

Fast ForwardSM

Accelerating Innovation Fund

This project is funded through a collaboration between Fast Forward, LLC, established by the National MS Society to speed potential therapies into drug development and clinical trials, and EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany. Fast Forward and EMD Serono committed \$3 million in 2009 to support innovative early-stage projects directed towards the development of therapies to prevent, treat, or reverse nervous system damage in MS. This was the first "Request for Proposals" (RFP) issued under the auspices of a multi-year collaboration between Fast Forward and EMD Serono to accelerate innovation and commercial development of MS therapies. Merck KGaA, the parent corporation of EMD Serono, Inc., will provide up to \$19 million in total funding for the collaboration.

<i>Primary Investigator</i> Michael Leach, PhD CenTRion Therapeutics, LTD	<i>Project Title</i> Novel triazine compounds for the treatment of multiple sclerosis	<i>Amount to be Committed</i> \$275,000 Term – 12 months
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About the Company

CenTRion Therapeutics Ltd was founded in the United Kingdom by a team of researchers investigating central nervous system (the brain, spinal cord, plus optic nerve) drug discovery. As employees of Wellcome Research Laboratories, this team was involved in taking drugs such as lamotrigine (Lamictal[®]) from bench to market. They came together again at the University of Greenwich. Led by Michael Leach, PhD, they formed CenTRion, and are utilizing the environment and facilities within their university to develop a fast-track, low-risk approach to discovery and preclinical development of treatments for CNS disorders, primarily MS.

Project Background & Goals

Multiple sclerosis occurs when the immune system attacks the brain and spinal cord, damaging the myelin that protects and insulates nerve fibers, and the nerve fibers (axons) themselves. Degeneration of axons is thought to be the major determinant of long-term neurological disability in MS, and no current MS treatments focus primarily on directly preventing this damage. Sodium channels – tiny pores along axons that are essential to nerve impulse



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conduction – are thought to contribute to axonal destruction, and recent findings suggest that molecules capable of blocking sodium channels may protect axons.

The CenTRion team played an active role in the development of the epilepsy drug lamotrigine, a sodium channel blocker that has shown preliminary benefit against MS relapses. But they think that this drug will only have a weak effect in MS at doses approved to treat epilepsy, so they are investigating alternative sodium channel blockers. The team has developed more than 200 similar compounds and has screened these candidates for sodium channel-blocking activity, oral availability, penetration of the central nervous system, and side effects. With funding from the Fast Forward/EMD Serono initiative, the team is now assessing the neuroprotective abilities of several compounds in preclinical models of acute and chronic, progressive courses of EAE, an MS-like disease, and conducting other testing necessary to develop a compound ready for human testing.

Protecting nerve cells and fibers and preventing disease progression is a vast unmet need in MS treatment. This project has tremendous potential to begin to answer this need by bringing a specific and potent treatment strategy closer to the point of clinical trials in people with MS.