

Fast ForwardSM

Fast Forward was established by the National Multiple Sclerosis Society, as part of the organizations' promise to people living with MS — a unique end-to-end commitment to MS research and treatment.

As a critical part of this comprehensive approach, **Fast Forward** is devoted to bridging the gap between promising research discoveries and drug development — providing critical funding for proof of concept and preclinical development activities. Filling this gap ensures that promising discoveries do not languish on a shelf waiting for funding, development resources and expertise, or the engagement of biotechnology and pharmaceutical organizations. **Fast Forward** is all about speeding the process between research discoveries and their entry into clinical trials — faster — resulting in more and effective treatments for the more than 2 million people worldwide living with MS.

Since its founding in 2007, **Fast Forward** has engaged in a global effort to identify and fund MS drug discovery and development programs through two funding streams: the **General Fund** (\$30 million philanthropic fund), and the **Collaborative Fund** (\$30 million collaborative industry fund). Significant progress continues to be made, as summarized below.

Fast ForwardSM

General Fund Progress



Amplimmune, Inc., Rockville, MD — A series A VC-backed (InterWest and Wellcome Trust) company spun out of Johns Hopkins University that is developing a novel biological molecule that redirects immune responses in MS. Amplimmune is collaborating with Dr. Steven Miller (Northwestern University) to conduct preclinical studies to demonstrate the efficacy of AMP-110 in animal models of MS. Amplimmune is currently engaged in raising its Series B financing.

Project Summary: Development of recombinant B7-H4-Ig fusion protein as a therapeutic treatment for multiple sclerosis.

Fast Forward Project Funding: \$500,000 to support the development of an immune therapy called AMP-110, which would target the inflammatory response in MS. AMP-110 has already shown efficacy in other autoimmune diseases.



Apitope International, Bristol, United Kingdom — A series B, VC-backed (LRM and Vesalius Biocapital) company developing a tolerizing therapy, ATX-MS-1467, for MS. Subsequent to Fast Forward's investment, the company entered into a \$200 million licensing and development agreement with Merck Serono to underwrite additional development of the ATX-MS-1467 program.

Project Summary: The use of peptide antigens for prevention and treatment of autoimmune disease.

Fast Forward Project Funding: \$1 million to support the design and conduct of a phase IIb proof of concept trial for the company's lead product ATX-MS-1467 in relapsing remitting MS.

Fast ForwardSM



Axxam SpA, Milan, Italy– A privately held company spun out of Bayer AG. Axxam is conducting a discovery program to identify lead compounds that target specific molecules on immune cells in MS and Type 1 diabetes. **Fast Forward** is co-funding the program with the Juvenile Diabetes Research Foundation.

Project Summary: Innovative immunosuppressant for potential prevention of type I diabetes, multiple sclerosis and other autoimmune diseases.

Fast Forward Project Funding Year 1: \$250,000 joint funding with the Juvenile Diabetes Research Foundation to support use of Kv1.3, a channel inhibitor, as a small molecule immune therapy for treatment in MS. Company is ready to complete validation in an animal model and move it into a clinic setting.

Fast Forward Project Funding Year 2: \$220,000 joint funding with the Juvenile Diabetes Research Foundation



Canbex Therapeutics, London, United Kingdom – A privately held company spun out of University of London. Canbex is developing an oral therapy that may treat the muscle spasticity that affects people with MS.

Project Summary: Development of a new treatment for spasticity associated with multiple sclerosis.

Fast Forward Project Funding: £242,500 in funding support for studies that will accelerate the testing of VSN16R, a small molecule compound that has shown good evidence of anti-spastic effects in laboratory models of MS and spasticity.

Fast ForwardSM



Five Prime Therapeutics, San Francisco, CA – A privately held venture capital backed company that is developing a range of therapies for human diseases.

Project Summary: Development of a pre-clinical testing of a biological molecule for the treatment of multiple sclerosis.

