# ANTERIS TECHNOLOGIES (ASX: AVR)

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## Who says you can't mend a broken heart?

**Meet Anteris Technologies.** A company that is **set to revolutionise the multibillion-dollar transcatheter aortic valve replacement (TAVR) market** through its suite of pioneering technologies, including the **world's first 3D single-piece aortic valve, DurAVR™**, which has been proven to **provide superior hemodynamics over the existing valves** currently dominating the market. DurAVR™, in combination with Anteris' patented ADAPT tissue technology, will be used in the treatment of aortic stenosis and will provide patients with **life-changing outcomes**. It also provides a much-needed solution to the challenges facing doctors today with existing solutions lacking durability.

| COMPANY SNAPSHOT | |
|---|---|
| **Name** | **Anteris Technologies** |
| **Ticker** | ASX:AVR |
| **Price (14/01/2022)** | A$16.2 |
| **30-day VWAP** | A$10.8 |
| **CAPITAL STRUCTURE** | |
| **Shares on Issue** | ~11M |
| **Options on Issue** | ~3M |
| **Market Cap** | A$179.7M |
| **Cash (30 Sep 21)** | ~A$28M |
| **Enterprise Value** | **~A$151.7M** |


*Source: Australian Stock Exchange*

## THE TRIPLE THREAT OF TECHNOLOGIES

### 1. ADAPT® - unique anti-calcification tissue technology platform

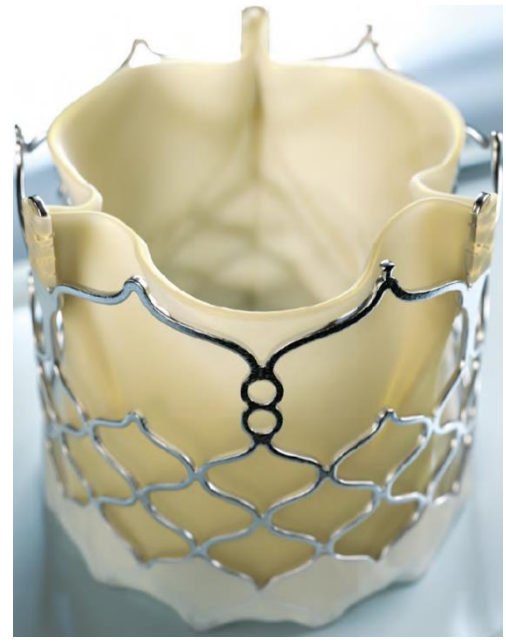
- **World's leading anti-calcification tissue technology** used in >20,000 surgical repair procedures globally
- Able to completely re-engineer xenograft tissue into a pure collagen bio-scaffold with **optimized strength and pliability, superior biocompatibility and unparalleled durability**
- Patented process that binds and detoxifies calcium binding sites and residual aldehydes resulting in **zero calcification for up to 10 years**
- Proven to show **38% and 34% less calcification than industry leading competitors**, Medtronic and Edwards Lifesciences, respectively
- ADAPT technology forms the cornerstone for multiple different products currently under development.

### 2. DurAVR™ – world's first 3D single piece aortic valve

- **Selected as "Best Innovation" at the world's leading interventional cardiovascular conference**, PCR London Valves, which is focused on transcatheter therapies for valvular heart disease
- **World's only artificial valve that is anatomically correct** resulting in an 85% increase in leaflet coaptation area & 35% reduction in leaflet stress
- **Ability to restore pre-disease hemodynamics** and **deliver superior hemodynamics** over industry leading competitor valves
- Demonstrates **no mechanical wear in ~750 million cycles** (equivalent to 15 years compared to competitor valves that last ~5 years)
- The **only viable valve for implantation into younger patients** who require a longer lasting solution than older patients
- **Removes the potential for valve-in-valve procedure** to replace existing artificial valve (due to degeneration), which creates risk of leakage and/or blocked vessels
- **Successfully implanted into five patients** as part of first-in-human study. An additional five patients are planned for treatment in Q1 of FY22 to conclude the study, paving the way for commercialisation

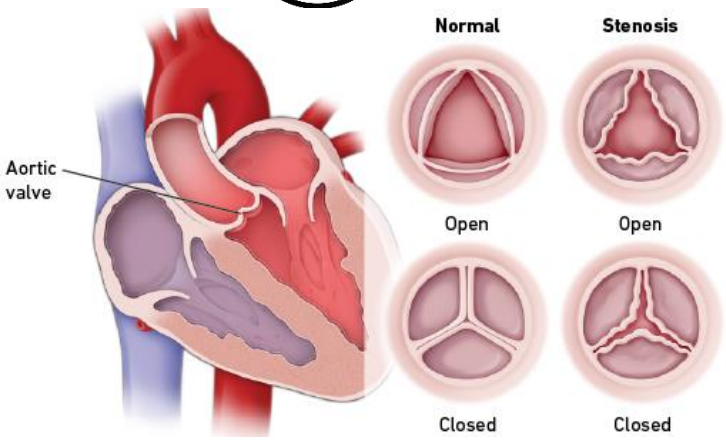
### 3. ComASUR – novel transfemoral delivery system to align valves

- Developed by the **world's leading cardiologists**
- Enables surgeon to **deliver DurAVR™ accurately and consistently** into the same position as the native valve (i.e. commissural alignment) using a minimally invasive technique
- **Not available with currently marketed products but highly desired by physicians**
- Shown to **reduce suture strain, improve leaflet durability and provide superior hemodynamic function**.



