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Companies covered: **AVR, CGS, IMM, 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 - Current)	66.1%
Cumulative Gain	1708%
Av. Annual gain (20 yrs)	19.7%

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Bioshares

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Extract from Bioshares –

Anteris – Positive Data from First Five Patients in 15 Patient Pilot Study

Anteris Technologies (AVR:$3.75) is commercialising a novel heart valve for the treatment of aortic stenosis. The DurAVR valve is novel because it's formed as a single piece, in contrast to how separate leaflets are structured to form other aortic replacement valves.

The aim of the 3D DurAVR valve program is to develop a valve that is more durable than current devices and achieves superior hemodynamic performance. Anteris' ADAPT anti-calcification tissue processing technology offers the potential for heart valves to be implanted in younger patients. This durability benefit relates to ADAPT's superior ability to strip bovine or porcine pericardium of cellular DNA, significantly resisting the tendency to calcify. Evidence has accumulated that shows no calcification in ADAPT treated tissue more than ten years after treatment.

Anteris' novel 3D single piece design is already showing improvements in hemodynamics, according to data emerging from a 15 patient trial of the DuAVR valve at the Universitys Hospitals, Leuven, Belgium, for which the principal investigator is Professor Bart Meuris.

The single piece design is closer in shape to native heart valves, which allows for more natural motion of the leaflet, has an 85% increase in coaptation area and a 35% reduction in leaflet stress according to Meuris. (Coaptation refers to the way in which the leaflets fit together. Incomplete coaptation results in regurgitation.)

The outcomes of the trial will be two hemodynamic measures at six months, mean pressure gradient and EOA (effective orifice area).

PCR London Valves

At a recent PCR London Valves e-session for the Best Innovation session, Professor Bart Meuris was one of three surgeons invited to present on a current innovation.

Meuris presented data for five patients at discharge who have been implanted with Anteris Technologies' 3D DurAVR valve. While the eventual goal is to have the 3D DurAVR valve implanted using a catheter, the current trial has the patients being implanted using conventional open surgery methods. A sixth patient has been successfully implanted, however, data for that patient was not included.

The table that follows (next page) records peak gradient, mean gradient and EOA for these patients, along with selected data from trials of two competing TAVR devices, Medtronic's Corevalve Evolut and Edward Life Sciences' Sapien device.

Mean (pressure) gradient is a measure of blood pressure. EOA is a measure of the openness of the valve. The data for these devices is relevant because it is expanding the opportunity for aortic heart valves to be implanted in younger patients and at the same time increasing the appeal of TAVR devices relative to surgically implanted devices.

Continued over

The Corevalve Evolut TAVR arm was superior to the surgical arm achieving better measures for mean gradient and EOA at two years post-implant. ELS's PARTNER 3 trial did not deliver as strong a difference for its Sapien device, between the TAVR arm and the surgical arm at two years for hemodynamics; the mean gradient figure of 11.8 mmHg was superior in the TAVR arm, compared to 13.6 mmHg in the surgery arm, with both arms recording an EOA of 1.7 at two years. (Note however that the primary endpoint at two years was met, which was mortality, stroke or re-hospitalisation of 11.5% in the TAVR arm being superior to 17.4% in the surgery arm.)

What is distinctive about the data emerging from the trial of the 3D DurAVR valve is the strong trend towards normal values, or healthy human measures, with obvious differences emerging between the 3D DurAVR valve and the TAVR trial data for the Corevalve Evolut and Sapien valves.

Aortic valve mean gradients in healthy humans are 5 or less. Across five patients, DurAVR has achieved mean gradients (in units of mmHg) at discharge of 5, 15, 6, 7 and 4, respectively, and an average of 7. In contrast, for TAVR-implanted Corevalve Evolut's mean gradient at one month was 8.4 and for the Sapien device, 12.8.

Professor Meuris said that the second patient in the study had "high gradients because it had a very narrow aortic annulus, of 18 to 19 mm, which meant it was to be expected that they would have slightly higher gradients."

EOAs in healthy humans range from 3.5 cm^2 to 4 cm^2 . For the five implanted patients, DurAVR has achieved EOAs of 2.9 cm^2 , 1.5 cm^2 , 3 cm^2 , 2.3 cm^2 , and 2.5 cm^2 respectively, with an average of 2.4. cm^2 . Corevalve Evolut's EOA at one month was 2.2 cm^2 and Sapiens was 1.8 cm^2 .

Meuris concluded his presentation stating "there is still an issue with long term durability and hemodynamics in the current devices that we are using now. We are in the process doing this first-in-man study, looking at the feasibility of this single 3D pericardial valve, with ADAPT technology incorporated into it. The results show for the moment, excellent hemodynamic behaviour, with very low gradients, high effective orifice values and low velocities. This technology is very well suited for later development into clinical use a tanscatheter device."

Summary

In a small number of patients, the 3D DurAVR valve is producing evidence of being highly competitive against two leading valves.

Selected Discharge TTE Data for Five Patients Surgically Implanted with Anteris DurARV 3D Valve, October 2020

	Valve Size	Peak gradient (mmHg)	Mean gradient (mmHG)	EOA (cm2)
	27	11	5	2.9
	23	26	15	1.5
	27	11	6	3
	27	13	7	2.3
	25	8	4	2.5
Average			7	2.4

Selected Echocardiography Comparator Data

Healthy human			<5	3.5 - 4
Leuven Hospital Registry (1,400)		23	11	1.9
Corevalve Evolut TAVR arm				
baseline			44.8	0.8
at 1 month			8.4	2.2
at 2 years			9.0	2.2
Corevalve Evolut Surgery arm				
baseline			44.2	0.9
at 1 month			10.5	2.0
at 2 years			12.3	2.0
Sapien PARTNER 3, TAVR Arm				
baseline			49.4	0.8
at 1 month			12.8	1.7
at 2 years			11.8	1.7
Sapien PARTNER 3 Surgery Arm				
baseline			48.3	0.8
at 1 month			11.2	1.8
at 2 years			13.6	1.7

Medtronic Corevalve data is for patients with echocardiograph data

Should these positive results from the first five patients be repeated with the remaining patients in the trial, the company's confidence in initiating a feasibility study of the 3D DurAVR implanted by catheter (TAVR) will be boosted considerably.

An unknown aspect of 3D DurAVR TAVR device is how surgeons will adapt to a new technique required to implant the device.

An outstanding issue for the company is its low cash balance, which stood at $4.8 million at September 30, 2020, and a Survival Index of 0.3. (See *Bioshares* 867)

Anteris Technologies is capitalised at $22 million.

Bioshares recommendation:
Speculative Hold Class B

Bioshares

Sources: Anteris Technologies, Meuris presentation at PCR Valves London 2020
Popma et al, N Engl J Med 2019; 380:1706-1715; Mack et al, N Engl J Med 2019;380:1695-705
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How Bioshares Rates Stocks

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

Sell

Corporate Subscribers: Cogstate, LBT Innovations, Opthea, ResApp Health, Pharmaxis, Dimerix, Adalta, Actinogen Medical, Patrys, Cyclopharm, Antisense Therapeutics, Imugene, Exopharm, Immutep, Neuroscientific Biopharmaceuticals, Invex Therapeutics, Anteris Technologies