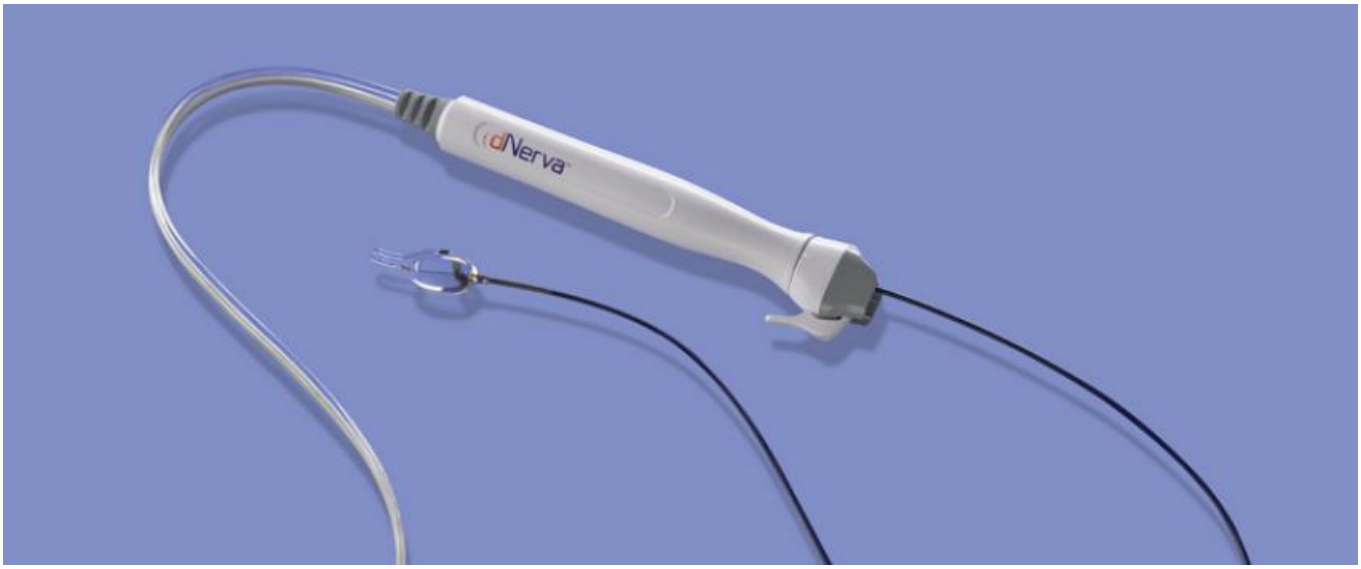
Evaluate Vantage

September 11, 2019

Nuvaira hopes to go with the flow in COPD

Elizabeth Cairns



If its study of lung denervation hits, Nuvaira could get US approval and maybe swing a trade sale.

You've heard of renal denervation – get ready for lung denervation. US group Nuvaira has just begun its US pivotal trial of dNerva, a system that attenuates parasympathetic nerve function in the lung, with the intention of opening up constricted airways in patients with COPD.

"What you need in today's world to successfully commercialise a product is overwhelming clinical data," Dennis Wahr, Nuvaira's chief executive, tells *Vantage*. And the company has shown its confidence – or possible healthy appetite for risk – by picking a challenging primary endpoint for its new study.

The dNerva catheter is inserted into the patient's lungs via their mouth, and emits electrical energy through the walls of the bronchi to ablate the pulmonary nerves that surround them. In this it mirrors the technique of renal denervation, a therapy under investigation for hypertension, in which the energy transmitted through the walls of the renal arteries to the sympathetic nerves on the outside.

It is the only such device in development, Mr Wahr says.

Pivotal

The Airflow-3 trial will randomise more than 500 patients to either radiofrequency ablation of the lung nerves or a sham treatment, with the aim of reducing moderate or severe COPD exacerbations.

"It's very rare that people will take on trying to prove a reduction in exacerbation rate because previous therapies have really been unable to do that," Mr Wahr says.

It is true that both Astrazeneca and Glaxosmithkline, for instance, have approved triple-drug combination COPD therapies that reduced moderate to severe exacerbations over other drugs (*Astra cannot breathe easy despite first triplet approval, June 19, 2019*). But Airflow-3 is enrolling patients already on these bronchodilators, so must demonstrate an effect over and above pharmacological therapy.

In the company's phase IIb trial of dNerva, Airflow-2, which recruited 82 moderate-to-severe patients with high symptom burden despite optimal medical management, the risk of severe COPD exacerbation requiring hospitalisation was significantly lower (p=0.039) in the treatment group compared with the sham group through 12.5 months of randomisation.

The magnitude of benefit was a 25% reduction in recurrent exacerbation rate, Mr Wahr says, describing this as

“meaningful”.

2022

If Airflow-3 can match this, the device will be well positioned for US premarket approval. Being unique, no reimbursement codes yet exist for technology like dNerva, so the company needs the Airflow-3 data to be good enough to convince payers, too.

US approval could come in about two and a half years, Mr Wahr says. At that point a buyer might emerge, and here Nuvaira’s early history comes into play. The group, then named Holaira, was spun out of The Foundry, the Californian incubator with an enviable record of developing companies that appeal to buyers (*Fire1 gets €40m for hush-hush heart monitor, February 8, 2018*).

“We’re growing the company. I think that’s the only way you can do it,” says Mr Wahr. “If the Airflow-3 and data duplicate the results of Airflow-2, I suspect there probably will turn out to be large companies that would certainly see this as potentially attractive, but that’s not our primary goal at this point.”

Even if Mr Wahr’s suspicion is well-founded, the company will probably remain independent until the spring of 2022 at the earliest. It is reasonably well-funded, its last VC round pulling in $79m from investors including Versant and Endeavour Vision – the deal was the fourth largest medtech VC round this year.

These investors have not taken a risk-free bet, of course. Devices intended to have a direct therapeutic effect on COPD – as opposed to inhalers or nebulisers intended to deliver drugs – do not have a flawless track record. Last summer an FDA adcom was unimpressed by BTG’s Elevair lung implant, and the group’s acquisition of the original developer, Pneumrx, for $230m in 2014, has been little short of a disaster.

Moreover the clinical value of renal denervation in hypertension remains unproven despite several groups committing themselves to large clinical trials. Nuvaira is bringing an unverified technique to a disease in which devices have stumbled; its pivotal trial will indeed have to yield overwhelmingly good data if the company is to achieve the goals it has set itself.

Nuvaira's VC funding

Date	Round	Investment ($m)	Investors
Feb 11, 2019	Series E	79	US Venture Partners; Advanced Technology Ventures; Endeavour Vision; Lightstone Ventures; Morgenthaler Ventures; Qiming Ventures; Richard King Mellon Foundation; Split Rock Partners; Versant Ventures; Vertex Venture Holdings; Windham Venture
Apr 3, 2014	Series D	42	Vertex Management; Advanced Technology Ventures; Morgenthaler Ventures; Split Rock Partners; Versant Ventures; Windham Venture
Feb 11, 2013	Series C	10	Advanced Technology Ventures; Morgenthaler Ventures; Split Rock Partners; Versant Ventures
Sep 20, 2012	Series B	11	Advanced Technology Ventures
Oct 1, 2010	Series A	3	Split Rock Partners; Versant Ventures
	Total	**145**	

Source: EvaluateMedTech.