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Bioshares

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Edition 926

Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies

Companies covered: **AVR, CGS, PXS, TLX**

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-35.8%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - May '14)	26.6%
Year 14 (May '14 - May '15)	23.0%
Year 15 (May '15 - May '16)	33.0%
Year 16 (May '16 - May '17)	16.8%
Year 17 (May '17 - May '18)	-7.1%
Year 18 (May '18 - May '19)	-2.3%
Year 19 (May '19 - May '20)	39.5%
Year 20 (May '20 - May '21)	86.8%
Year 21 (May '21 - May '22)	-15.6%
Year 22 (May '22 - Current)	-3.7%
Cumulative Gain	1553%
Av. Annual gain (21 yrs)	19.0%

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Extract from Bioshares –

Anteris Technologies - Aortic Valve Outperforms Surgical and TAVR Competitors

Aortic heart valve company Anteris Technologies (AVR: $23.10) had multiple presentations at the major US conference TCT (Transcatheter Cardiovascular Therapeutics) held in Boston last month. The event has around 11,000 specialists in the field attending and was founded by Dr Martin Leon, who has joined the Anteris Medical Advisory Board earlier this year.

Technology Background

The Anteris valve will compete with two other biological material heart valves, the Sapien 3 (from Edwards Lifesciences) and the CoreValve Evolut R (from Medtronic). Both can be implanted via a catheter, called a TAVR (transcatheter heart valve replacement) procedure, rather than surgically via the chest. Its appeal is its shaped single piece 3D design (unlike the three-piece competing valves), and the biologic material used (from bovine pericardium tissues) which has been implanted in over 35,000 patients.

Currently around half of aortic valve replacements are conducted through open chest surgery and half by TAVR. By 2028, it is expected that around 75% of procedures will be by TAVR. Over the last decade the average age of implant recipients has fallen from 85 to 73, driving the need for a more durable product that is resistant to calcification. Anteris' ADAPT tissue processing has shown to be resistant to calcification over 10 years from an earlier pediatric heart tissue repair study.

To date its aortic heart valve, called the DurAVR THV, has been implanted into 13 disease complicated patients. Findings from these first implants were presented at TCT and are summarised below.

Updated Results from Clinical Study

There were several key findings from the first 13 patients treated, based on data obtained at 30 days after implant. Dr Michael Reardon, a cardiac surgeon from Houston Methodist Hospital, said that the first 13 patients were mostly difficult cases. Of these 77% were women, who have smaller annuluses which is more challenging, some were bicuspid valves, some had heavily calcified leaflets, and some had a heavily calcified annulus, with the average age being 74 years.

The three doctors involved with the study were Dr Chris Meduri, an interventional cardiologist at the Karolinska University in Sweden and also the Anteris CMO, and cardiac surgeons Dr Vinnie Bapat (Abbott Northwestern Minneapolis) and Dr Susheel Kodali (Columbia University Medical Center).

Finding 1 - Safety

At 30 days after implant, there were no device failures or implant issues, including no bleeding complications, stroke or any need for surgical reintervention.

Continued over

Finding 2 - Normal Hemodynamics
One surprise from the study is that the DurAVR THV restored blood flow to more normal hemodynamics with consistent laminar flow. This can be attributed to a much more native-like leaflet function according to Dr Chris Meduri.

In a separate study looking at 22 patients, normal heart valves were compared with DurAVR THV and other TAVR or surgical implanted valves such as the Sapien 3, Evolut R and CEP Magna Ease. Meduri said that DurAVR THV is the first valve that has restored normal-like aortic flow, with no significant difference in flow between a healthy valve and the DurAVR THV valve. The other commercially available valves deliver a significantly worse aortic flow than what occurs in a healthy valve.

Finding 3 - Mean Pressure Gradient and EOA
The mean pressure gradient was reduced from 49 mmHg before implantation to 9 mmHg following the implant.

The effective orifice area was increased from 0.5 cm^2 to an average 2.0 cm^2 (normally 1.45cm^2 and 1.83 cm^2 achieved for the Sapien 3 and Evolut for that sized valve). "To get an average EOA of 2.0 cm^2 for a 23mm valve is excellent," said Dr Susheel Kodali. And the EOAi (indexed effective orifice area) value of 1.15 was 'quite remarkable' according to Dr Kodali.

Finding 4 - Good Coaptation
A mean coaptation length, where the leaflets meet, was 8.3 mm, which was better than the standard target of 8.0 mm according to Dr Reardon.

Competing Devices 20 Years Old

CEO Wayne Paterson said that the current valves were designed 20 years ago. But patients being treated are now younger and the science and understanding has evolved. "The valve in your body is not a three-piece valve with hundreds of sutures in it which causes limitations."

