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C-Pulse always keeps heart failure at bay

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Dealing with the common diseases in an innovative manner is becoming a trend these days and not surprisingly, Australia is playing a crucial role in this. Sunshine Heart, a US-based company which is listed in Australian Stock Exchange, has developed a unique method to help the patients with class III or ambulatory class IV heart failure.

The company's C-pulse Heart Assist system has been making news, with the company receiving $23 million through an initial public offer (IPO) held in the US during October 2012. *BioSpectrum* speaks with Dr Elaine Stead, VP, corporate development, Sunshine Heart to find out more about the device, the company and the future that this device holds for the patients.

Please tell us about Sunshine Heart?
The company was founded in 2000 by the inventor Dr Will Peters and his business partner, Mr Crispin Marsh a patent

attorney, around the early intellectual property developed by Dr Will Peters for the C-Pulse device. Following, early investment by Australian based venture capital the company was eventually incorporated and listed on the ASX in 2004. Currently, the company has 16 employees and is headquartered in Minneapolis, Minnesota, US.

How does the company deal with funding issues?
Funding and continued access to it is an issue for all companies, particularly those in the medical technology or biotechnology space as development of healthcare products is a capital hungry exercise and can have long development times. Despite this, Sunshine Heart has always been able to raise capital.

It is important for companies to look at all forms of capital or funding, to access the right type of capital for the specific stage of development, to define and communicate value building milestones to investors and most importantly, to have a plan A, B, C and D.

Could you kindly tell us how the C-Pulse Heart Assist system was developed?
The C-pulse Heart Assist system was invented and developed by Dr Will Peters, a cardiac surgeon and founder of Sunshine Heart. His novel idea and device was developed based on the existing and well validated intra-aortic counter pulsation technology. Intra-aortic counter pulsation, is a well validated technology originally developed in the 1960's and used for acute periods of time (less than six hours) to treat various cardiac afflictions, but most commonly for weaning patients after cardiac bypass surgery and following myocardial infarction (heart attacks).

It consists of an inflatable balloon placed inside the aorta that inflates and deflates in synchrony with the heart beat to assist blood flow and reduce the workload of the heart. While this device is highly beneficial, as it is placed inside the aorta using a catheter, it can only be used acutely, and is not a feasible approach for long term relief or therapy.

Dr Peters' idea was to use the technology of counter pulsation to provide the same work load and blood flow benefits to the heart but in a way that allows the therapy to be applied outside the blood stream and thus could be implanted permanently for longer term benefits for those patients who needed chronic therapy, such as heart failure patients.

It was this idea that led to the birth of the C-pulse Heart Assist device, which consists of an inflatable balloon within a flexible cuff wrapped around the aorta just above the aortic valve. This inflatable balloon applies a 'thumbprint' pressure to the aorta when it inflates. Like traditional counter pulsation technology the timing of inflation and deflation is synchronized with the heart beat such that inflation occurs when the valve is closed, increasing coronary perfusion to the heart and deflates when the aortic valve opens, generating a vacuum like effect assisting the blood flow from the heart to the rest of the body.

The balloon cuff can be implanted minimally invasively, using an incision that is the same size used for pacemarker implantation. This cuff is then connected via sensing leads to the left ventricle to sense the heart beat/valve opening and also to a percutaneous lead that exits the patient at the abdomen and connects to an external battery and pump that sits on a patients waist.

The device has been trialed in 20 patients with moderate to severe heart failure which demonstrated that the device had both a strong safety profile and was able to provide symptomatic relief for Class III/ambulatory class IV heart failure patients.

How is C-Pulse different from the other solutions that are available to treat clinical symptoms associated with class III and class IV heart failure?
Heart failure is a progressive disease. Patients with class III heart failure have been given drug therapy such as beta blockers, diuretics and ACE inhibitors and resynchronization therapy (if indicated), yet they are still symptomatic and their heart failure has continued to progress. Class III heart failure patients are symptomatic even with mild exertion and suffer symptoms such as dizziness and shortness of breath.

Walking to the letterbox would be difficult for these patients and so their quality of life is severely compromised. Following drug therapy and cardiac resynchronization therapy, the only other treatment option for heart failure patients are life supporting devices such as left ventricular assist devices (LVAD's), artificial hearts and heart transplants.

These treatments are considered heroic measures, are highly invasive and carry risk of serious adverse events (clots, bleeding, stroke, death) and only implemented when the patient is in class IV heart failure and at risk of imminent death. For class III heart failure patients, who are refractory to drug therapy, there is no current treatment option, they are simply left to get worse and progress to class IV.

Please tell our readers about how cost-effective is C-Pulse?
While a precise cost benefit analysis cannot yet be determined as we are still in clinical trial stage in the US and have not yet had reimbursement approval in Europe, there are a number of metrics that we believe demonstrate the economic benefit trend of the C-pulse device:

Heart Failure is the leading cause of re-hospitalisation in the developed world with 25 percent of patient re-hospitalised for worsening heart failure after 30 days and 50 percent of Class III/IV heart failure patients are re-hospitalised by six months.

