Transcatheter Heart Valve Therapy

Larry L. Wood
Corporate Vice President,
Transcatheter Heart Valves

Edwards

Leader in ~$3B Global Transcatheter Heart Valves

- Primary growth drivers: **indication** expansion, **technology** advances, and therapy **awareness**
- We are investing in **groundbreaking trials** beyond severe symptomatic Aortic Stenosis (AS) patients
- We believe the prevalence of **aortic stenosis is large**, and **treatment rates are low**
- Robust pipeline investments expected to generate **transformational** new product launches
- Global TAVR opportunity **beyond 2021 is significant**

Expect the TAVR opportunity to exceed $5B by 2021

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2017 Highlights

- Underlying **sales growth** expected to be around the **midpoint** of our previous **20-25% range**, higher than our original estimate of 15-20%
- PARTNER 3 main study **completed enrollment**; CT Sub-study continues to enroll
- **Received FDA Approval** for aortic and mitral valve-in-valve procedures using SAPIEN 3
- Data presented at TCT 2017 TAVR With SAPIEN 3 should be the **preferred strategy** based on **clinical and economic** considerations
- SAPIEN 3 Ultra System and CENTERA positioned for launches in 2018
- EARLY TAVR trial has **begun enrollment**

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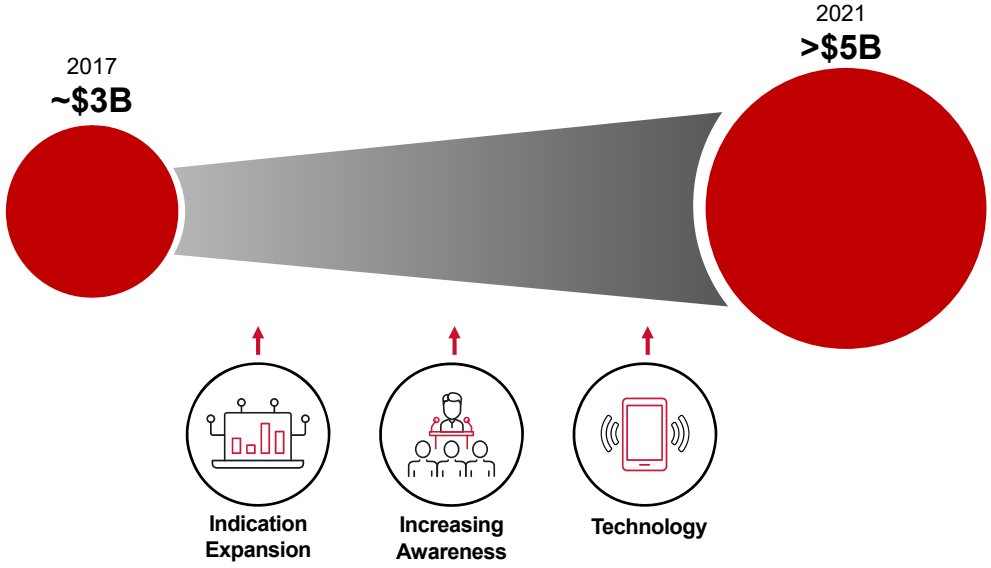
Global TAVR Opportunity Expected to Grow Mid-Teens CAGR



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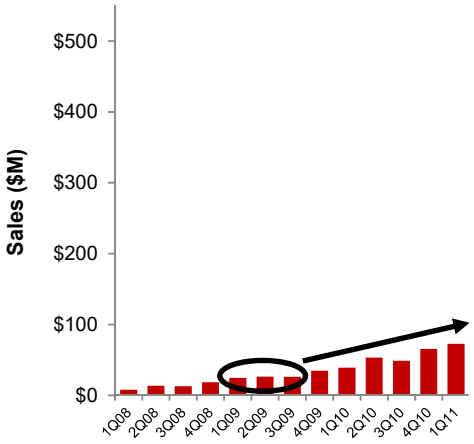
Technology and Strong Clinical Evidence Have Been the Primary Growth Drivers to Date

Edwards' Global TAVR Sales by Quarter[1]



