Edwards Bets on Treating Degenerative Regurgitation Via Mitral Repair with Harpoon Investment

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Harpoon Medical Executive Vice President Peter Boyd

December 10, 2015 – Harpoon Medical Executive Vice President Peter Boyd told *FierceMedicalDevices* that cardiology titan Edwards Lifesciences acquired an option to purchase the startup so that it can someday offer a solution for both functional and degenerative mitral valve disease patients.

Together they form a population that's three to four times larger than those suffering from aortic valve disease, a market that Edwards expects to treat to the tune of more at least $1.2 billion in 2016, thanks to the success of its Sapien TAVR franchise. Like other industry leaders, Edwards hopes the transcatheter mitral valve story plays out similarly.

Harpoon Medical will use the proceeds to fund a large, single-arm multicenter clinical trial designed to obtain a CE mark, which will begin enrollment next year. Boyd declined to disclose the company's timeline for European approval.

Mitral disease consists of two types of regurgitation: functional and degenerative. Both cause the blood in the heart to flow backward into the left atrium, but for very different medical and anatomical reasons. Crucially, Boyd said there is strong evidence that degenerative MR is better treated by mitral valve repair, while the data---such as a recent study of nontranscatheter surgical implants in the *New England Journal of Medicine*--is increasingly pointing toward mitral valve replacement as the optimal solution for functional MR.

Like several other industry leaders, Edwards has already covered its bases on the functional MR front by purchasing transcatheter replacement player CardiAQ Valve Technologies for $350 million in cash. Abbott is the only large company with a strong presence in transcatheter mitral valve repair thanks to the commercially successful MitraClip, which it purchased in 2009.

The option to acquire Harpoon Medical for an agreed upon price in return for an investment of an undisclosed sum in the Baltimore-based company rounds out Edwards' minimally invasive mitral valve disease portfolio, assuming both devices achieve commercialization, a milestone that is far from certain given the early stage of minimally invasive technology to treat mitral valve disease.

But Harpoon Medical's Harpoon System boasts some strong clinical data; the company reported at the TCT conference in San Francisco that all 10 patients in a feasibility study of its investigational minimally invasive mitral valve repair technology experienced a reduction or elimination of mitral valve regurgitation (MR).

Boyd said that out of the 55,000 open heart mitral valve surgeries in the U.S., 70% are for degenerative cases. The risks of open heart surgery keep many patients in on the sidelines, with 1.4 million Americans suffering from degenerative mitral valve disease alone, and even more in Europe (2.2 million).

"What Edwards and others see is that if you can come up with a much less invasive solution where you don't have to have open surgery, and you can still get good results in a large percentage of patients, there's an opportunity to dramatically expand the number of patients who actually receive treatment," he said.

Citing Edwards' Dec. 9 investor day presentation, during which the investment in Harpoon was announced, Boyd said that 60% of people with severe untreated severe mitral valve degenerative mitral valve disease are dead within 5 years.

He also described the nature of degenerative MR, and the mechanism of action of the Harpoon Medical's Harpoon System, as well as its advantages over open heart surgery.

"The problem with degenerative disease is that some of the mitral valve's native chords have either broken or stretched. Because they've broken or stretched or both, when the heart beats instead of the two sides of the valve lining up together, one side goes out of position," he said. "What our technology has been designed to do is to go and place that chord on the leaflet while the heart's beating so you don't have to worry about stopping the heart."

It works similarly to today's standard-of-care open heart surgeries for the condition, which involve implantation of Gore-Tex sutures to serve as replacement chords, with two crucial differences.

The procedure enabled by the Harpoon System (and its minimally invasive competitors) doesn't involve cutting open the chest nor stopping the heart from beating, sparing the patient from risky open-heart surgery and the use of a heart-lung machine, which is otherwise deployed while the heart is temporarily prevented from beating.

"Adjusting the length of those chords while the heart is stopped can be challenging, because when the heart stops and is flaccid, the shape same isn't the same," Boyd said. "It works better in the hands of a high-volume surgeon. For somebody who does that procedure 5 times a year, which is the national average, getting the length of those chords right is more challenging."

Thus, performing beating heart surgery improves not only safety, but possibly efficacy as well. "With our device you put those 3 or 4 chords and then when you're done, the surgeon can adjust those chords in real time," he said.

The Harpoon System does not involve the use of a delivery catheter because it is delivered transapically through a small incision in the chest. "The way that Edwards thinks about their product portfolio, which they've talked to us about, is when we're doing beating heart procedures, we refer to those as transcatheter," Boyd said, noting that two of the recently acquired development-stage transcatheter mitral valve replacement devices are also delivered transapically.

In contrast to transcatheter mitral valve repair, the replacement devices are going to be used to treat functional MR, Boyd said. Functional MR occurs when the heart becomes enlarged due to a traumatic event such as a heart attack.

When the normal-sized mitral valve is not big enough to cover the newly enlarged hole, "if you go back to first principles you can make a scientific explanation for why maybe in that situation it's better to actually replace the valve with a new bigger valve," he said.

Edwards' $350 million purchase of transcatheter mitral valve replacement company CardiAQ Valve Technologies triggered three additional acquisition from Abbott, Medtronic and smaller HeartWare worth more than $1.5 billion in aggregate.

Will Edwards' latest move lead to a similar scramble to buy the 8 to 10 companies on the repair side of the minimally invasive mitral valve disease market?

Boyd says it's likely: "My sense of the industry is that the mitral market is a very, very big market, most people are saying at least three, maybe four times bigger than the aortic valve market, and so I think there is still room for the big companies to invest in and possibly acquire other mitral valve technologies. I think most of the bets in the replacement space, at least for the next year or two, have been made. If you see more option type deals in mitral space in the next 12 to 18 months, my guess is that they will be more on the repair side than the replacement space."