



FIERCEMEDICALDEVICES'S 2014 FIERCE 15

by Stacy Lawrence & Varun Saxena

It's not easy to be a med tech startup. But it does look like it's getting a bit easier. Here we've taken a look at some of the most promising private med tech companies--those that embody a huge leap forward as well as those that offer meaningful improvement upon the past.

This year, medical device venture fundraising could actually increase for the first time since 2007. That's driven by the increasingly connected healthcare environment. VCs are going wild for digital health, the promise of convergence between our healthcare systems and all the mobile, cloud, wireless and wearable technologies you could possibly imagine.

During the first half, financing to "digital health" companies was \$2.3 billion; that's up from a total of less than \$2 billion for all of 2013, according to venture firm and industry analyst Rock Health. Now, digital health doesn't equate precisely to medical devices, but it does include many of the latest tech trends in the sector.

Even the more traditionally defined "medical devices and equipment" segment is finally regaining financing traction as IT investors become increasingly familiar and well versed in it. According to the National Venture Capital Association, these companies raised \$1.25 billion during the first half; that's up from \$1.09 billion during the same

period in 2013. Med tech venture financing cratered that year at \$2.1 billion.

The high-water mark for medical device venture financing was in 2007 with \$3.7 billion and 315 deals; since then it's fallen off every year. That year, med tech venture money was 62% of what went to the biotech sector; during the first half of 2014 that figure was a meager 43%.

Right now, med tech is the odd and ungainly combination of the established medical device sector along with all the promise and excitement that the go-go technology sector brings to the table.

A couple of the companies on our Fierce 15 list have successfully navigated this terrain. Both are in the cardiac monitoring space, which is seeing tremendous integration of wireless and mobile tech: cardiac arrhythmia monitoring patch company iRhythm and smartphone ECG plug-in maker AliveCor. iRhythm can be worn as long as 14 days, giving physicians a new diagnostic tool for disorders that may not conveniently present themselves during a single diagnostic test. And AliveCor can actually substitute for much more expensive cardiac diagnostic equipment--opening up the opportunity for affordable care to a whole new underserved population.



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Other startups on our list are looking to serve up treatments that are better than or complementary to existing drug options. These include Reshape Medical, which could have the first obesity device approved in the U.S. market in more than a decade, and Oraya Therapeutics, whose low-voltage, stereotactic, targeted X-rays could help wean patients off frequent use of wet AMD therapeutics--a lucrative biopharma category. In addition, central nervous system companies Tal Medical and NeuroPace are aiming to aid the underserved populations by providing, respectively, a rapid-acting, effective depression device and an antiepilepsy neural implant. Finally, Vertex (\$VRTX)-backed Holaira is developing its COPD renal denervation device.

The remaining startups on our list are working to reimagine existing medical devices. These include the first FDA-approved sleep apnea implant from Inspire Medical Systems; Gynesonics' uterine fibroid ablation device, an alternative to the increasingly defamed power morcellator during surgery; a hearing aid from EarLens that uses a light-based method to pull sound into the

ear rather than to merely amplify it; a novel transcatheter aortic valve replacement tool from Direct Flow Medical that improves placement and decreases complications versus the TAVR options from dominant players Medtronic (\$MDT) and Edwards (\$EW); and Breathe Technologies, with its lightweight, wearable ventilator that helps patients get better faster.

On the diagnostics side, we chose Astute Medical, with its acute kidney injury test that's the first approved by the FDA; CorTechs Labs, which has a novel software to improve brain volume imaging that could improve diagnoses of diseases such as Alzheimer's; and Infraredx with its first-in-class intravascular imaging system.

Whatever the task they've undertaken, each of these Fierce 15 companies will be worth watching in the coming years as the unprecedented intersection of medical devices with information technology continues to unfold. ■



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Based: Plymouth, MN

Founded: 2008

CEO: Dr. Dennis Wahr

Website: www.holaira.com



The Scoop: Drug options for chronic obstructive pulmonary disease (COPD) are only modestly effective. Holaira is betting that its lung denervation device can improve COPD treatment, either as a replacement for drugs or in addition to them.