1. Adjusted sales excluding impact of sales return reserves and Germany stocking.

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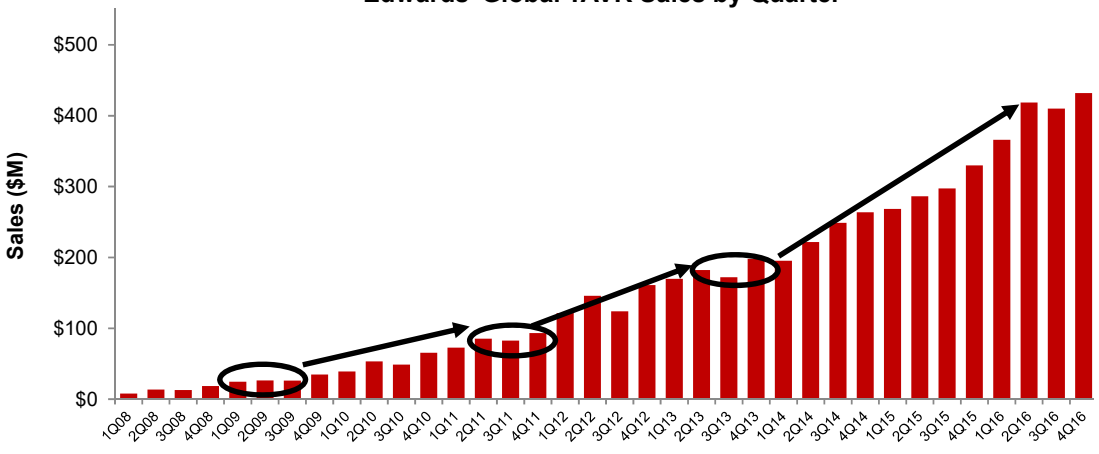

1. Adjusted sales excluding impact of sales return reserves and Germany stocking.

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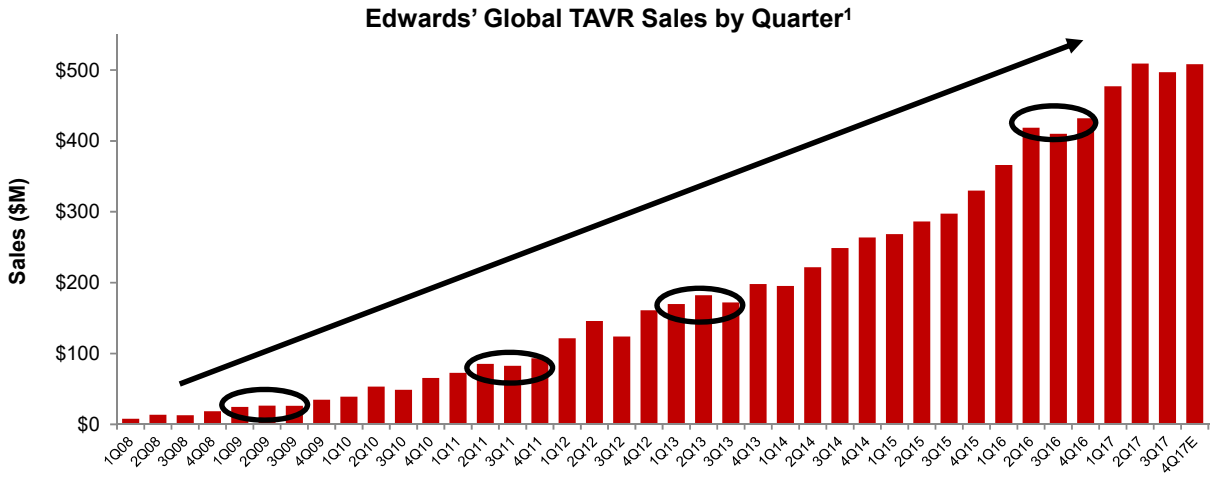
While Not Linear, TAVR Growth Since Introduction Has Grown to ~$3 Billion Industry Revenue



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Indication Expansion Allows Us to Reach More Patients