## ‘AS’ the story goes

Aortic stenosis (AS) is defined as the narrowing of the heart’s aortic valve due to the accumulation of calcium deposits that increases with age. The aortic valve acts as a one-way door out of the left ventricle and into the aorta, which subsequently pumps oxygenated blood to the rest of the body. Needless to say - it is important. The build-up of calcium deposits around the valve opening results in an increase in blood pressure as the heart ‘works harder’ to circulate blood around the body. If left untreated, approximately 50% of patients with severe AS will not survive longer than ~2 years.



*Source: Anteris Technologies*

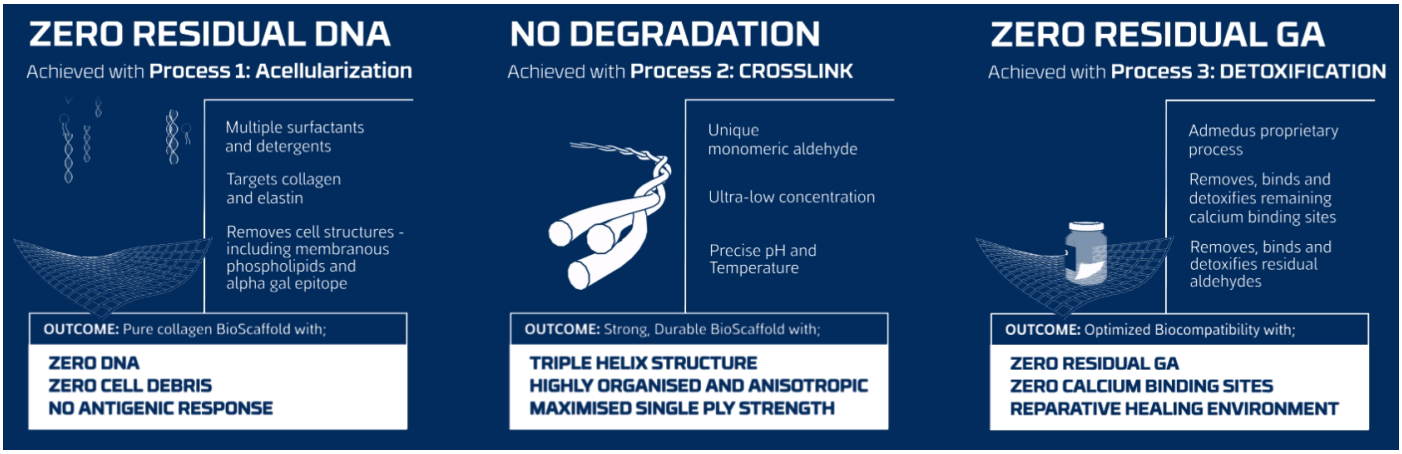
Historically, the only way to fix the problem was through surgical aortic valve replacement (SAVR), or as it’s more commonly known, open heart surgery. Unfortunately, due to its invasiveness and lengthy recovery time, SAVR is unsuitable for older ‘high risk’ patients, leaving them with no viable alternative to extend their life. This changed when TAVR was introduced and approved by the US Food and Drug Administration (FDA) for use in high-risk patients in 2012. TAVR is a minimally invasive alternative to SAVR that uses a catheter to deliver a replacement valve and can be completed in as little as 20 minutes. Since its introduction, TAVR has continued to grow in popularity and is now considered the preferred treatment for patients with severe AS. **It is anticipated that by 2025, TAVR treatments will represent 62% of procedure volume and 87% of market revenue**, **representing a CAGR of 15.6%.**

*Source: Anteris Technologies*

Replacement valves used in TAVR procedures typically only last approximately 5 years before losing their efficacy due to a build-up of calcium and mechanical fatigue. This has historically been a sufficient time frame due to the mean age of TAVR recipients being 85 (near life expectancy). In 2019, the landscape changed drastically when the FDA approved TAVR procedures to be performed on younger, lower-risk patients. This meant that the mean age of TAVR recipients suddenly plunged from 85 to 73, meaning that valves which lasted ~5 years were no longer sufficient. In some instances, this would result in younger patients requiring a replacement for the initial valve in a procedure known as “valve-in-valve” surgery, whereby the new valve is placed via a catheter onto the orifice of the failed valve, which gets pushed aside. Valve-in-valve procedures carry a risk of leakage if the previously implanted valve is damaged or not securely placed. Further, there is a possibility that the partially detached valve leaflet from the previously implanted valve could block a blood vessel, leading to further complications. **Therefore, the inability of currently available valves in the market to last longer than ~5 years is a significant issue burdening both physicians and patients**. As a result, on the back of the FDA approval in 2019, an acute need for a more durable, longer lasting heart valve presented itself - and Anteris set out to deliver just that.

