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Merck KGaA marches to its own beat in bioelectronic medicine

by Susan Schaeffer, consulting editor

A pair of deals between Merck KGaA and two different startups signals the German company's interest in exploring bioelectronic medicines. But it's hard to tell what Merck's interest might augur for broader pharma appetite, because Merck's business model makes it an outlier among its peers.

Robert Spoelgen, Head of Bioelectronics at Merck, told *BioElectRx Business Report* that Merck considers bioelectronic medicines a "future pillar of medicine."

"Today, bioelectronic devices are used for patients that do not find an adequate solution with traditional pharmaceuticals," he said. "But we have good reasons to believe that our devices could offer an effective treatment for a broad range of patients."

Merck announced on June 29 that it would collaborate with neuroloop GmbH to develop a neurostimulation device for chronic inflammatory diseases. neuroloop is a spin-off of the University of Freiburg, the Freiburg University Medical Center, and the Aesculap AG surgical division of medtech company B. Braun. The startup is developing a closed-loop implantable device that allows selective stimulation of fibers in the vagus nerve.

According to Merck, neuroloop has a novel multichannel cuff electrode based on thin-film technology. Merck believes the technology can complement drugs used by patients with chronic inflammatory diseases by delivering localized therapeutic effects. The company said the electrode is capable of highly selective stimulation of specific fibers within the vagus nerve, which is expected to minimize side effects.

A second deal, announced July 8 with the Innervia Bioelectronics subsidiary of Inbrain Neuroelectronics S.L., covers co-development of graphene-based bioelectronic vagus nerve therapies targeting severe, chronic inflammatory, metabolic, and endocrine diseases. Innervia is developing intelligent systems that both record and modulate vagus nerve signals using graphene electrodes.

Merck expects the graphene technology to increase energy efficiency in neurostimulators, enabling digital personalized treatment of severe and chronic diseases such as inflammatory disorders, Laura Matz, Merck's chief science and technology officer, said in a statement announcing the deal.

Energy efficiency becomes more important for devices that both sense and respond to nerve activity, because reading, analyzing, and transmitting data consume more energy than neurostimulation alone. The need for increased power is at odds with the need to miniaturize devices for implantation. Thus

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graphene, with its single-atom thickness and unique electrical and thermal conduction properties, may kill two birds with one stone.

Both deals were done by the Merck Innovation Center, a group tasked with forming and incubating new businesses outside Merck's current R&D scope. The company hasn't disclosed further details about the deal terms, target indications, or development plans.

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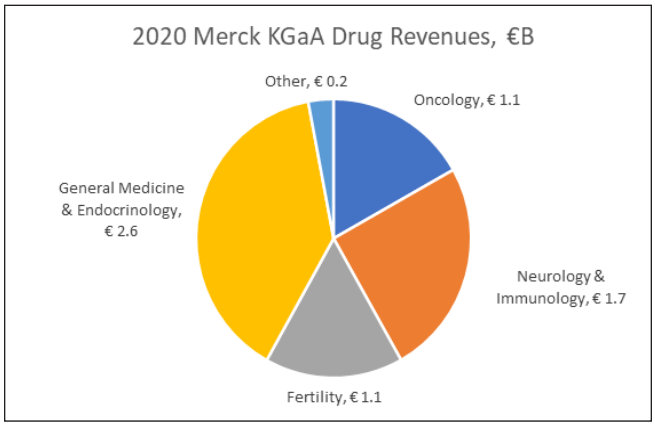
> Head of Bioelectronics at Merck

Unique strategy

Examining Merck's history helps to understand how bioelectronics may fit into its strategy, which is unique among midcap pharmas.

While other European midcaps spent the early 2000s splitting up unrelated business units into stand-alone, pure-play pharmaceutical or chemistry companies, Merck has remained steadfastly committed to a risk-diversification strategy that involves building out three distinct "business sectors" in prescription medicines, laboratory supplies and equipment, and performance materials used in electronics.