Indication Expansion

Increasing Awareness

Technology

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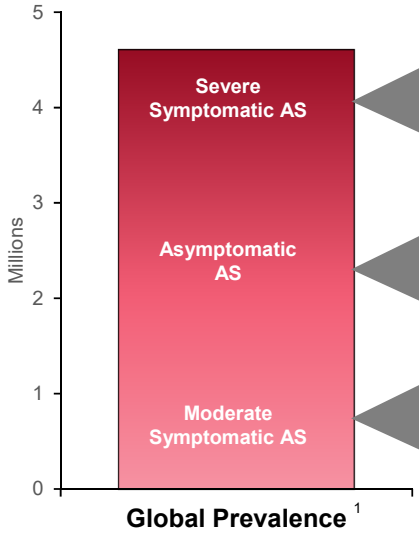
Groundbreaking AS Trials Expand Addressable Patient Population



- Inoperable, High and Intermediate risk indications **approved**
- **Significant opportunity** – Treatment rates remain low
- **PARTNER 3** - Low risk trial underway

- **EARLY TAVR** – Asymptomatic trial underway
- Addresses a large unmet need

- **TAVR UNLOAD** – 'Moderate AS with Heart Failure symptoms' trial underway

TAVR UNLOAD is a Investigator Initiated Trial Supported by a Funding Grant from Edwards Lifesciences

1 Nkomo 2006, Iivanainen 1996, Aronow 1991, Bach 2007, Freed 2010, Lung 2007, Pellikka 2005, Brown 2008, Thourani 2015, and internal estimates.

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PARTNER 3 Main Study Enrollment Complete; CT Sub-Study Continues to Enroll

THE PARTNER 3 TRIAL

- **Nested sub-studies are important to indication expansion**
- **Expect data to be presented at ACC 2019**

Sub-Studies

- Aortic ViV (n=125)
- Mitral ViV (n=50)
- Mitral ViR (n=50)
- Bicuspid (n=75)

Severe, Calcific Aortic Stenosis Patients at Low Operative Risk
Heart team agrees the patient has low risk and STS < 4%

Assessment by Heart Team: Transfemoral access → No → **Alternative Access TAVR**

Yes → 1:1 Randomization

TAVR (SAPIEN 3 valve)	**Surgical AVR** (surgical bioprosthetic valve)
CT Imaging Sub-study	CT Imaging Sub-study
Actigraphy/Quality of Life Sub-study	Actigraphy/Quality of Life Sub-study

Primary Endpoint: Composite of all-cause mortality, all stroke, and re-hospitalization at 1 year post procedure.
Follow-up: 30 day, 6 months, and annually through 10 years

U.S. FDA approval anticipated in late 2019

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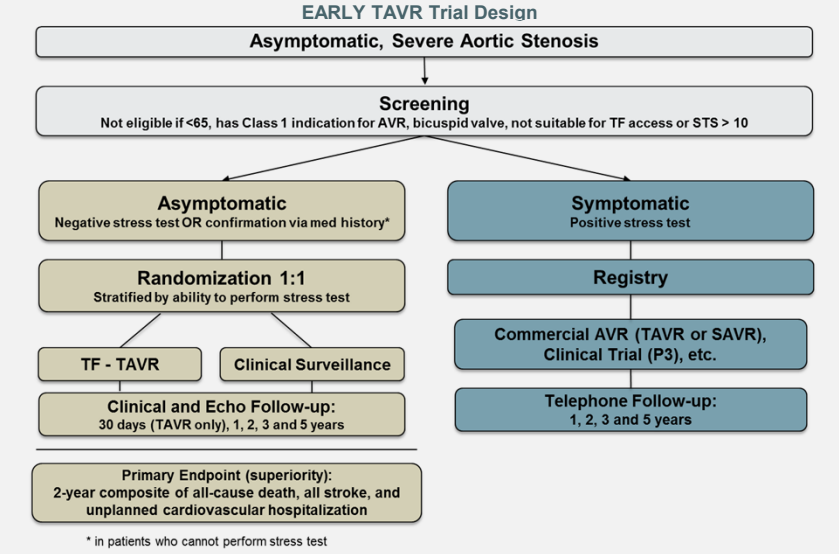
Indication Expansion into the Severe Asymptomatic AS Patient Underway

THE EARLY TAVR TRIAL

- **Treating Severe Asymptomatic AS early may:***
  - Prevent irreversible myocardial damage
  - Reduce risk of sudden death without preceding symptoms
  - Offer an even safer procedure than after developing symptoms and advancing age



* Genereux P. Natural history, diagnostic approaches and therapeutic strategies for patients with asymptomatic severe AS. JACC 2016: 2263-88

