Transcatheter Mitral & Tricuspid Therapies

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Corporate Vice President
We Will Lead and Transform Treatment for Patients with Mitral and Tricuspid Diseases

Mitral and Tricuspid Diseases are complex, varied and prevalent; patients are in significant need of safe and effective therapies

Multiple therapy options are needed; our portfolio strategy positions Edwards for leadership

Commitment to innovate across therapies, build practice-changing evidence, and drive therapy adoption

Expect the Global Mitral & Tricuspid Transcatheter opportunity to reach $1B+ by 2021 and ~$3B by 2024

Expect strong cadence of transformational therapies; 3 commercially available in Europe in 2019

PASCAL and EVOQUE not available for commercial sale
TMTT is Building on a Long History of Experience, Knowledge and Commitment

1960

First surgical mitral valve replacement
Starr-Edwards Silastic ball valve

1st surgical mitral and tricuspid annuloplasty rings

MONARC™ TMVR coronary sinus device

Developed 1st surgical mitral and tricuspid annuloplasty rings

1st TMVR project - percutaneous Alfieri stitch device

FORTIS™ TMVR with paddles to anchor valve to leaflet

Launch of the Carpentier-Edwards Physio tricuspid annuloplasty ring

First in human PASCAL Mitral Valve Repair System

Cardioband Tricuspid system CE marked

Today

EVOQUE first in human

Cardioband acquisition

SAPIEN M3 first in human

CardiAQ™ acquisition

FORMA first in human

TMVR Dock™ For use with commercial TAVR device

Mobius™ 1st TMVr project - percutaneous Alfieri stitch device

*1 Product not commercialized. FORMA, PASCAL, SAPIEN M3 and EVOQUE are not available for commercial sale.
Mitral and Tricuspid Patients are in Significant Need of Better Treatment Options

Mitral and Tricuspid Regurgitation are **prevalent and undertreated**

Patients experience **debilitating symptoms** and **high mortality rates**

- **Painful symptoms**
- **Frequent hospitalizations**
- **Ineffective medical management**

Mitral and Tricuspid Regurgitation: 4.5M U.S. Prevalence

Aortic Stenosis: 1.2M

<2% Treated

1. Sourced from Internal Models; 2. Addressable patient populations
Wide Range of Etiologies May Require Different Treatments for Optimal Patient Outcomes

**Tricuspid Regurgitation**
- Secondary (Functional)
  - Annular Dilation
  - Tethering
- Primary (Degenerative)

**Mitral Regurgitation**
- Mixed
  - Flail & Prolapse
  - Annular Dilation
- Secondary (Functional)
  - Tethering
- Primary (Degenerative)
  - Rheumatic & Other
  - Leaflet Prolapse

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TMTT is Building a Transcatheter-Based Portfolio to Optimally Treat All Patients

Developing world-class evidence across the portfolio with 5 early feasibility trials, 4 pivotal trials, and 3 EU post market follow-up studies in 2019
PASCAL: Advancing Leaflet Repair
EU Commercial Launch; Pivotal Trial Enrolling

**Innovation**

**Spacer** fills regurgitant area to reduce Mitral Regurgitation

**Clasps** allow for individual leaflet capture and ability to fine-tune leaflet position

**Broad, curved paddles** reduce stress on native leaflets

**Evidence**

*In early clinical experience at 6 months¹:

- 95% of patients with MR <2+
- Clinically significant quality of life improvements
- PASCAL shown to be safe and feasible in high risk / inoperable patients

100+ patients treated; positive outcomes

**2019**

**Clinical**

- CLASP IID DMR U.S. Pivotal Trial enrolling
- CLASP IIF FMR U.S. Pivotal Trial initiation expected in late 2019
- Tricuspid EFS enrolling

**Commercial**

- PASCAL Mitral European launch by mid-year

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CLASP IID Pivotal Trial Approved and Enrolling

Patients with Symptomatic Primary Mitral Regurgitation

- Patient not a candidate for mitral valve surgery (as assessed by Heart Team)
- Echo Evaluation by Core Lab: Suitable for MitraClip and/or PASCAL Implant?
  - Suitable for either PASCAL or MitraClip
  - Suitable for PASCAL only

2:1 Randomization n=300*

Edwards PASCAL n=200
MitraClip n=100
Edwards PASCAL

* Not including roll-in patients, up to 3 cases per site

Principal Investigators:

- Scott Lim – Interventional Cardiologist, UVA
- Robert Smith – Cardiac Surgeon, Baylor
- Linda Gillam – Echocardiologist, Morristown
Cardioband: Establishing Annular Reduction as First-Line Therapy for Functional Disease
Scaling Supply and Reducing Procedure Time