## Time to ADAPT

At the heart of Anteris' success to date is its patented ADAPT® tissue technology, which has already been used in over 20,000 surgical repair procedures globally. **ADAPT® is the only bioscaffold to demonstrate zero calcification over 10 years across multiple applications.** The proven technology can be broken down into three processes that are outlined in the diagram below. In summary, ADAPT® works by detoxifying and removing cell structures and calcium binding sites to produce a pure collagen bioscaffold (an artificial structure) with **zero DNA and zero calcium binding sites**. This is an important feature in the context of aortic stenosis, being a disease of calcification. Therefore, by incorporating ADAPT® technology into its development, DurAVR™ is a significantly more durable heart valve than competing valves, which are prone to calcification over time.




*Source: Anteris Technologies*

## A world's first - DurAVR™

**DurAVR™ is the world's first and only 3D single-piece aortic valve**. Through its unique design, combined with ADAPT® technology, DurAVR™ addresses the key areas that lead to the degradation of current valves. These include:

1. **ZERO CALCIFICATION**: As mentioned earlier, aortic stenosis is a disease of calcification. Heart valves are formed by thin and pliable leaflets that become stiff as calcium accumulates, which eventually causes the valve to narrow (or become 'stenotic'). This increases blood flow pressure and can ultimately result in cardiac arrest or sudden death. Therefore, **the requirement for replacement valves to have anti calcification properties is immense.** Existing replacement valves on the market display calcification over time (and thus, lose their efficacy). This is thought to be either due to glutaraldehyde, which attracts calcium (discussed further below), or an immune reaction caused by the artificial valve being implanted into a foreign body.

2. **ZERO GLUTARALDEHYDE:** Prior to implantation, valves are typically fixed in glutaraldehyde, which helps to stabilise the tissue against the proteolytic and/or enzymatic degradation that occurs once it is implanted. It also helps to decrease the thrombogenicity and immunogenicity by cross-linking and masking the antigens, which reduces the potential for a hyperacute rejection by the recipient. Essentially, glutaraldehyde makes the valves 'immunologically inert' and also helps to increase the storage life. Immediately before implantation, the valves are thoroughly washed in saline to remove the glutaraldehyde. Despite this, aldehyde residues typically remain, rendering the material less biocompatible and more prone to calcification. Unlike its competitors, Anteris, through its ADAPT® process has been proven to produce zero residual glutaraldehyde.

3. **SUPERIOR UNIBODY DESIGN:** Existing replacement valves on the market involve a complex, three-piece valve construction, and therefore, are not anatomically correct. As a result, recipients typically have higher blood pressure due to suboptimal blood flow, which is heightened during periods of increased cardiac output. To overcome this, Anteris developed specialised machinery and a novel processing technique to reduce the thickness of native pericardia and yield tissue with the desired thickness to make its 3D single-piece aortic valve. As part of a major manufacturing breakthrough, Anteris was able to prove absolute equivalence between the processed

tissue and native tissue. In other words, it is considered to be "human-like". As a result, DurAVR has been shown to **increase leaflet coaptation area by 85% and reduce leaflet stress by 35%.** The zone of coaptation refers to the rough area on the top side of the valve's surface. Any irregularities in the coaptation zone can prevent the valve from functioning properly and increase the stress of surrounding leaflets, leading to poor hemodynamics.

3. **LESS SUTURES** – Sutures are the stitches holding together the edges of a wound or surgical incision. Existing replacement valves are manufactured with hundreds of sutures per valve, which causes them to be 'mechanically compromised'. DurAVR™ requires just 20-30 sutures and has shown zero suture tears in up to 600 million cycles of testing (noting that the FDA requires a minimum of 200 million cycles of testing). This translates to a lower manufacturing cost and a more reliable product as it is less likely to fatigue (as observed in competitor valves).

## Delivered differently – ComASUR

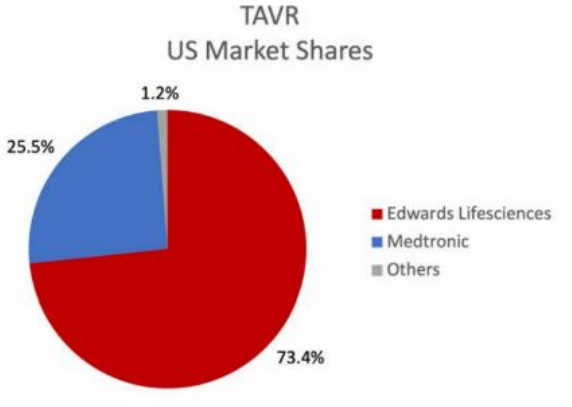
As part of its suite of technologies, Anteris has also developed the ComASUR catheter – a commissural alignment device. ComASUR helps surgeons to accurately position the replacement valve by tracking through the aortic arch and aligning it with the native valve, providing better blood flow and reducing the potential for error. The system is highly demanded by physicians because it addresses the limitations of current delivery systems available on the market that are more prone to error.

