Multiple Sclerosis Society of Canada-Brain Canada-Biogen

Platform Support and Team Grant

MS Progression Cohort

Request for Applications (RFA)

About Multiple Sclerosis Society of Canada

Multiple Sclerosis is Canada's disease with 100,000 Canadians living with MS. The MS Society provides services to people with multiple sclerosis and their families and funds research to find the cause and cure for this disease. We have a membership of 17,000 and are the only national voluntary organization in Canada that supports both MS research and services. Since our founding in 1948, the core support of the MS Society has been from tens of thousands of dedicated individuals, companies and foundations in communities across Canada. The Society receives almost no funding from government.

Since 1948, the MS Society has provided over $150M towards MS research that furthers our understanding of MS, seeking new treatments and a cure. The MS Society is governed by a board of directors comprised of 14 volunteer members who are elected annually. There are seven regional divisions and more than 90 chapters that engage in many community-based activities. Some 1,500 volunteers serve on MS Society national, division and chapter boards and committees. An estimated 13,500 women and men are volunteers for service programs, fundraising events, public awareness campaigns and social action activities.

About Brain Canada

Brain Canada is a national non-profit organization that enables and supports transformative, original and outstanding brain research in Canada. For more than a decade, Brain Canada has made the case for the brain as a single, complex system with commonalities across the range of neurological disorders, mental illnesses and addictions, brain and spinal cord injuries. Looking at the brain as one system has underscored the need for increased collaboration across disciplines and institutions, and a smarter way to invest in brain research that is focused on outcomes that will benefit patients and families.

The Canada Brain Research Fund is a public-private partnership established between Brain Canada and Health Canada to encourage Canadians to increase their support of brain research, and maximize the impact and efficiency of those investments. Brain Canada is raising $120 million from private and non-federal sources, which is being matched by the Government of Canada on a 1:1 basis. The Fund supports "the very best Canadian neuroscience, fostering collaborative research and accelerating the pace of discovery, in order to improve the health and quality of life of Canadians who suffer from brain disorders."

About Biogen Canada Inc

Through cutting-edge science and medicine, Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative diseases. Founded in 1978, Biogen is a pioneer in biotechnology and today has the leading portfolio of medicines to treat multiple sclerosis (MS), has introduced the first and only approved treatment for spinal muscular atrophy (SMA) and is at the forefront of neurology research for conditions including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS). Building on its heritage in biologics, Biogen also manufactures and commercializes biosimilars of advanced biologics.

RATIONALE

People affected by Multiple Sclerosis (MS) continue to voice an urgent need for treatments that will halt and reverse their progression, but in order to achieve this, researchers must first understand why and how progression in MS occurs. Prospective and retrospective longitudinal studies allow researchers to observe a disease over time and gather important biological, healthcare, economic, and real-world information. MS is a chronic disease that evolves over time, and the best approach to understanding and measuring progression is to establish a unique Canadian cohort of people who can shed light on the following key questions: why do certain individuals progress? How does progression affect their physical symptoms, adherence to and impact of treatments, and their ability to obtain employment and participate meaningfully in the community and healthcare system? Ultimately, this information will influence the management of all forms of MS, and the development of solutions that enable people living with MS to live an improved quality of life, and serve as a resource and model for the study of other neurological diseases.

In the last few years, various countries (Germany, US, Switzerland and Netherlands) have begun developing cohort studies of people living with MS. These cohort studies follow a group of people over time who have, or are at risk for developing, MS; collect health information to understand how the condition develops and how to best treat it; provide important tools for understanding the cause, the course, and prognosis of the disease. In addition, there is growing interest and a need to understand the impact the disease has on healthcare resource utilization, employment and meaningful outcomes for those affected.

The Multiple Sclerosis Society of Canada (MSSC), Brain Canada and Biogen are pleased to announce a new and innovative research initiative to study disease progression in people living with MS in Canada. This multi-stakeholder partnership is a novel opportunity to support MS research with the intent to build a national cohort of MS patients. This funding opportunity has the overall goals of serving as an open access tool to stimulate continued MS research in Canada that will benefit the MS patient, research and clinical communities and serve as a resource and model for the study of other neurological diseases.