**Innovation**

- **Supra-annular** placement preserves native anatomy
- **Stepwise anchor deployment** enables individualized treatment based on valve anatomy
- Beating-heart procedure allows for **real-time confirmation of results**

**Evidence**

In early clinical experience from CE Mark Trials:

- Durable reduction of **MR** with significant quality of life improvements, sustained at 2 years\(^1\)
- Significant reduction in **TR** with clinically meaningful quality of life improvements, sustained at 6 months\(^2\)

**2019**

**Clinical**

- ACTIVE TR U.S. Pivotal Trial initiating in late 2019
- ACTIVE MR U.S. Pivotal Trial enrollment paused to evaluate trial design

**Operations & Innovations**

- Scaling to produce a stable supply
- Procedural time improvements

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1. Maisano, TCT 2018; 2. Nickenig, TCT 2018
EVOQUE & SAPIEN M3: Two Innovative Transfemoral Mitral Valve Replacement Platforms

Leveraging decades of experience in mitral valve replacement & transcatheter valve delivery…

...to target safe and effective replacement to eliminate mitral regurgitation

PERIMOUNT
Leading surgical mitral tissue valve

SAPIEN Platform
~3,000 transcatheter mitral procedures

FORTIS (internal)
Valve anchoring

CardiAQ (acquisition)
Transseptal valve delivery

EVOQUE

SAPIEN M3

EVOQUE and SAPIEN M3 not available for commercial sale
EVOQUE: Pursuing Safe & Effective Transfemoral Valve Replacement to Eliminate Mitral Regurgitation

Continued Clinical Learnings

**Innovation**

- Low-profile, Transfemoral delivery system with enhanced maneuverability and depth control
- **Low ventricular projection** preserves LVOT\(^1\)
- Unique anchoring mechanism respects native anatomy
- **Two valve sizes** integrating Edwards leaflet design and tissue treatment

**Evidence**

- **In early clinical experience:**
  - 100% MR grade 0-1+ in 12 consecutive patients followed to 1 yr\(^2\) with CardiAQ (first-gen device)
- **First EVOQUE cases successfully completed**

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1. Left Ventricular Outflow Tract; 2. Herrmann, TCT 2018

2019

Continued Early Feasibility Studies to drive future clinical and regulatory strategies
SAPIEN M3: Pursuing Safe & Effective Transfemoral Valve Replacement to Eliminate Mitral Regurgitation

U.S. Pivotal Trial

**Innovation**

Low-profile, Transfemoral easy-to-use delivery system

**Modified SAPIEN 3 29mm valve** leverages proven design

**Docking system** facilitates valve anchoring;

**Retrievability** allows for optimal device placement

**Evidence**

In 15 patient EFS early clinical experience:

- High technical success, 93% reduction of MR to 0 or 1+; no deaths from any cause at 30 days¹

Experience in 30+ patients

**2019**

Continued Early Feasibility Studies

Plan to initiate U.S. Pivotal Trial in late 2019

ⁱ Makkar, TCT 2018
**FORMA: Innovating Simple Leaflet Coaptation Therapy for Advanced Tricuspid Regurgitation**

**Continued Clinical Learnings**

**Innovation**

- Simple design allows for **short procedure times** and easy implantation

- **Spacer** allows for treatment of the most severe patients

- **Two sizes** provide treatment options for a wide range of patients

**Evidence**

*In 30 patients implanted with first gen device*¹:

- Significant sustained reduction of TR at one year

- Sustained cardiac function and quality of life improvements at one year

*Successful cases with updated device*

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¹. Perlman, TCT 2018

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2019

Continued Early Feasibility Study with updated device to define future clinical and regulatory strategies
Expansive Clinical Activity in 2019 to Build Evidence Across the TMTT Portfolio

5
Early Feasibility Studies

4
Planned Pivotal Trials

3
EU Post Market Follow-Ups
Experience, Momentum and Commitment Uniquely Position Us to Transform Patient Care

60+ years

12 Clinical Studies

2 Complex Diseases 7 Platforms 600+ employees

Experience

Momentum

Commitment
2019 Underlying Global Sales Outlook

~$40M

2019E

Underlying Global TMTT Estimated Sales

Tailwinds

- COAPT validation of transcatheter mitral therapies
- Growing base of well trained SHD¹ physicians

Headwinds

- Competition for clinical trial patients
- Cardioband supply progressively improving
Executive Summary

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