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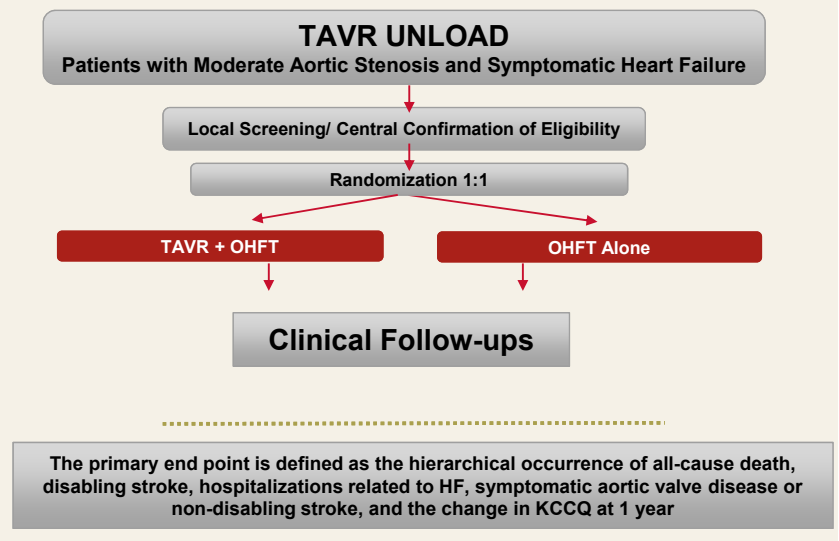
TAVR UNLOAD is Focused on the Moderate AS Patient Population

- **Investigator led trial funded by Edwards Lifesciences**
  - An international, multicenter, randomized, open-label study
  - Coexistence of moderate AS and Heart Failure is not infrequent
  - Trial aims to test the hypothesis that TAVR on top of Optimal Heart Failure Therapy (OHFT) improves clinical outcomes



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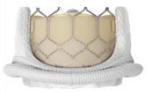
SAPIEN 3 Indication Now Includes Valve-in-Valve Procedures, Approved Exclusively with TVT Registry Data



Aortic Valve-in-Valve

- Indicated for failure of a surgical bioprosthetic aortic valve (Valve-in-Valve) in high-risk patients

Mitral Valve-in-Valve

- Indicated for failure of a surgical bioprosthetic mitral valve (Valve-in-Valve) in high-risk patients

Addresses new patient population that is outside of currently served severe symptomatic aortic stenosis patients

Received FDA approval on Jun 05, 2017 for both Aortic & Mitral Valve-in-Valve procedures

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TAVR Valve-in-Valve Therapy is an Attractive Option for Treatment of a Degenerated Bioprosthesis

Currently, aortic valve-in-valve therapy is 3-4% of our U.S. sales

Data from Brown et al. Journal of Thoracic and Cardiovascular Surgery Jan 2009; Goldstone et al. "Mechanical or Biologic Prostheses for Aortic-Valve and Mitral-Valve Replacement". NEJM Nov 2017 and Internal estimates. U.S. data shown.

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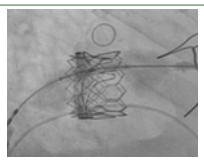
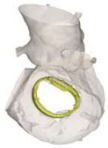
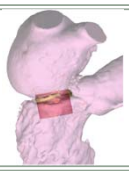
We Have Also Gained Significant Experience with the SAPIEN Platform in the Mitral Position

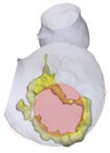
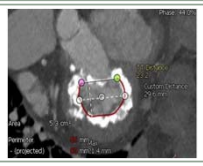
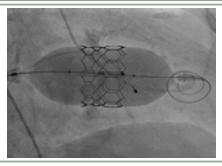
Valve-in-Valve
FDA APPROVED


Valve-in-Ring
Currently being studied in MITRAL trial


Valve-in-MAC*
Currently being studied in MITRAL and SITRAL trials

In addition, SAPIEN M3 (SAPIEN 3 with a dock) is being studied in the mitral position

