<td>• Treat patients contra-indicated for warfarin</td>
</tr>
<tr>
<td>EVOLVE</td>
<td>50</td>
<td>3</td>
<td>• Evaluate next generation WATCHMAN®</td>
</tr>
<tr>
<td>PREVAIL</td>
<td>31</td>
<td>≤50</td>
<td>• Same endpoints as PROTECT AF</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Revised inclusion/exclusion criteria</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Initiate enrollment October 2010</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,620</strong></td>
<td></td>
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</table>
PROTECT AF Clinical Trial

• Prospective, randomized study of WATCHMAN® LAA Device vs. long-term warfarin therapy in patients with non-valvular AF and CHADS2 score ≥1

• 2:1 allocation ratio device to control

• 800 patients enrolled from February 2005 to June 2008
  ▪ 93 roll-in; 707 randomized

• 59 enrolling centers (U.S. & Europe)

• Follow-up requirements
  ▪ TEE follow-up at 45 days, 6 months and 1 year
  ▪ Clinical follow-up biannually up to 5 years
  ▪ INR monitoring every 2 weeks for 6 months and monthly thereafter

Intent-to-Treat: Primary Efficacy Results

Primary efficacy endpoint:
- stroke (ischemic or hemorrhagic)
- cardiovascular or unexplained death
- systemic embolism

<table>
<thead>
<tr>
<th>Cohort</th>
<th>WATCHMAN®</th>
<th>Control</th>
<th>Relative Risk (95% CI)</th>
<th>Posterior Probabilities</th>
<th>Non-inferiority</th>
<th>Superiority</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate (95% CI)</td>
<td>Rate (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>600 pt- yrs</td>
<td>4.4 (2.6, 6.7)</td>
<td>5.8 (3.0, 9.1)</td>
<td>0.76 (0.39, 1.67)</td>
<td>0.992</td>
<td>0.734</td>
<td></td>
</tr>
<tr>
<td>900 pt- yrs</td>
<td>3.4 (2.1, 5.2)</td>
<td>5.0 (2.8, 7.6)</td>
<td>0.68 (0.37, 1.41)</td>
<td>0.998</td>
<td>0.837</td>
<td></td>
</tr>
<tr>
<td>1065 pt- yrs*</td>
<td>3.0 (1.9, 4.5)</td>
<td>4.9 (2.8, 7.1)</td>
<td>0.62 (0.35, 1.25)</td>
<td>&gt;0.999</td>
<td></td>
<td>0.900</td>
</tr>
<tr>
<td>1350 pt- yrs</td>
<td>2.9 (2.0, 4.3)</td>
<td>4.2 (2.5, 6.0)</td>
<td>0.69 (0.42, 1.37)</td>
<td>&gt;0.999</td>
<td></td>
<td>0.830</td>
</tr>
<tr>
<td>1500 pt- yrs</td>
<td>3.0 (2.1,4:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.846</td>
</tr>
</tbody>
</table>

Results are consistent over time, demonstrating approximately a 30% reduction in primary efficacy, stroke and mortality risk

Presented by Holmes, MD, TCT 2010

*Published Results: Holmes D R et. Al, Lancet 2009;374:534-42
Intent-to-Treat: All Cause Mortality

<table>
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<tr>
<th>Cohort</th>
<th>WATCHMAN® Rate (95% CI)</th>
<th>Control Rate (95% CI)</th>
<th>Relative Risk (95% CI)</th>
<th>Posterior Probabilities*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Non-Inferiority</td>
</tr>
<tr>
<td>600 pt-yrs</td>
<td>3.4 (1.8, 5.4)</td>
<td>4.9 (2.3, 7.8)</td>
<td>0.69 (0.33, 1.66)</td>
<td>0.991</td>
</tr>
<tr>
<td>900 pt-yrs</td>
<td>2.9 (1.7, 4.4)</td>
<td>4.7 (2.5, 7.1)</td>
<td>0.61 (0.32, 1.32)</td>
<td>0.999</td>
</tr>
<tr>
<td>1065 pt-yrs*</td>
<td>3.0 (1.9, 4.5)</td>
<td>4.8 (2.8, 7.1)</td>
<td>0.62 (0.34, 1.24)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>1350 pt-yrs</td>
<td>3.1 (2.1, 4.4)</td>
<td>4.4 (2.6, 6.1)</td>
<td>0.70 (0.43, 1.36)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>1500 pt-yrs</td>
<td>3.2 (2.3, 4.5)</td>
<td>4.5 (2.8, 6.2)</td>
<td>0.71 (0.46, 1.28)</td>
<td>&gt;0.999</td>
</tr>
</tbody>
</table>

*No adjustment made for multiple comparisons

29% lower relative risk in WATCHMAN® Group

Presented by Holmes, MD, TCT 2010
*Published Results: Holmes D R et. Al, Lancet 2009;374:534-42
CAP Results versus Early and Late PROTECT AF: Progression of Procedural Success and Safety

Procedure Metrics

- **Implant Success (%):**
  - Early (n=271): 88%
  - Late (n=271): 91%
  - CAP (n=460): 95%

- **Procedure Time (Min):**
  - Early (n=271)
  - Late (n=271)
  - CAP (n=460)

- **P** values:
  - Implant success = 0.001*
  - Proc. time < 0.001*

Procedure Outcomes

- **Proc/Device Rel. Safety AE w/in 7 days**
  - Early (n=271)
  - Late (n=271)
  - CAP (n=460)
  - P=0.006*
  - P=0.018*
  - P=0.039*

- **Serious PE w/in 7 days**
  - Early (n=271)
  - Late (n=271)
  - CAP (n=460)

- **Proc. Rel. Stroke**
  - Early (n=271)
  - Late (n=271)
  - CAP (n=460)

*From tests for differences across three groups: early PROTECT AF (1st 50%), late PROTECT AF (2nd 50%), and CAP*

Reddy VY et al, Circulation AHA 2011
PREVAIL Study Overview

**Study Objective:** To provide additional information on the safety and efficacy of WATCHMAN LAA Closure Technology

**Study Design:** Prospective, randomized (2:1) study of WATCHMAN versus long-term warfarin therapy

**Scope and Duration:**
- Currently Enrolling
- Up to 475 patients (75 roll-in, 400 randomized) at up 50 U.S. Centers
  - 25% randomized patients must be enrolled by new operators

**Key entry criteria**
- Calculated CHADS$_2$ score of 2 or greater. Patients with a CHADS score of 1 may be included if any of the following apply:
  - Female age 75 or older
  - Baseline LVEF $\geq$ 30 and < 35%
  - Aged 65-74 and has diabetes or coronary artery disease
  - Aged 65 or greater and has congestive heart failure
Conclusions

Thromboembolism in AF is a major cause of morbidity and mortality
   – Although Oral Anticoagulation is Effective, many patients will not tolerate it
e   due to the risk of major bleeding

WATCHMAN LAA Closure Device occludes the Left Atrial
Appendage preventing embolism of LAA thrombi

- In Protect-AF (800 patients, 1500 patient-years of follow-up), the
device was non-inferior to oral anticoagulation in patients at high-risk
of thromboembolism with a trend toward improved outcomes

The PREVAIL, ASAP and EVOLVE trials will provide further
information on the safety and effectiveness of the device, the
indicated population and next generation technology