In the US, the heart failure related re-hospitalisation rate is such an economic burden, that in October this year the Affordable Care Acts Hospital Readmission Reduction Program was instituted and includes a penalty system to incentivize hospitals to ensure their heart failure related rehospitalisation rates meet a defined benchmark rate of less than 24.7 percent at 30 days. If hospitals exceed this benchmark then they risk repayment of reimbursements as a penalty. As such, we believe any approach that allows hospitals to reduce heart failure related re-hsopitalisation will be actively supported by hospitals.

In our pilot study trial, at least 17 of the 20 patients had been hospitalized due to worsening heart failure in the year prior to receiving our implant. Post implant, the re-hospitalisation rate at 12 months was 15 percent. Reducing this clinical and economic burden is such a priority that the FDA have approved the primary endpoint for our clinical trial with the C-pulse device to be the demonstration of a reduction in hospitalization rate due to worsening heart failure or heart failure related mortality. Other cost effective benefits we believe the C-pulse device offers compared to Class IV devices is:

In our pilot study, the average number of days in hospital was nine compared to 19 for patients who received a Left Ventricular Assist Device (LVAD). Our average number included those patients who received the C-pulse device both via minimally invasive approach and via a thoracotomy (which is a more invasive and requires additional post-operative care). Those patients who receive the C-pulse device implanted in a minimally invasive manner only require approximately four days in hospital.

Our device is currently sold for US$59,000 while it's being evaluated in premarketing and post marketing clinical trials, which is significantly lower than Class IV devices such as LVAD devices which cost in the order of US$150,000 and is in excess of the medicare/payer reimbursement level for these devices/procedures ($130,000).

When was the first patient implanted with the C-Pulse and so far how many patients have been treated with C-Pulse?
The first patient implanted was in 2005. However, since this time the device has undergone several modifications and improvements to improve the safety, robustness and convenience for the patient and the surgeon. For example, now the device consists of a single unit that comprises the battery and pump which is lighter and quieter, making it more convenient for the patient and the aortic cuff is pre-sutured to save time for the surgeon and reduce the time taken to complete the surgery (currently about 1 hour for minimally invasive procedures).

Our pilot study of 20 patients was completed in 2011 and demonstrated the C-pulse device had a strong safety profile (no serious adverse events - device related deaths, strokes, bleeding), In addition the device showed promising efficacy trends.

Overall patients showed a statistically significant improvement in heart failure status (1.2 Class improvement at 12 months) and quality of life measures . Two patients were permanently disconnected from the device after reporting no further heart failure symptoms and were discharged from a heart failure program. Close to 15 percent of patients were rehospitalised for worsening heart failure at 12 months post implant, compared to 85 percent re-hospitalisation rate for the same patients in the 12 months prior to receiving implant.

Drug Therapy improvements. All patients were either discontinued, reduced or unchanged from their diuretic drug therapy. All four patients who were receiving inotropes were successfully weaned within 48 hours of receiving the device. Improvements in Ejection Fraction and Left Ventricular End Diastolic Diameter (LVEDD or heart size). Currently, the device has only been approved for sale in Europe following awarding of CE Mark in July this year.

Will C-Pulse be available to the patients directly or through prescription only?
The C-pulse device will not be available to patients directly. The patients need to consult with their cardiologist about whether C-pulse device might be an effective therapeutic option for them.

Which is the biggest market for C-Pulse?
Class III and ambulatory class IV heart failure. These patients represent about 25 percent of the heart failure patients. Medtech analysts who cover the cardiovascular market and have written research on Sunshine Heart (Craig Hallum, Canacord, Cowen, RBS Morgans) have estimated the conservative market for the C-pulse device is in excess of $2.5 Bn (this is based on current device costs and conservative penetration).

How important is the latest regulatory milestone that Sunshine Heart has achieved? What are the conditions set by the FDA for providing marketing approval for C-Pulse?
The US market is the largest addressable market for the C-pulse device and obtaining marketing approval for the US is one of the company's primary goals. Conditional approval by the FDA of the IDE application is an important milestone in this process and getting the green light to commence the pivotal trial, which if successful, we believe will be sufficient to obtain marketing approval for the device in the US, is a key step toward this goal.

The conditions the FDA have set involved making minor changes to the informed consent, providing the Charters for the Data Safety Management Committee and Clinical Events Committee, minor revisions to the Investigator agreement, minor labeling updates and a few minor modifications to the study design not affecting the endpoints. Importantly, there were no substantive changes to the clinical trial design structure or endpoints.

Are there any other solutions that Sunshine Heart is offering to deal with heart failures?
The C-pulse device is the company's lead technology however it is also developing a fully implantable version to reduce the risk of exit site infection to the patient, make the device more patient friendly and broaden the market opportunity of the therapeutic device.

What are the future plans of the company?
In the last six months the company has achieved three key milestones, including getting the CE mark, FDA approval of the IDE, and raising of $23 million in capital through US IPO. The company's immediate plans are to execute the market strategies that will enable us to commence and roll out the US pivotal clinical trial and ensure that site engagement and patient recruitment meets our forecast timelines.

We will also begin a structured roll out in Europe, initially in Germany and Italy, and conduct a post marketing clinical trial (of approximately 50 patients) for reimbursement purposes. Largely, the companies resources (both human and financial) will be focused on these two key strategies and markets.