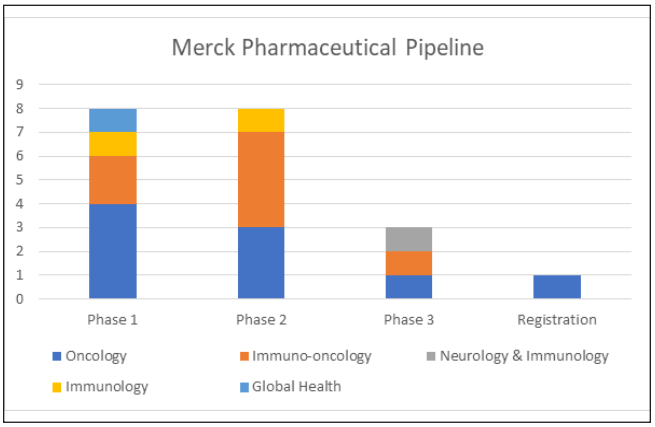


The bioelectronic medicine deals would tap into expertise in both the pharmaceutical and electronics sectors, and the therapeutic areas of inflammation, endocrinology, and metabolic diseases align with Merck's pharmaceutical focus. Merck reported €6.6 billion in pharmaceutical revenues for 2020. Drugs for cardiometabolic and endocrinology diseases accounted for 39%, while multiple sclerosis drugs accounted for 25%.

Its pipeline of investigational drugs is dominated by cancer and immuno-oncology programs, with just two programs for indications that could be considered as chronic inflammatory diseases: enpatoran, a Phase I candidate to treat lupus; and evobrutinib, a Phase III candidate for MS.

The company also has numerous early-stage research collaborations and licensing deals for drug candidates to treat inflammatory and metabolic/endocrine diseases.

While Spoelgen acknowledged that medical devices—including bioelectronic medicines—will require a different commercial infrastructure than Merck's pharmaceuticals business, he said the company expects bioelectronic medicines to benefit from "our long track record working with doctors and patients."



Sizing up the competition

It's not clear whether Merck will find itself in competition with the more established Galvani Bioelectronics—and Galvani's majority owner, GlaxoSmithKline plc—although both are working in inflammatory and endocrine/metabolic diseases.

Galvani's first program to enter clinical testing entailed the use of neurostimulation to prevent systemic inflammation during esophagectomy, which completed a feasibility study in October 2020. On October 19, 2021, according to clinicaltrials.gov, Galvani began two studies testing stimulation of the splenic nerve bundle to treat rheumatoid arthritis. Neither program addresses indications in which Merck has

disclosed development programs or marketed drugs. Although Merck was developing candidates for osteoarthritis, it announced the intention to partner them out in late 2019.

However, Galvani also has published on the design of a spatially selective multi-electrode cuff array for vagus nerve neuromodulation, and is reported to have at least one preclinical program in metabolic/endocrine disorders.

Other bioelectronic medicine players in chronic inflammatory diseases include SetPoint Medical Corp., whose Micro-Regulator platform is in pilot testing for RA and in proof-of-concept testing for Crohn's disease. SetPoint also has a preclinical program in MS. Micro-Regulator is an implantable device for controlling the inflammatory response by selective stimulation of the vagus nerve.

In metabolic/endocrine disorders, potential competitors include MedAutonomic, whose gastric pacemaker is in feasibility testing for type 2 diabetes and obesity; and Metavention, whose transcatheter-based Metabolic Neuromodulation Therapy is in feasibility testing to treat type 2 diabetes.

B. Braun
Melsungen, Germany
www.bbraun.com

Galvani Bioelectronics
Stevenage, U.K.
www.galvani.bio

GlaxoSmithKline plc (LSE:GSK; NYSE:GSK)
London, U.K.
www.gsk.com

Inbrain Neuroelectronics S.L.
Barcelona, Spain
www.inbrain-neuroelectronics.com

MedAutonomic
Concord, CA
www.medautonomic.com

Merck KGaA (Xetra:MRK)
Darmstadt, Germany
www.merckgroup.com

Metavention
Maple Grove, MN
www.metavention.com

neuroloop GmbH
Freiburg im Breisgau, Germany
www.neuroloop.de

SetPoint Medical Corp.
Valencia, CA
www.setpointmedical.com