On a question of why the DurAVR THV is outperforming other valves with respect to durability, Paterson said all the other biologic valves have residual DNA, whereas the DurAVR THV has almost no residual DNA. Paterson stressed that ADAPT treated tissue has been implanted into 35,000 patients around the world, with data showing that this tissue does not calcify (having more anti-calcification data that any other group).

Expert Panel Discussion at TCT on DurAVR THV

An expert panel session was held at TCT, chaired by Dr Martin Leon and also involved Dr Chris Meduri, Dr Thomas Modine, Dr Rebecca Hahn and Dr Michael Reardon

Dr Bapat was asked what would make clinicians change over to the DurAVR THV valve from existing devices. Dr Bapat said that the changes from first to second to third generation devices have been based on improved hemodynamics and improved durability.

Dr Meduri said that each of the panellists are part of valve programs that conduct over 500 TAVR procedures a year, but almost half are being implanted into patients less than 65 years of age.

Dr Meduri said that ease of use is critical. The DurAVR THV can be installed using a balloon expansion process (rather than self-expandable), which is the easiest to implant, as well as achieving commissural alignment. This will also be a driver of adoption in the short term, with the tissue science adding to the appeal.

Dr Thomas Modine, a cardiac surgeon from Bordeaux, said that an appealing characteristic of the DurAVR THV is that it anatomically mimics nature. Dr Martin Leon highlighted that having less sutures to the frame is going to make an important difference (100 sutures for the DurAVR THV compared to around 800 for existing devices).

Dr Modine said that DurAVR THV has a larger effective orifice opening (2.83 mm^2) compared to the Sapien 3 (2.30 mm^2) and the Evolut R (2.41 mm^2), which is a fantastic outcome.

Dr Rebecca Hahn, Professor of Medicine at Columbia University Medical Center, is fascinated with the DurAVR THV leaflets, which are shaped like native leaflets. There is less closing pressure according to Dr Hahn as they are shaped to be in a closed position. There is also little or no reverse blood flow, which means laminar and not turbulent blood flow can be achieved, delivering improved hemodynamics. This also translates to improved patient outcomes with respect to functional benefits and quality-of-life for the patient.

Dr Reardon said that the following characteristics or features are sought in an aortic heart valve: a short frame to maintain coronary access, near normal hemodynamics, commissural alignment of the valve, and a valve that is easy, reliable and dependable to implant.

Dr Reardon said the hemodyamics of this valve were absolutely stunning. And the safety and implantability for the first 13 patients was absolutely stunning. The hope is that this valve will provide what is more like a native valve that has the ease and predictability of a balloon expanding platform.

Dr Leon said that normalising hemodynamics through the aortic valve would be an enormous advance. Dr Modine said it has been one of the most exciting projects he has been involved with. Dr Rebecca Kahn said that the ability to improve outcomes with the DurAVR THV from valve-in-valve procedures is very enticing, as is the ability to gain such results from small annulus patients in women and smaller patients. "This is a valve for everyone, including the patients who need to have a repeat valve-in-valve (procedure)."

Summary

Early data from Anteris Technologies' first clinical study in 13 patients appears to deliver most if not all of the aspects for an ideal aortic heart valve. It can be implanted via a catheter, the tissue is resistant to calcification, it can be delivered with an easier to use balloon expansion process whilst maintaining proper alignment (commissural alignment), and it can achieve almost normal, laminar blood flow.

Whilst the early data is excellent, larger studies of the DurAVR THV will be required. In that process it is likely the technology will

– Anteris cont'd

DurAVR THV Laboratory Data

DurAVR THV was compared directly with the Sapien 3 and the Corevalve Evolute R TAVR valves in a pulse duplicator in a bench study. The Anteris valve achieved a greater effective orifice area of 2.83 mm^2 (compared to 2.30 mm^2 and 2.41 mm^2 for the Sapien 3 and the Evolute respectively) and a lower pressure gradient across the valve of 5.9 mmHg (compared to 8.8 mmHg and 8.3 mmHg for the competition).

In another bench study a DurAVR THV was placed inside a Sapien 3 valve (valve-in-valve procedure). The effective orifice area actually increased from 2.01 cm^2 to 2.29 cm^2, and the pressure gradient fell (from 11.3 mmHg to 9.3 mmHg), which reduces the energy required for the heart to pump the blood through the valve. One application being considered is a study implanting the DurAVR THV into an existing Sapien 3 valve in a valve-in-valve process.

An emerging market dynamic is repairing existing valve implants through a valve-in-valve procedure, which is expected to become 30%-40% of the market, according to Dr Meduri. Dr Vinnie Bapat, one of the world's leading experts in valve-in-valve procedures, believes that lifetime management of patients with replacement valves is going to become an increasingly important indication.

gain interest from one of its main competitors, given the level of interest from its extensive scientific advisory panel.

Anteris is capitalised at $321 million.

Bioshares Recommendation: **Speculative Buy Class A**

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For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Some Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages of commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

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