



FastForwardSM

General Fund

This project is funded by the National Multiple Sclerosis Society through Fast Forward, LLC, in order to accelerate the commercial development of MS treatments. The Society and Fast Forward connect university-based MS research with private-sector drug development and fund small biotechnology/pharmaceutical companies to develop innovative new MS therapies and repurpose FDA-approved drugs as new treatments for MS.

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| <i>Primary Investigator</i> Marie Österlund, Ph.D., Karo Bio AB Huddinge, Sweden | <i>Project Title</i> IND-enabling preclinical studies with a new ER beta agonist for neuroprotection in MS | <i>Amount to be Committed</i> \$500,000 Term – 10 months |
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About the Company

Karo Bio is a pharmaceutical company focused on the research and development of innovative drugs for large medical needs, by targeting nuclear receptors. The company advances drug development projects mainly within the therapeutic areas of neurodegeneration, inflammation, autoimmune diseases and cancer. The company has a number of strategic agreements and collaborations with international pharmaceutical companies.



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Project Background & Goals

MS involves the progressive destruction of myelin, the substance that insulates and protects nerve fibers. The nerve fibers themselves may also be destroyed. Myelin is produced by supporting cells called oligodendrocytes. Although natural, spontaneous myelin repair occurs in people with MS, this process is often not sufficient to reverse the damage caused by the disease. The brain contains immature oligodendrocyte precursor cells (OPCs) that are capable of becoming mature myelin-making oligodendrocytes, but seem to be dramatically decreased in MS lesions, which are areas of disease activity or damage. Finding a way to increase OPC numbers is a potentially promising therapeutic strategy for MS because myelin repair requires the production of new oligodendrocytes.

Karo Bio's lead compound, KB3944, is a selective estrogen receptor beta (ERbeta) agonist. An agonist is a chemical that binds to a receptor and triggers a response. Karo Bio has preliminary evidence that KB3944 significantly increased OPCs, and their development into mature oligodendrocytes. In mice with EAE, an MS-like disease, KB3944 reduced disease activity and protected against the loss of myelin and nerve fibers. Now Karo Bio is exploring this compound further to determine how it is metabolized, any toxic effects, and what the optimal dose might be.

These studies will help fine-tune a potentially promising therapeutic strategy for ultimately repairing the nervous system and restoring function to people with MS.