MAC = Mitral Annular Calcification

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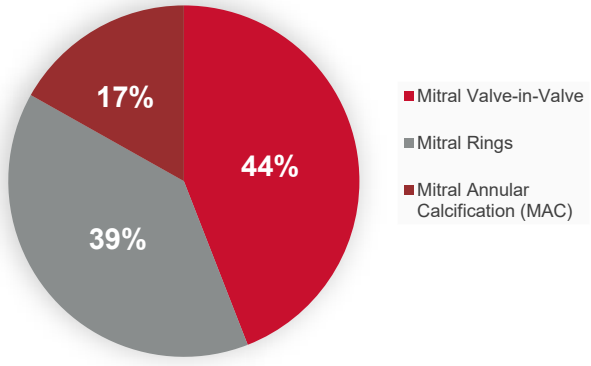
Over 1,700 Mitral Procedures Performed with the Edwards SAPIEN Platform

Breakdown of ~1,700 Mitral Procedures Performed with the Edwards SAPIEN Valve Platform*



1. Investigator Sponsored Trial Supported by a Funding Grant from Edwards Lifesciences

Our experience to date continues to strengthen our confidence of SAPIEN 3 in the mitral position

*Includes trial, compassionate and reported cases.

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Increasing Awareness and Bringing Treatment to Patients is Our Primary Focus Moving Forward

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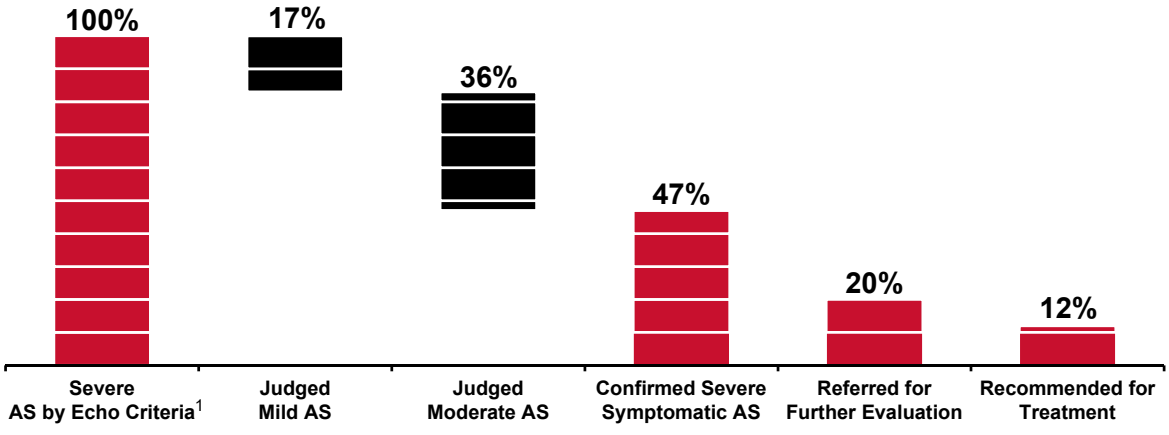
Subset of 47,000 Echoes at 5 Hospital Systems Demonstrates Opportunities to Improve Under-Treatment of AS Patients



Multiple opportunities to improve diagnosis, referral and treatment

1. Subset met at least one severe AS criteria (based on AHA/ACC guidelines) at screening/ECHO. Analysis is as of October 25, 2018.

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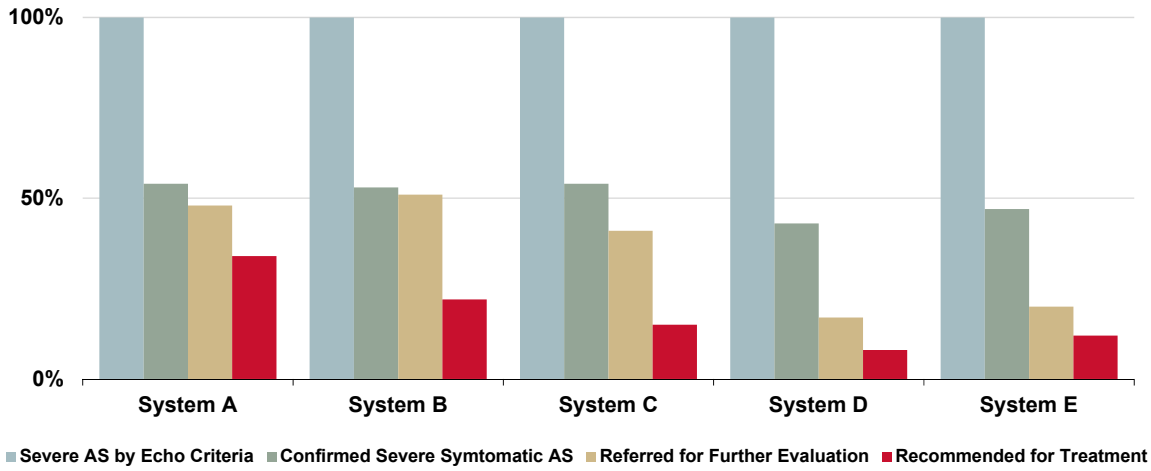
Similar Trends Exist in Each Hospital System