In July 2021, Anteris was awarded a 20-year patent for the sterilised packaging system associated with its ComASUR device. This patent enhances the intellectual property barrier and commercial value of Anteris' technologies, as well as helps to protect against product counterfeit.

Anteris has completed a series of acute animal studies that have demonstrated the feasibility of the DurAVR™ transcatheter heart valve (THV) and its bespoke ComASUR delivery system. Post-implant echocardiography and CT scans have confirmed the functionality of the DurAVR™ THV with stable positioning and good hemodynamic function. These studies represent a critical part of the test plans agreed with the FDA as part of its regulatory approval process.

## The (not so) competitive landscape

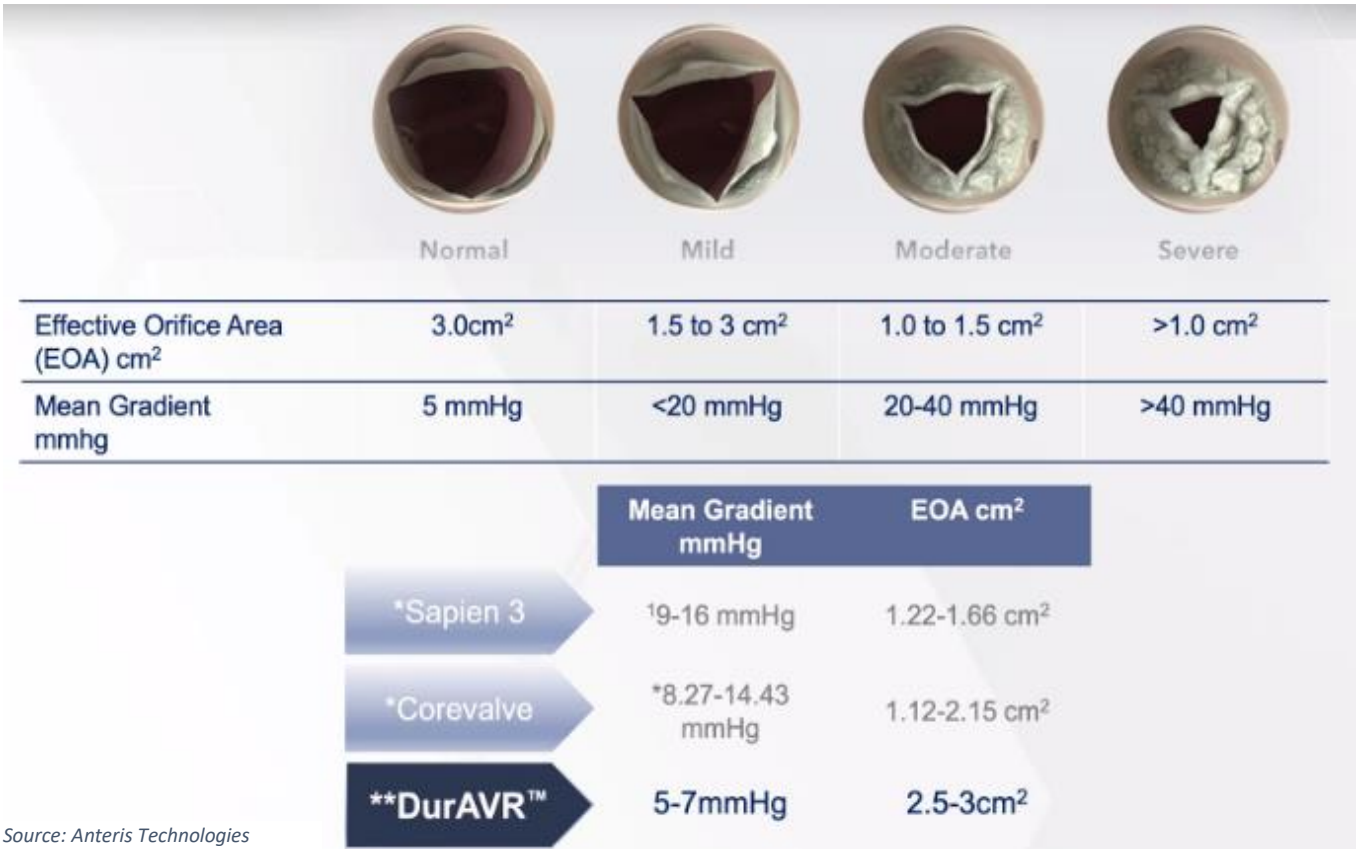
Currently, the market is dominated by two key players, Edwards Lifesciences (Edwards), which offers the Sapien valve, and Medtronic, which offers CoreValve. Collectively, these companies represent a whopping 98.9% of the US TAVR market (as shown opposite). Both valves feature a tri-leaflet design with the main difference being that Sapien is balloon expandable, while CoreValve is self expanding. Self expanding valves are generally viewed by physicians to be less predictable due to the ability of the valve to move around. As a result, balloon expandable valves are more highly desired by physicians, which contributes to the greater market share of Edwards over Medtronic.