COPD is characterized by persistent airflow limitation caused by progressive narrowing of the airways. This leads to shortness of breath,

wheezing, chest tightness and a productive cough. More than 190 million people worldwide, including 15 million U.S. adults, have COPD, according to the company. There are no curative drugs, they are only for symptom management.

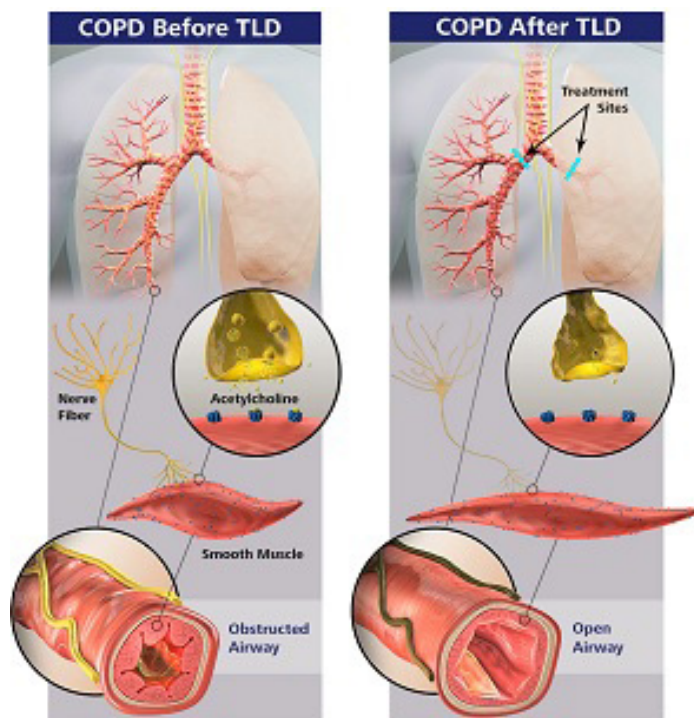
What makes Holaira fierce: Holaira's technology is a catheter-based system used in a procedure called Targeted Lung Denervation (TLD). Like anticholinergic COPD drugs, such as Spiriva and Atrovent, TLD targets the parasympathetic innervation of the lungs. The one-time bronchoscopic procedure ablates the nerves at the top of the lungs, thereby relaxing the airways beyond it.

"By interrupting those nerves, the airways can dilate," said Holaira President and CEO Dr. Dennis Wahr in an interview with *FierceMedicalDevices*. "This mechanism is how the anticholinergic drugs like Spiriva work. Spiriva works by blocking the parasympathetic system. It releases acetylcholine and when that hits the lungs it causes them to constrict."

He continued, "Pharmaceuticals block the acetylcholine. What we do is working on the same pathway, which we do by ablating the nerves upstream." He added that in its clinical trials, Holaira is using the same clinical endpoints as drugs, primarily FEV1 (forced expiratory volume), the 6-minute walk test and improvement in quality of life.

The company has done two feasibility studies in a total of 37 patients. It hasn't released detailed data yet but expects to have data published in a peer-reviewed publication in the coming weeks.

Although he couldn't offer any feasibility data details, Wahr



said the company was able to raise a \$42 million round on the strength of preclinical data earlier this year.

The Series D round closed in April; it was led by Vertex Venture Holdings with participation from Windham Venture Partners, Advanced Technology Ventures, Morgenthaler Ventures, Split Rock Partners, and Versant Ventures.

What to look for: Wahr said this financing will be sufficient to complete a Phase II study that has already started enrolling. He added that the company will pursue a clinical path that is more akin to drug testing including preclinical, Phase I, Phase II and Phase III, rather than the more typical medical device path from feasibility directly to pivotal testing.

Wahr noted that he thinks medical device development should be more similar to the track for drugs, citing \$100 million to \$140 million and 8 to 10 years as the norm for development of a novel device aiming for a PMA.

Holaira expects to have full Phase II data, including 12 months of follow-up, by the end of 2016. The Phase III trial would take an additional two years after that, pushing a potential FDA approval out into 2019. ■