Fast Forward Project Funding: \$800,000 to fund the advancement of a biologic targeting specific cells of the innate immune system.



Provid Pharmaceuticals, Monmouth Junction, NJ – A privately held medicinal chemistry company developing a small molecule, PV-267, that disrupts abnormal functioning of the immune system in MS. Provid is collaborating with Dr. Thomas Forsthuber (University of Texas – San Antonio) to conduct preclinical validation studies with PV-267.

Project Summary: MHC Class II inhibitors for multiple sclerosis

Fast Forward Project Funding Year 1: \$50,000 to support R&D costs for their MS program, PV-267, which is expected to lead to the generation of small molecules that interact with immune cells and disrupt antigens from attacking the brain.

Fast Forward Project Funding Year 2: \$260,000 to enhance immunology and safety data to support further development of PV-267.

Fast ForwardSM



Athersys, Cleveland, OH – A publically traded biopharmaceutical company engaged in the discovery and development of therapeutic product candidates. The Company is developing an adult stem cell platform for the treatment of MS, including progressive forms of the disease. Athersys is collaborating on this project with Robert H. Miller, PhD, Vice President for Research at Case Western Reserve University School of Medicine.

Project Summary: Development and testing of Multistem[®] allogeneic stem cell product for treatment of multiple sclerosis.

Fast Forward Project Funding: \$640,000 to fund the advancement of this program to the clinical development stage.



Lineagen, Salt Lake City, UT – A privately held commercial diagnostics business with leading programs in autism spectrum disorder (ASD), multiple sclerosis (MS), and chronic obstructive pulmonary disease (COPD). Lineagen is developing gene and biomarker based clinical assays for MS.

Project Summary: Development and validation of clinical biomarker for use in blood-based tests to speed the diagnosis of multiple sclerosis.

Fast Forward Project Funding: \$622,000 to establish and validate a broad array of biomarkers for MS, including genes associated with predisposition for the disease, and blood-based markers that have diagnostic and prognostic potential. This project is being conducted in collaboration with the University of Utah.

Fast ForwardSM

CoNCERT Pharmaceuticals Inc.TM

Concert Pharmaceuticals, Lexington, MA – A clinical stage biotechnology company focused on applying the company’s DCE PlatformTM (deuterated chemical entity platform) to create novel and differentiated small molecule drugs. Concert is advancing a therapy for spasticity and pain in MS.

Project Summary: Development of C-21191 for treatment of spasticity and neuropathic pain associated with multiple sclerosis.

Fast Forward Project Funding: \$750,000 to help advance development of its C-21191 agent toward clinical trials in people with MS.

DIOGENIX

DioGenix, Gaithersburg, MD – A molecular diagnostics company intent on commercializing novel molecular tests for neurological diseases where the current standard of care lacks diagnostic certainty. The company’s lead program is focused on improving the ability of neurologists to diagnose and treat patients that have, or are suspected of having, Multiple Sclerosis.

Project Summary: Development of a blood-based diagnostic test for multiple sclerosis.

Fast Forward Project Funding: \$479,000 to accelerate the progress of this program which, if successful, will lead to a simple blood test that can aid physicians in the clinical diagnosis and monitoring of MS.

Fast ForwardSM



Ezose Sciences Inc., Pine Brook, NJ – A glycomics-focused company that leverages its unique, high-throughput glycan analysis technology to discover and develop new biomarkers and therapeutic targets, and provide glycoform analytical service to support biologic and biosimilar drug development. Ezose’s proprietary GlycanMap® technology platform brings a new dimension to biomarker discovery by enabling glycomics research on a scale comparable to that of genomics and proteomics.

Project Summary: Development of novel “glycans” - sugar complex – biomarkers that might be useful as signposts for diagnosing multiple sclerosis and also for determining disease subtypes.

Fast Forward Project Funding: \$390,000 to support the discovery of new biomarkers and targets that can improve the diagnosis and management of multiple sclerosis and enhance the efficacy of developing new therapeutic options.