*Source: Anteris Technologies*

The limitation of these competitor valves is that they were initially designed for the treatment of aortic stenosis in high-risk patients (i.e. prior to the FDA approval of TAVR procedures in low-risk patients in 2019). Therefore, both valves were designed predominantly to overcome the issue of SAVR procedures (open heart surgery), meaning the **design focus was on valve delivery via a catheter as opposed to normal hemodynamic performance and/or durability**. This differs to DurAVR™, which has been designed specifically to overcome the issue of existing TAVR devices with a focus on providing superior hemodynamic performance and durability, such that it is suitable for use in younger, low-risk patients that require a valve to last for longer than 5 years.

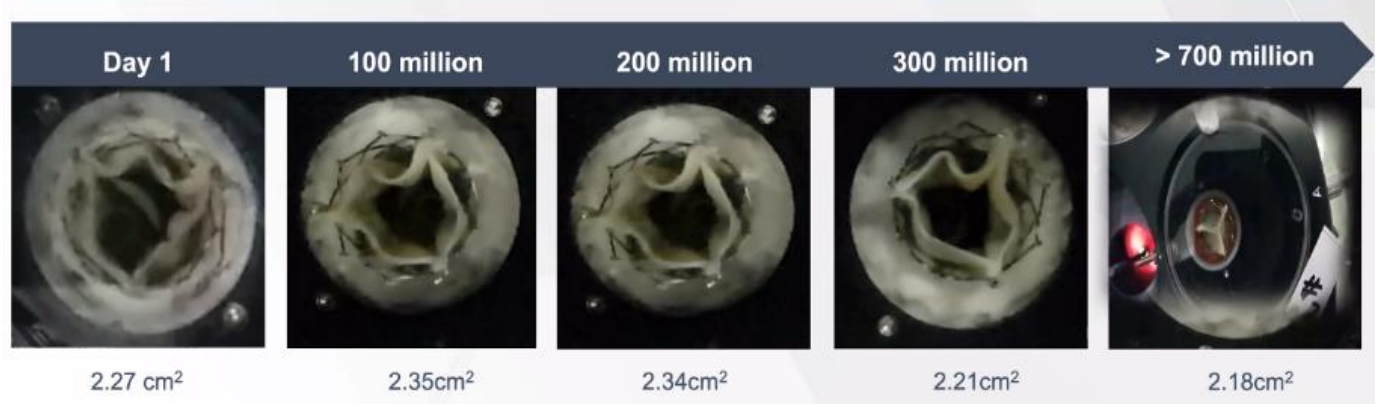
This change in design focus is paramount to the superiority of DurAVR™ over its competitors, which becomes clear when the valves go head-to-head in a comparison of mean gradient and effective orifice area (EOA), as presented in the table below. Gradient refers to the difference in pressure across the two sides of a heart valve and is measured in millimetres of mercury (mmHg), while EOA is the minimal cross-sectional area of the flow jet that is downstream to the aortic valve and is the standard parameter used for the clinical assessment of aortic stenosis severity. The higher the gradient and the smaller the EOA, the greater the severity of stenosis.




*Source: Anteris Technologies*

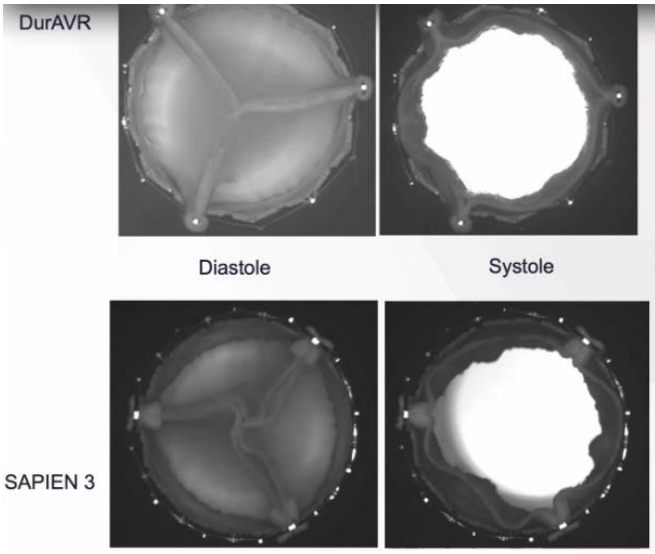
As presented above, DurAVR™ is not only statistically superior to competing valves, it is the only valve that is able to restore the valve to be within the normal range. In other words, **DurAVR™ takes the patient out of stenosis, while competitor valves only reduce the severity of the stenosis.**