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Our Experience Has Driven Us to Expand Patient-Centric Services with Hospital Systems

Patient Identification

Standardizes & improves quality of echo evaluation for SHD patients

Physician Communication

Enhances communication of disease severity findings to ordering physician

Care Path Navigation

Streamlines care pathway to enable efficient patient management process from detection to care plan

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Increasing Awareness is Crucial in Addressing Low Treatment Rates

Digital Outreach – For patients and their families to learn about disease and treatment options

Patient Education – Inform patients and reinforce the patient engagement

Direct to Patient

Experienced Clinical Educators educating referring physicians on Therapy and patient selection

Connecting patients to the right HCP[1] by guiding the pathway through diagnosis and referral

Direct to Referrer

Leveraging field expertise and relationships to tailor awareness programs to regional audience

Educating HCPs at the regional level through podium and scientific meetings, and conferences

Regional Programs

1. HCP = healthcare provider

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Our R&D Pipeline Continues to Strengthen Our Long-Term Position

Indication Expansion

Increasing Awareness

Technology

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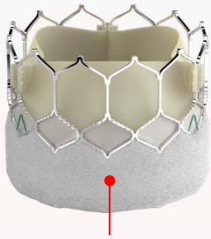
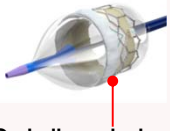
Edwards SAPIEN 3 Ultra System Further Elevates the Performance Benchmark of SAPIEN 3

SAPIEN 3 ULTRA with AXELA



Unique skirt design
For enhanced sealing performance

Ergonomic handle design
Allows for single-handed control



On-balloon design
Streamlines the procedure

- **14F Axela Sheath** for all valve sizes
- Next generation seamless expandable sheath
- Designed for dynamic expansion and contraction, and improved haemostasis

Expect CE Mark by late 2017 or early 2018, and U.S. approval in late 2018

The SAPIEN 3 Ultra System is not available for commercial sale.

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CENTERA CE Mark Approval Expected by End of 2017, U.S. Pivotal Trial Planned in 2018

- **Low incidence of cardiovascular mortality**
- **Low incidence of disabling stroke**
- **Low incidence of permanent pacemakers**
- **No reported moderate or severe paravalvular regurgitation**

Clinical Outcomes at 6 Months
AT Population

Safety Endpoints	KM % (n) (N=203)	
	30 Days	6 Months
All-Cause Mortality	1.0 (2)	5.0 (10)
Cardiovascular Mortality	1.0 (2)	2.0 (4)
Disabling Stroke¥	2.5 (5)	3.0 (6)
Myocardial Infarction	1.5 (3)	1.5 (3)
Coronary Artery Obstruction Requiring Intervention	0.5 (1)	0.5 (1)
Major Vascular Complications	6.4 (13)	6.4 (13)
Life-Threatening or Disabling Bleeding	4.9 (10)	4.9 (10)
New Onset Atrial Fibrillation	8.0 (16)	11.0 (22)
New Permanent Pacemaker - (As Treated)	4.9 (9)	5.5 (11)
Patients without Prior Permanent Pacemakers	5.3 (9)	5.9 (11)

PCR london valves *All Values are CEC adjudicated; KM (%) Estimate; According to VARC-2 Guidelines ¥ two <24h; two 2d, 5d, 16d

CENTERA

CENTERA valve with unique valve geometry shows sustained clinical outcomes at 6 months

CENTERA is not available for commercial sale.

