



EINDHOVEN,
NETHERLANDS

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YEAR FOUNDED

2017

WHO'S BEHIND IT

Hubert Martens, CEO, who founded Sapiens Steering Brain Stimulation and led its product development; Daniël Schobben, Business Development, who previously founded Intrinsic-ID; Wim Pollet, Medical & Clinical Affairs, MD, formerly Medical Director of Sapiens; Michel Decré, Neurotechnology expert, formerly Sapiens scientific founder

UNMET CLINICAL NEED

A drug-free therapy for chronic migraine

SOLUTION

A novel neurostimulation platform that is able to treat known neural targets with a device that is well suited for implantation on the head and scalp

FUNDING TO DATE

A €3.1 million seed round raised in 2018, with the participation of Brabant Development Agency (BOM), Thuja Capital Seed Fund II, Netherlands Enterprise Agency, founders and employees of Salvia, and a recent investment by Brabant Startup Fund

Neuromodulation

SALVIA BIOELECTRONICS: A NEUROSTIMULATION PLATFORM FOR MIGRAINE

The founders of Salvia BioElectronics aim to give migraine sufferers back their lives. Building on research around known neural targets in migraine, the start-up is working to develop the right form factor for stimulation that is effective, safe, and affordable.

by
MARY STUART



They ride again. The core team of Sapiens Steering Brain Stimulation, which was sold to **Medtronic plc** for \$200 million three years after its founding, have started up a new company, **Salvia BioElectronics BV**, to apply their formula for success.

Sapiens Steering Brain Stimulation offered improved technology—an advanced lead with targeting precision for deep brain stimulation—to boost the efficacy of an established therapy working on known targets. Salvia BioElectronics will do the same, with a new neuromodulation technology capable of addressing known neural targets in migraine, while better addressing the needs of those who suffer from these debilitating headaches.

camaraderie they'd enjoyed from working together for so many years, and decided it was time to solve another clinical problem together. They settled upon migraine, and, says Hubert Martens, in the tiniest, most inexpensive office on the Eindhoven Campus, they began sketching out a new vision on a whiteboard.

It's an understatement to describe a migraine as a headache; disabling brain disorder is more apt. Martens says that as the team did research into the populations and therapies for migraine, he was surprised to learn that the World Health Organization categorized severe migraine attacks in the highest disability class among active psychosis, severe depression, and quadriplegia. Due to its high prevalence, migraine also ranks high as a major public health problem; it is the second largest cause worldwide of "years lost due to disability," just behind low back pain (according to Steiner, T.J., "Migraine is *first* cause of disability in under 50s: will health politicians now take notice?" *Journal of Headache and Pain*, Feb. 21, 2018).

People who suffer from migraines experience episodes of throbbing, pulsating pain, usually in one area of the head, sometimes accompanied by nausea, vomiting, and sensitivity to light, and these can last anywhere from a few hours to a few days. Ten percent of patients experience migraines for at least 15 days a month, a condition described as chronic migraine. In the US, 36 million people suffer from migraines, the majority of them women, who are three times more likely than men to get these attacks.

It's an understatement to describe a migraine as a headache; disabling brain disorder is more apt, according to Martens.

After the Medtronic acquisition, the Sapiens team—Hubert Martens, Daniël Schobben, Wim Pollet, MD, and Michel Decré—had continued on with Medtronic from their headquarters at the High Tech Campus in Eindhoven, Netherlands. When it was time, two years ago, for Medtronic to move the operations to the US, the team thought about the

Pharmaceutical treatments for migraine fall into two categories—preventive and abortive—the latter attempting to lessen the symptoms or shorten the duration of the attack. A wide choice of drugs in both categories has historically served some patients extremely well, some for only a time before they stop working, and some, not at all. The limitations of drugs include, as noted, limited efficacy, contraindications when patients are on other medications, side effects such as nausea, and the propensity for patients to worsen over time because of a phenomenon known as medication overuse headache. Up to 80% of migraine sufferers discontinue their preventive meds within one year (according to Hepp Z., *et al*, “Adherence to oral migraine-preventive medications among patients with chronic migraine,” *Cephalalgia*, 2015; 35(6):478-88).

The migraine problem has not been solved for many, spurring on therapy developers in both the pharmaceutical and medical device industries. The newest drug, the once-monthly injectable biologic *Aimovig* from **Novartis AG** (which gained FDA approval in 2018), shows promise as a preventive therapy that significantly reduces migraine days.

Device companies, for their part, have repurposed implantable spinal cord stimulators to stimulate occipital nerves (at the back of the head) and trigeminal and supraorbital nerves (near the eyebrow) to manage headaches. Other companies developing non-invasive, home based therapies are targeting the vagus nerve (for example, the FDA-cleared *gammaCore* device from **electroCore Inc.**) or are using transcranial magnetic stimulation (the modality of **eNeura Inc.**, which is also selling an FDA-cleared device for home use).

But patient and clinician surveys taught *Salvia*'s founders that patients wanted something unobtrusive and as easy to use as taking drugs that achieved optimal stimulation of target nerves over long periods of time. According to that list of requirements, none of the existing neuromodulation platforms is ideal, Martens says. Conventional leads can't be placed on the head unobtrusively and without suffering from breakage and skin erosion, whereas non-invasive devices can't make intimate contact with the nerve to get targeted delivery of stimulation with low levels of energy (because high levels are painful to the patient) and are moreover subject to patient compliance.

Those are the issues *Salvia Bioelectronics* has set out to address with a new technology. “It is a great opportunity to build on clinical evidence with a technology specifically developed for this indication,” says Martens. He points out that because of the clinical work done by manufacturers of spinal cord stimulation systems “there is indeed literature about stimulating the occipital and other nerves, and the benefits of providing a wider stimulation coverage across multiple nerves.”

The company is at an early stage, and isn't ready to disclose the finer details of what it is doing; indeed, at the date of this writing, its website doesn't yet mention that the starting application is migraine. Martens offers that *Salvia*'s platform delivers stimulation not by a conventional lead, but by “A highly integrated bioelectronics foil” that can be placed below the skin to cover the nerves of the head. “In terms of our device design, we think a lot about the anatomy of the head and scalp and the limitations they present,” he says. The bioelectronics foils

are thin, and unobtrusive. “When we approached patients with our early prototypes, it was important to them that it would be unnoticeable.”

It was also important for patients to regain control of their lives, since migraineurs might spend days lying in agony with the shades pulled down. It can be particularly devastating because it affects people in the prime of their lives; the peak incidence of migraine occurs in people in their 30s. As noted, women are three times more likely to develop migraines, and, Martens says, “We have spoken to women who have decided not to have a family because of the disease.” Martens says *Salvia* wants “to give patients control over their therapy,” by allowing them to apply the best possible therapy settings on a day-to-day basis.

The next milestone for the company is the completion of a Series A round. Funding to date of €3.1 million, raised in May 2018, is largely non-dilutive, coming from the Brabant Development Agency (BOM), The Brabant Startup Fund, Thuja Capital Seed Fund II, Netherlands Enterprise Agency, the start-up's founders and employees, and support from the Eurostars and ECSEL programs of the European Commission.

Martens points out that in contrast to *Sapiens Steering Brain Stimulation*, which grew up around a concept developed within Philips Healthcare, *Salvia Bioelectronics* started from scratch. He is happy to say “It's only been 18 months since we hired the first people. We have a prototype, we have patents filed, we have clinical collaborations that give us feedback from patients and physicians, and we have secured our seed funding. I'm very proud of this team.” 