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Sehr gut: Autobahn roars out of stealth mode with $76M, new leitmotif in MS

By Randy Osborne

San Diego-based Autobahn Therapeutics Inc.'s $76 million series B round will let the firm advance lead candidate ABX-002, a thyroid hormone receptor beta agonist therapy for multiple sclerosis (MS) and adrenomyeloneuropathy (AMN), a rare genetic disorder, plus a portfolio of central nervous system (CNS) programs that leverage the company's brain-targeting chemistry platform.

The science originated with Tom Scanlan at Oregon Health & Science University, whose "lifetime of work in the area" let him devise a "very novel, clever way" of deploying thyroid hormone's role in myelin production to invent small-molecule receptor agonists that stimulate regrowth of the nerve-fiber sheath, CEO Kevin Finney told *BioWorld*. "We're starting with a position of validated human genetic biology" that involves oligodendrocyte progenitor cells, which differentiate to form myelin and which are stimulated by thyroid hormone. The brain-targeting aspect leverages the enzymatic activity and tissue distribution profile of fatty acid amide hydrolase, with prodrug technology that maximizes the on-target effects without systemic activity.

Kevin Finney, CEO, Autobahn

As a therapeutic space, MS is plenty crowded with approved drugs but still regularly generating news of those moving through pipelines. Just last week, Basel, Switzerland-based Novartis AG said the FDA delayed action for three months on the sBLA for its candidate, Arzerra (ofatumumab, OMB-157). Wainwright analyst Raghuram Selvaraju gave the drug, partnered with Genmab A/S, a 95% chance of approval; Arzerra was first cleared in October 2009 for chronic lymphocytic leukemia. Big pharma player Bristol Myers Squibb Co. has had better luck, and recently launched Zeposia (ozanimod), cleared in March of this year for MS. RBC analyst Brian Abrahams, in a note weighing Zeposia, called it "an important additional entrant" in the jostling market.

"If the patient's winning that day, then they're remitting," Finney said. "If the inflammatory process is winning the next day, then they're flaring. It's a battle, but these MS patients are progressing" and the hunt is underway for better prospects. "Does the world really need another immunosuppressant in MS?" he asked rhetorically. Autobahn's therapy would be used in tandem with other therapies. "We think it could work with all mechanisms," he said. "Obviously, we'll let our science bear that out. Our initial proof-of-concept studies are going to be [in] all comers."

Research into the MS proceeds apace. Work published this month in *Neuron* showed how astrocytes, star-shaped glial cells of the CNS, can transform into neuron-killers in an inflammatory setting, making diseases such as MS advance faster. The effort, led by the New York Stem Cell Foundation, made astrocytes derived from human induced pluripotent stem cells (hIPSCs) for the testing. In late May, investigators at RMIT University in Melbourne, Australia, reviewed 113 studies, discovering a link between changes in gut mucus and the development of neurological disorders such as MS. Findings appeared in *Frontiers in Cellular and Infection Microbiology*.

AMN is a form of X-linked adrenoleukodystrophy that tends to surface in an affected person's late twenties, according to the NIH. Signs and symptoms may include progressive stiffness and weakness of the legs, ataxia, speech difficulties, adrenal insufficiency, sexual dysfunction and bladder control issues. Some with AMN also turn up with brain involvement, which can lead to behavioral abnormalities, vision loss, hearing problems and/or seizures. Specifically, the disorder is caused by mutations in the ABCD1 gene. Treatments that address symptoms include steroid replacement therapy for adrenal insufficiency.

Soon after starting its work, Autobahn was contacted by a man with AMN who had started a patient advocacy group. He had been active before the disease struck but developed lower-body dysfunction that "ended up looking very similar to MS," Finney said. A blood test that measures the levels of very long-chain fatty acids and/or genetic testing for the ABCD1 mutation in the ABCD1 gene can be used to confirm the diagnosis. Next comes magnetic resonance imaging (MRI) of the brain to determine whether cerebral involvement has set in or the disease is limited to the spinal cord. Generally, AMN affecting the brain and spinal cord bears a worse prognosis. About 40% to 45% of people with AMN show some degree of cerebral involvement on MRI. In some cases (10% to 20%), the brain disease becomes severely progressive and may lead to cognitive decline, behavioral abnormalities, physical disability and death.

The company is funded for three years, and phase I trials are expected to begin this time next year. "We haven't quite decided

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if we're going to take our lead program, pursuing two indications, and develop a franchise in a bottle" or nominate a second drug and pursue one in each indication, Finney said. The goal is to conduct four proof-of-concept studies in parallel, preparing for a phase IIb in MS and potentially a phase II/III registration study in AMN.

Arch Venture Partners and Cowen Healthcare Investments co-led the series B round, with participation from BVF Partners LP, Biogen Inc., Bristol Myers Squibb, Pfizer Ventures, Invus, Section 32, Samsara Biocapital and Alexandria Venture Investments.

Formed in late 2019, Autobahn launched with a series A round of $18 million, led by Arch. The company lists 11 staffers and expects to employ "a little under 20" by the end of this year, mostly in R&D, Finney said. Its name derives from the German highway system, high-speed and interconnected like the CNS, he said.

Asked how the COVID-19 pandemic is affecting operations, Finney said that "a couple of weeks ago, I said, 'Nothing,' and it's still almost nothing." A quarter of the team was hired virtually, he said, and Autobahn's lab is open; the company also use contract research organizations. "We're already very close to the clinical sites in the U.S., and there are one or two clinical sites in northern Europe that are well known in MS and AMN," he said. "We don't anticipate any problems with recruiting over the next year and a half to two years. I don't think we're going to miss a blink."