UNIVERSITY OF CAMBRIDGE

University of Cambridge, Cambridge, UK – Research at the Universities of Cambridge and Edinburgh has led to the identification of a key pathway called, “retinoid X receptor” (RXR) and its role in the brain in patients with MS. This group has showed that when stimulated, this receptor causes nervous system repair (remyelination) in animal models of CNS demyelination and thus represents a novel target for stimulating nervous system repair in humans. The project grew out of findings from a Nervous System Repair and Protection Initiative funded through the Society’s Promise: 2010 campaign.

Project Summary: Identification of retinoic acid gamma agonist ‘hit like’ molecules which plays a role in forming new myelin in multiple sclerosis. This project aims to identify compounds that slow or stop worsening symptoms associated with loss of myelin.

Fast Forward Project Funding: \$200,000 to support the virtual screening program to identify selective small molecule agonists of RXR gamma involved in repairing demyelinated axons in multiple sclerosis.

Fast ForwardSM



University College London, London, UK – Research at the University College London has led to the development of a possible therapy to protect nerve damage. This group is developing a molecule similar to Cyclosporin (cyclophilin D inhibitor), which has been investigated as a possible neuroprotective agent in conditions such as traumatic brain injury, and has been shown in animal experiments to reduce brain damage associated with injury.

The project will focus on identifying and developing a new experimental compound and testing to see if it can induce neuroprotective effects while eliminating immune suppressive effects in the CNS in an animal model of MS.

Project Summary: Development and testing of a selective cyclophilin D (CyP-D) blocker for neuroprotection in multiple sclerosis.

Fast Forward Project Funding: \$285,000 to support the synthesis and optimization of a variety of chemicals similar to cyclosporin A, which has been shown to inhibit cyclophilin D, in protecting nerve damage in MS.



University of Miami, Miami, FL – Research at the University of Miami has led to the development of a possible therapy for treatment of cognitive impairment in MS. A group of researchers at the University of Miami Miller School of Medicine MS Center, in conjunction with Accera, is currently undertaking a study to examine the safety, tolerability, and efficacy of Axona for the treatment of cognitive dysfunction in MS. Previous research suggests that there may be flaws in how glucose is metabolized in the brains of individuals with MS. If these metabolic abnormalities are contributing to cognitive dysfunction in MS, Axona may provide a therapeutic strategy to treat MS-related cognitive problems. This double-blind, randomized, placebo-controlled study will be conducted by this group and will enroll 158 people with MS at the University of Miami Miller School of Medicine MS Center over the next three years who

Fast ForwardSM

have experienced cognitive problems to determine whether Axona can help restore cognitive function to people with MS.

Accera, Inc., Broomfield, CO - A privately-held, commercial-stage, healthcare company focused on the discovery and development of innovative clinical applications to address acute and chronic neurodegenerative diseases. The company is now examining the effects of Accera's medical food product, Axona, on cognitive impairment in patients with MS.

Project Summary: Clinical trial at the University of Miami to determine potential benefits of Accera's medical food product, Axona, on cognitive impairment in people with MS.

Fast Forward Project Funding: \$544,750 to support a double-blind, randomized, placebo-controlled study of Axona for cognitive impairment in MS.

Collaborative Fund Progress

Fast Forward has formed a 5-year \$19 million strategic alliance with EMD Serono/Merck KGaA to speed drug development through the MS pipeline through mutually agreed upon seed-to-early-stage projects.

In the first year of the collaboration, 4 drug development programs in the area of neural repair and protection were selected for funding. Under the terms of the collaboration, EMD Serono/Merck KGaA will have the option to in-license these programs at their completion. A list of the projects is below.

2009

The following are the recipients from the ***Accelerating Commercial Development Fund***:

innatetherapeutics

Fast ForwardSM

Innate Therapeutics Limited, Auckland, New Zealand (Project Director – Simon Wilkinson) will receive \$550,000 over 15 months to conduct a phase IIa clinical trial in patients with progressive forms of MS using MIS416, a naturally occurring agent derived from bacteria.