Over the next five years, due to the suboptimal design of competitor valves, the patient's stenosis begins to progress again towards severe stenosis as the valve is overcome by calcification and mechanical fatigue. In comparison, **DurAVR™ has been shown to exhibit no wear in over 700 million cycles – the equivalent of 15 years.** This is largely attributable to its unibody design that dramatically enhances its structural integrity, ADAPT technology that removes all DNA and glutaraldehyde, and the ComASUR delivery system that ensures accurate valve delivery.




*Source: Anteris Technologies*

The superiority of its unibody design when compared to the tri-leaflet design of its competitors can be visualised in the figure opposite that shows DurAVR™ and Sapien in both diastole (closed) and systole (open). The differences in these images are supported by the metrics in the table, which translates to better blood flow for DurAVR™.



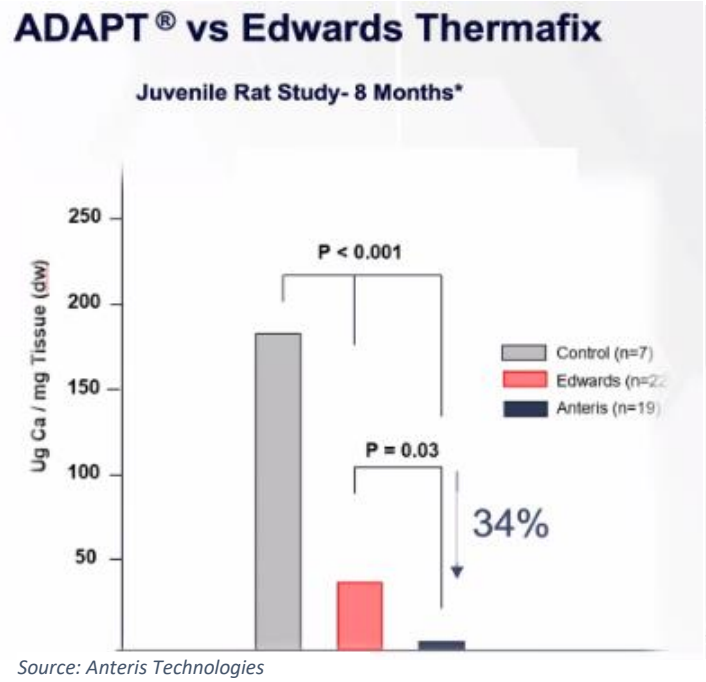

| | DurAVR 25mm | Sapien 26mm |
|---|---|---|
| **EOA** | **2.5 cm²** | **1.9 cm²** |
| GOA (geometric orifice area) | 2.7 cm² | 2.5 cm² |
| Mean Pressure Drop (Across Valve) | 7.3 mmHg | 11.1 mmHg |
| Pressure Required To Open Valve | 97 mmHg | 99 mmHg |
| Valve 'Open' Duration (per cycle) | 312 ms | 286 ms |

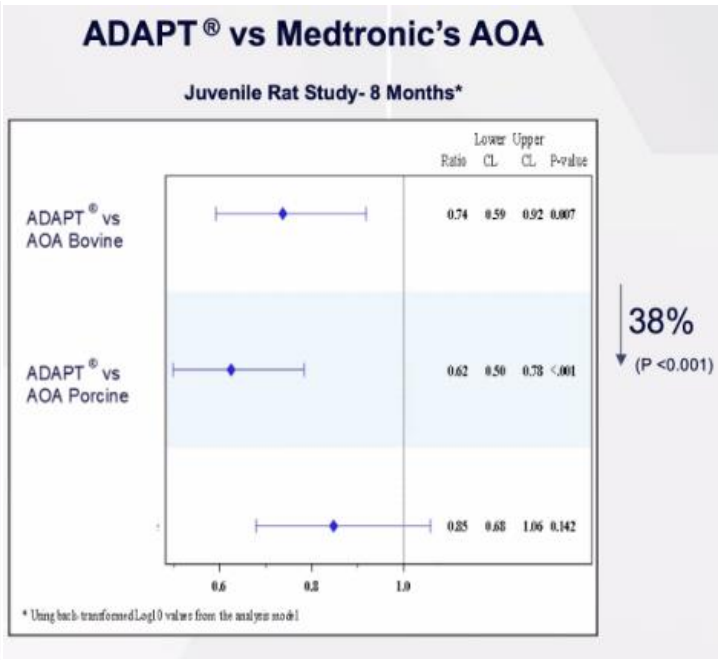
*The valves were tested using the same Pulse Duplicator. Testing was performed at Normotensive conditions.

