Agenda

• Unmet Clinical Need
  ➢ VVI(R) pacemaker
  ➢ Leadless pacemaker / S-ICD coordination

• Boston Scientific’s Leadless Pacing System

• Safety Considerations
  ➢ Performance criteria: contemporary pacemaker data
  ➢ Encapsulation and device replacement
  ➢ Implanter training

• Benefit-risk Considerations
Unmet Clinical Need

The unmet need for bradycardia therapy:

• Although contemporary VVI pacemakers have been shown to be safe and effective, the combination of a PG + endovascular lead may be associated with risks of:
  - Infection
  - Venous occlusion
  - Tricuspid regurgitation
  - Remedial actions that require lead extraction

• Avoiding the need for a lead directly connecting the subcutaneous space with the endovasculature may help mitigate risks
Unmet Clinical Need (cont.)

The unmet need for patients at risk of sudden death:

• For patients at-risk of SCD without an indication for pacing, an S-ICD may help avoid complications associated with a transvenous (TV) ICD lead

• S-ICD patients\(^1,2,3\) may develop a need for:
  - Pacing support (0.06%-2.4% per year)\(^4\)
  - ATP for recurrent monomorphic VT (0.4%-1.8% per year)\(^4,5\)

• Today, patients requiring ATP or pacing support have only TV options

• A leadless pacing system that could coordinate with an S-ICD offers an alternative to a TV system, while also avoiding the known risks of ICD leads

5. N=811; mean follow-up 45.5 months. Poole JE, Gold MR. Who should receive the subcutaneous implanted defibrillator? The subcutaneous implantable cardioverter defibrillator (ICD) should be considered in all ICD patients who do not require pacing. *Circ Arrhythm Electrophysiol.* 2013;6:1236-1245.
Boston Scientific - Key Components of Leadless Pacemaker System*

- **Pulse Generator**
- **Delivery**
- **Programmer**
- **Accessories**
- **Retrieval**

*Concept device or technology. Not available for sale.
Boston Scientific - Key Components of Leadless Pacemaker / S-ICD Coordinated System*

*Concept device or technology. Not available for sale.
1. Leadless pacemaker will sense and treat bradycardia independently from the S-ICD

2. ATP schemes are built into the leadless pacemaker, but can be activated only by the S-ICD or the programmer

3. S-ICD will continue to sense tachycardia, then command ATP in the leadless pacemaker prior to a shock

*Concept device or technology. Not available for sale.*
Use cases for a leadless pacemaker with the S-ICD:

A
- S-ICD implanted first
- Leadless pacemaker implanted later

B
- Leadless pacemaker implanted first
- S-ICD implanted later

C
- Leadless pacemaker + S-ICD implanted together

*Concept device or technology. Not available for sale.*
Leadless technology safety considerations include:

• Requirement for TV leads to:
  ➢ Pass an overall freedom from adverse event endpoint
  ➢ Show adequate performance with respect to individual adverse events

• Nature and severity of complications in TV pacing systems vs leadless pacemaker

• Physician and patient information to ensure appropriate risk awareness and avoidance

• Risk of adverse events with leadless pacemaker should be, at worst, comparable to TV pacemaker
• Perform a safety endpoint evaluation - compared aggregated rate of all device-related complications vs pre-defined performance goal
• Separately evaluate the components of this aggregated rate to ensure that each one is within the bounds of acceptability

*Boston Scientific envisions that a similar approach will be taken for leadless pacemakers as TV pacemakers*
Event-specific Performance Goals

Data collected from a recently completed large, long-duration TV brady lead trial* can serve as a comparative, contemporary dataset for traditional pacemakers

<table>
<thead>
<tr>
<th>Major System Complication¹</th>
<th>Observed Complication Rate through 24 Months²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Single-chamber PM (N = 213)</td>
</tr>
<tr>
<td>Perforation</td>
<td>0.0%</td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>0.6%</td>
</tr>
<tr>
<td>Dislodgment</td>
<td>1.4%</td>
</tr>
<tr>
<td>Embolization</td>
<td>0.0%</td>
</tr>
<tr>
<td>Other (e.g., infection, arrhythmia)</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

¹Definition matches what was used in Micra Trial
²24-month (BSC) versus 6-month observational period (Micra)

*Caution: Investigational Device. Limited by US law to investigational use only. Not available for sale.
Event-specific Performance Goals

Data collected from a recently completed large, long-duration TV brady lead trial* can serve as a comparative, contemporary dataset for traditional pacemakers

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<tr>
<th>Major System Complication</th>
<th>Observed Complication Rate through 24 Months$^2$</th>
<th>Single-chamber PM (N = 213)</th>
<th>Dual-chamber PM with RA Lead Excluded (N = 1143)</th>
<th>Total (N = 1356)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforation</td>
<td>0.0%</td>
<td>0.5%</td>
<td>0.4%</td>
<td></td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>0.6%</td>
<td>0.2%</td>
<td>0.2%</td>
<td></td>
</tr>
<tr>
<td>Dislodgment</td>
<td>1.4%</td>
<td>1.1%</td>
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<td></td>
</tr>
<tr>
<td>Embolization</td>
<td>0.0%</td>
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<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Other (e.g., infection, arrhythmia)</td>
<td>3.8%</td>
<td>5.1%</td>
<td>4.9%</td>
<td></td>
</tr>
</tbody>
</table>

$^1$Definition matches what was used in Micra Trial

$^2$24-month (BSC) versus 6-month observational period (Micra)

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Retrieval / Extraction Challenges - Encapsulation

**Canine Chronic Functional***
(90 days post implant)

**Ovine Chronic Functional***
(90 days post implant)

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Device Replacement Considerations

Clinician / Patient shared decision making related to options
Leadless delivery tools and techniques differ significantly

Boston Scientific has a long history of training physicians on novel technologies

- Endocardial ICD leads
- Cardiac Resynchronization Therapy
- S-ICD
- WATCHMAN

Phase I
Self-Study and Expectation Setting

Phase II
Professional Training Event

Phase III
Initial Cases and Building Confidence through Cadence

Phase IV
Transition to Independence
Benefit-risk Considerations

Benefit-risk considerations differ according to the clinical use:

• For VVI pacing, a well-established therapy already exists with excellent short- and long-term safety

• Intrinsic risks associated with endovascular leads connected to a subcutaneous pocket

• For appropriately selected patients at high risk of complications from endovascular leads, leadless pacing will offer a positive benefit-risk as long as the rate of life-threatening complications can be proven to be acceptably low
Benefit-risk Considerations (cont.)

For patients with an S-ICD who manifest a need for ATP or brady pacing, the benefit vs risk of a leadless pacemaker / S-ICD Coordinated System* needs to be evaluated against the alternative of device explant with implantation of a new TV-ICD.

For both of these scenarios, a patient-centered approach to individualized benefit-risk assessment will be of paramount importance.

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Complication Rates from TV Studies

Data from 8 prospective pre-market pacemaker lead approval trials\(^1\) (N=3761) were pooled to establish representative TV rates for various event types

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Weighted Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforation</td>
<td>0.3%</td>
<td>0.0 – 1.7%</td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>0.4%</td>
<td>0.0 – 1.1%</td>
</tr>
<tr>
<td>Dislodgment</td>
<td>1.5%</td>
<td>0.8 – 2.1%</td>
</tr>
</tbody>
</table>

\(^1\)Data source:
- Boston Scientific INGEVITY™ Active Fixation and Passive Fixation Pace/Sense Lead Clinical Study. 12-month Follow-up Clinical Report.*
- Medtronic Revo MRI™ SureScan™ Pacing System Clinical Study. Summary of clinical results.

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