Cognosci Inc., Research Triangle Park, NC (Project Director – Feng Qiao Li, PhD) will receive \$330,000 over 12 months for the efficacy testing of COG112, a molecule that mimics actions of the cholesterol transporting protein, ApoE. In the funded studies, the company will evaluate the ability of COG112 to promote myelin repair in the central nervous system (CNS) in laboratory models of MS.

The following organizations will receive financing from the ***Accelerating Innovation Fund***:



CentRion Therapeutics Limited, a spin out of the University of Greenwich, UK, (Project Director – Michael Leach, PhD) will receive \$275,000 over 12 months for studies with compounds, related to lamotrigine, an approved epilepsy therapy, which some studies suggest also can protect nerve cells from damage. CentRion will conduct research to determine the safety and efficacy of its original neuroprotective compounds in laboratory models of MS.



Oregon Health & Science University, Portland, OR, (Project Director – Lawrence Sherman, PhD) will receive \$275,000 for the screening and efficacy of small molecule inhibitors of hyaluronidase, an enzyme that dissolves hyaluronic acid – a complex sugar molecule that accumulates in MS lesions. Dr. Sherman's group has found that by-products resulting from

Fast ForwardSM

breakdown of hyalunoric acid prevent myelin repair. This project will assess whether myelin repair blockage can be overcome by inhibiting the activity of hyaluronidase.

2010

The following are the recipients from the ***Accelerating Commercial Development Fund***:



Axxam SpA, Milan, Italy (Project Director – Michela Stucchi, PhD) will receive \$430,590 over 18 months to advance the development of small molecules that target the sodium-calcium exchanger NCX1 on axons. NCX1 functioning in reverse mode is thought to cause nerve cell death in MS. Axxam is developing molecules to prevent NCX1 activation and thus prevent axonal injury and ultimately clinical disability in MS.

The following organizations will receive financing from the ***Accelerating Innovation Fund***:



HOWARD FLOREY INSTITUTE

Howard Florey Institute, Carlton, Victoria, Australia (Project Director – Bevyn Jarrott, PhD) will receive \$275,000 over 12 months to advance the development of molecules that target Nav 1.6 ion channels. In MS, there is a change in these ion channels, which contributes to abnormal nerve function. This project will focus on molecules which could potentially prevent this abnormal function, thereby protecting axons from further damage.



The Gladstone Institutes/UCSF (Project Director- Katerina Akassoglou, PhD) will receive \$300,000 to conduct testing for the identification of small molecule inhibitors of microglial activation. Microglia are part of the resident immune system in the brain and spinal cord.

Fast ForwardSM

Activation of microglia in MS is thought to contribute to the inflammation and nerve cell damage associated with MS. In the funded studies, the investigators will focus on developing novel molecules that have the potential to inhibit the activation of microglia in MS.

2011

The following are the recipients from the **Accelerating Commercial Development Fund**



Axxam SpA, Milan, Italy (Project Director – Chiara Liberati, PhD) will receive \$402,000 over 12 months to identify antagonists of the chloride intracellular channel 1 expressed by activated microglia, which could form the basis for the development of potential new treatments for neurodegeneration in MS.



ACADIA[®]
Pharmaceuticals

ACADIA Pharmaceuticals / University of California, Los Angeles (UCLA) (Project Directors - Roger Olsson, Ph.D. and Rhonda Voskuhl, M.D.) will receive \$545,380 over 12 months to perform research to identify estrogen receptor beta agonist as a potential treatment of MS.



Vicore Pharma AB / Uppsala University and Charité - Universitätsmedizin Berlin (Project Directors: Professor Mats Larhed and Dr. Ulrike Steckelings) will receive \$531,300 over 18 months to perform research to identify angiotensin AT2-receptor agonists as a potential treatment of MS.