*Source: Anteris Technologies*

## A heart-to-heart battle

To further prove its superiority, Anteris has also completed numerous head-to-head anti-calcification studies comparing its ADAPT® tissue technology to its competitor equivalents - namely, Medtronic's AOA treatment, and Edward's Thermafix treatment. In both instances, ADAPT® tissue was proven to be superior to the market leaders with approximately 38% and 34% less calcium concentration when compared to Medtronic's AOA™ treated porcine arm and Edward's Thermafix treated valve respectively. Less calcific means less brittle over time which means less breakdown of the leaflets and therefore, greater durability. Given ADAPT® is already recognised as the world's best anti-calcification treatment (based on current data), when combined with the unique DurAVR™ design and ComASUR delivery system, Anteris appears poised to take on the medical device giants.




*Source: Anteris Technologies*

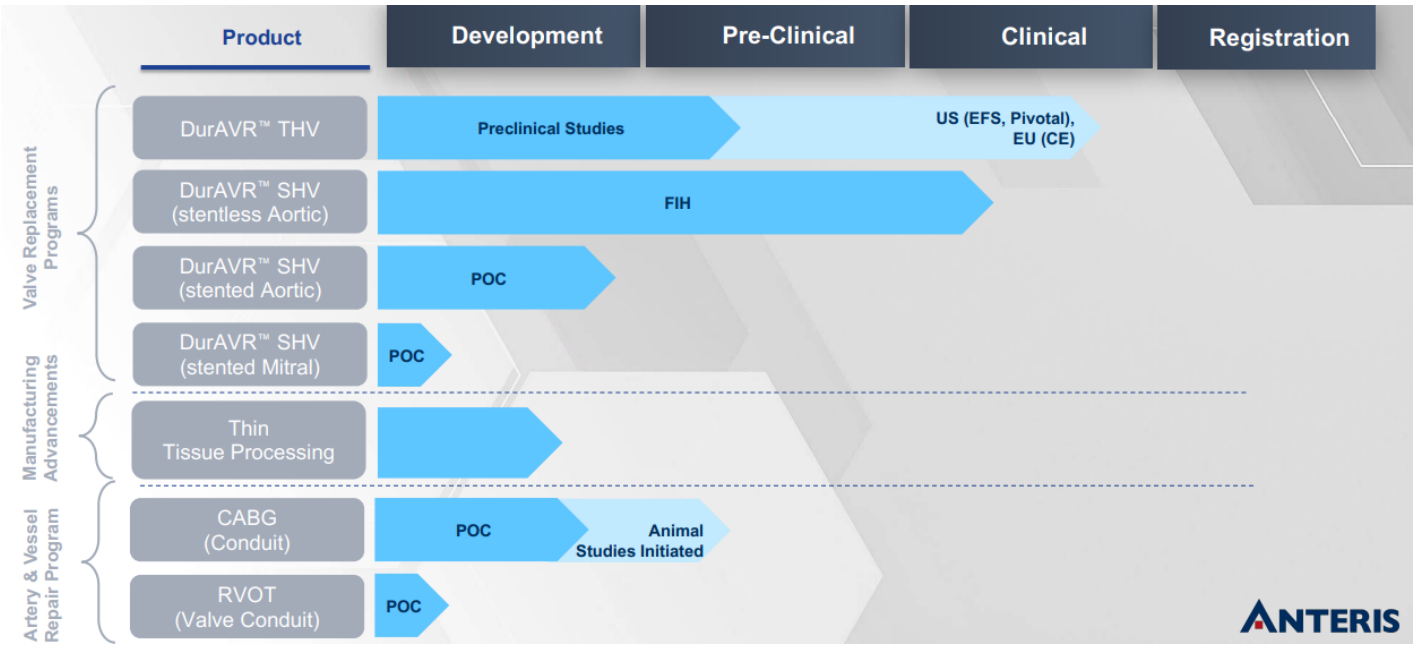
## Key milestones

In conducting its development activities and clinical programs (majority of which are required for regulatory approval), Anteris has hit a number of key milestones. This has included, but is not limited to, the following:

- **Successful completion of its first in-human 15 patient SAVR study of DurAVR™ in Belgium.** The trial aimed to replicate the successful results of a preceding animal study, whereby six sheep showed EOA with a range of 2-2.5cm2 (compared with 1.6-2cm2 in commercially available valves). The study focused on demonstrating efficacy and safety of DurAVR™ in humans. Patient outcomes exceeded the results of what is normally expected following a SAVR procedure
- As a result of the success in its first human trials, **Anteris was selected as "Best Innovation" at the PCR London Valves 2020 virtual conference**, being the leading interventional cardiovascular conference
- **Achieved outstanding performance in head to head study of ADAPT® tissue technology against Medtronic's AOA technology**, including 38% less calcium concentration in ADAPT® treated tissue
- **Successful in vivo demonstration of its ComASUR™ Transfemoral Delivery System**. This study was specifically designed to show the system's ability to access the arterial vasculature using minimally invasive techniques and track through the aortic arch to the aortic valve where a DurAVR™ THV was implanted
- **Successful completion of its Proof of Concept (PoC) animal study testing the viability of ADAPT® treated conduits in the carotid artery**. The conduits treated with ADAPT® showed no evidence of calcification, representing a major step towards ADAPT® treated prosthetic conduits for use in CABG (coronary artery bypass graft) surgeries
- **Achieved breakthrough in manufacturing for the tissue used in ADAPT® treated products from bovine pericardium**. This involved the development of specialised machinery that reduces the thickness of native pericardia such that it is of the desired thickness needed to make DurAVR™
- **Accepted into the innovation session at PCR London Valves meeting** as one of only six presentations selected out of 120 submissions
- **Successful completion of its final chronic animal study required by the FDA to commence US TAVR clinical trial**. The three-month study was carried out in six sheep to assess hemodynamic performance and in vivo response to DurAVR™. Results were positive across all study criteria
- **Successful implantation of DurAVR™ in five patients as part of its first-in-human (FIH) study.** The study has been designed to assess the correct position of the DurAVR™ valve at the proper anatomical location and the hemodynamic performance. Results to date have proven to be outstanding with all patients displaying superior hemodynamics at the 7 day follow up. The study will complete after an additional five patients undergo treatment in Q1 2022
- **Filed a provisional application for a new patent pertaining to ADAPT® that will allow for expanded manufacturing capacity ahead of commercialisation**. More specifically, the patent applies to particular aspects of the sterilization process allowing the safe transfer of product to manufacturer of valves, meaning Anteris will be able to start the manufacturing process in Australian facility and complete valve manufacture at the US facility.

## The fast track to commercialisation

With its seamless execution of clinical trial activities and undeniably impressive results to date, you might be wondering, what's next? Well, based on the product diagram below, it appears 2022 is poised to be an exciting year for Anteris as it continues to progress the development of its DurAVR™ and ADAPT based products in tandem. DurAVR™ remains the key focus as the company nears the completion of its EFS, after which it will commence its pivotal studies that will put the company on track for regulatory approval. Simultaneously, Anteris will also commence its CE registration study in Europe (discussed further below).




*Source: Anteris Technologies*

In relation to the EFS, the study will be concluded after the treatment of the next cohort of five patients that is due to occur within Q1 2022. The pivotal study will follow the EFS, which Anteris anticipates will be fast tracked due to the exceptional results of the human trials to date. This study will involve a larger cohort of human patients (~30) and is intended to demonstrate and confirm the safety and efficacy of DurAVR™. Anteris will also be able to include patients from the FIH trials as part of both the pivotal studies and CE registration study. Although, we note that it is not anticipated that there will be any issues in recruiting additional patients (which is a notoriously difficult and time-consuming part of clinical trial activities), due to the superiority of results thus far. Also noteworthy, is that Anteris intends to introduce Australian physicians and patients into the remaining studies, as well as set up an Australian Advisory Board, enabling it to conduct experimental studies in Australia.

The CE process is anticipated to commence towards the end of 2022, however we note that the US (FDA) has far more comprehensive technical standards and requirements when compared to Europe (CE), meaning it is unknown which jurisdiction will provide regulatory approval first.

Overall, while it is difficult to put an exact timeline on it, one thing we can be confident about is that Anteris looks likely to face an accelerated commercialisation pathway.. and that Edwards and Medtronic better watch out.

## So, why AVR?

It's quite simple – **DurAVR™ works better and lasts longer than any commercially available product**. Further, when you consider that the leading medical giants, Edwards and Medtronic, have a combined market cap of $250b and Anteris has a market cap of just $148m, the value proposition is clear.

With the stock price increasing by 68% in the last month alone, it's clear we aren't the only ones who are excited about Anteris – and you should be too. Here's a summary why:

- The TAVR market is a **US$10-11bn market that is anticipated to grow by a CAGR of 15.6%** into 2025
- **DurAVR** has been shown to **provide superior hemodynamics over the current market leaders**, creating the opportunity to revolutionise the industry and become the new, unsurpassed market leader. In addition, it also represents the **only viable valve replacement solution for younger patients** who require longer lasting, more durable valves to last their lifetime
- **ADAPT is the world leading anti-calcification treatment** that has been **used in over 20,000 patients globally**
- **ComASUR™ gives physicians the ability to deliver DurAVR™ accurately and consistently**. Furthermore, it is not commercially available with currently marketed products, however it is highly desired by physicians
- Collectively, the technologies **provide a solution to the clinical and anatomical challenges that patients and surgeons are burdened with in commercially available TAVR devices today**
- Anteris has an **extensive patent portfolio** (~40 applications) that enhances the intellectual property barrier around its key technologies, while adding to its products commercial value.
- Supported by a **highly competent management team** with vast experience in multi-national pharmaceutical companies and **proven track record in commercialisation.**

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