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Pulmonic Platform for New, Unmet Need

Treating patients with dysfunctional Right Ventricular Outflow Tract (RVOT) and/or Pulmonic valve

- Clinical unmet need for congenital heart disease patient population
- No interventional options due to large sizes, dynamic environments and elasticity
- Alterra adaptive prestent designed to conform to a wide variance of anatomies and facilitates retention of the SAPIEN 3 valve providing known hemodynamic benefits
- Alterra pivotal trial planned for ~Q3 2018

First-in-Human successfully completed in August 2017 at Cedars-Sinai Hospital

Alterra is not available for commercial sale.

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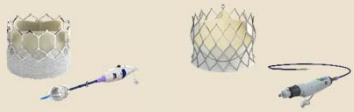
Expected Milestones in our Innovative Product Portfolio Extends Patient Reach and Drives Growth

2018	2019	2020+
		
SAPIEN 3 Ultra *EU & US Launches*	**Indication Expansion** ▪ *PARTNER 3 Low risk approval in U.S.* ▪ *EARLY TAVR enrolling*	**EARLY TAVR** *Approval*
CENTERA *US IDE Trial planned* *EU Launch*	**Alterra** *Pre-market approval submission*	**Programs under active development:** ▪ *Evolutionary product* ▪ *Revolutionary product* ▪ *SAPIEN M3 (SAPIEN 3 with dock)*

SAPIEN Evolutionary

SAPIEN Revolutionary

Dedicated to providing innovative solutions for our patients

All devices listed are not available for commercial sale.

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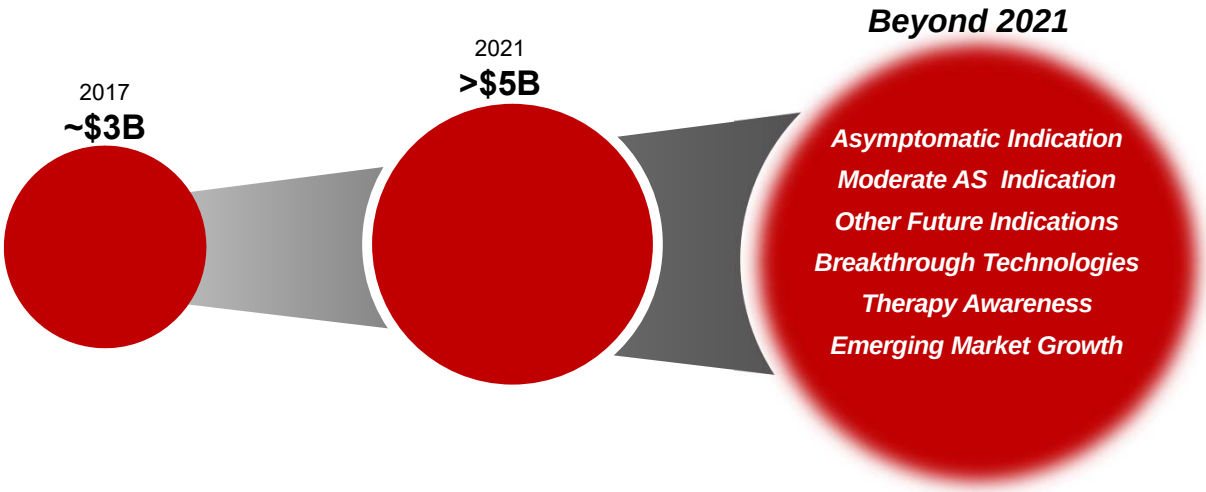
Global TAVR Opportunity Beyond 2021 is Significant



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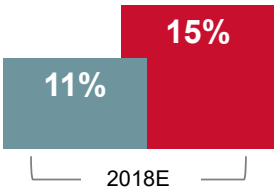
Underlying Global Sales Growth Outlook



Underlying
Global THVT
Estimated Sales Growth

2018 OUTLOOK

TAILWINDS

- **Improving diagnosis and referrals**
- **Improving TAVR economics**

HEADWINDS

- **Competitive entries**
- **Overall healthcare spending pressures**

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Executive Summary




Despite the rapid adoption of TAVR, less than 1 in 5 severe AS patients receives valve replacement therapy

Global TAVR opportunity beyond 2021 is significant