GRANT DETAILS

The purpose of this Request for Applications (RFA) is to establish a team of investigators to design a comprehensive study of people living with MS in Canada, and establish the feasibility of, and develop the infrastructure and protocols for, conducting retrospective and prospective studies over the period required to answer important questions related to progression in MS.

The competition will be structured in two parts:

- **Planning grant:** teams of investigators will first submit a Letter of Intent to seek a planning grant that will enable them to appropriately plan and develop their full application. The total funding envelope that is available for the planning grant is up to **$250,000 (CAD)** for 5 months. The planning grant payments will be made on a milestone/report basis. If more than one team is invited to the full application stage, they will share the planning grant.

The planning grant will provide the team(s) with resources to establish a team of researchers that, in collaboration, will design the study and conduct a landscape analysis of current resources that could assist with the development of the cohort. It is anticipated that the planning grant will enable the team to develop standard protocols, consider database infrastructure, develop work plans and budget, determine governance structure for the team of investigators and project, commence testing of protocols if required, hold meetings for the team of investigators, hire personnel to assist in developing a full application to the second stage of the competition. It is also expected that these studies will build on outcomes from previous studies following patients over time and from our current understanding of MS. Proposals should avoid duplicating work in other cohort studies that is already completed or underway and should seek to integrate resources that are currently available.

- **Full grant**: The work prepared with the planning grant will lead to the submission of a full application that will demonstrate the capacity of the team(s) to assemble a cohort of people with MS, collect data using a suitable database/infrastructure from the cohort and commence answering specific questions of this study related to progression in MS. Only one team representing multiple centers in Canada will be selected to receive the full grant. The total funding available is **$6,590,000 (CAD)** for up to 5 years (with the potential of additional funding depending on additional partners).

The successful team will design a cohort study that can ultimately answer one or more key questions in each of the three research domains:

- **Research Domain 1 – Mechanism of Progression**:
  - What are the pathophysiological mechanisms that trigger MS progression versus those that stabilize progressive disease?
  - What pathophysiological factors determine whether certain people with MS develop progressive disease and others remain stable?
  - What are some mechanisms that protect against neurodegeneration, why do they fail in progression, and how can they be harnessed?
- **Research Domain 2 – Treatments/Real World Evidence**:
  - Do early diagnosis and prevention strategies mitigate the risk of transitioning to a progressive course or lead to more favourable disability outcomes and, if so, by how much?
  - What is the impact of early versus delayed treatment with DMTs on the rate of disease progression?
  - How do the currently approved DMTs compare in terms of slowing the progression of people living with MS from the relapsing-remitting to the secondary progressive form of the disease?

- **Research Domain 3 – Impact:**
    - What are determinants of health-related quality of life in people living with or at risk of transitioning to progressive MS and how can they be integrated into a comprehensive care strategy?
    - What are the socioeconomic and societal impacts of MS progression, including those on the person with MS and their families, education status, employment and productivity costs, social welfare and long-term disability costs, etc.?
    - What approaches and measures best equip people affected by progression in MS regarding their self-care or shared decision-making with their healthcare providers.

The funding of this initiative from MSSC, Brain Canada and Biogen is only for a fixed period. The successful team is required over the course of the funding term to consider how they can sustain the study over a long period of time using funding from other sources. They should also consider and develop a preliminary business model that includes all possible sources of revenue, such as data access fees.

ELIGIBILITY

This competition is open to a team of three or more investigators who holds an M.D., Ph.D., or equivalent degree, have an academic or research appointment and is conducting research in a recognized Canadian institution.

A. Study Investigators

The Principal Investigator (PI) is responsible for overall scientific and administrative oversight of the grant and the collaborative members. The PI need not be a Canadian citizen. The PI should be an established, highly qualified scientist with adequate administrative and leadership experience and authority to manage grant operations.

The Co-Investigators (co-I) are responsible for overseeing elements within the individual study sites, including participant recruitment, data collection etc. and/or one of the research domains. The co-Is must meet the eligibility criteria for the PI, and should be established scientists and/or clinicians with demonstrated leadership and research management experience.

The team may also include Collaborators with specialized expertise needed for the project (e.g. those needed for specialized techniques, statistical analysis, etc.). Collaborators contribute indirectly to the proposed research activities. Collaborators may be from sites outside Canada.

Funds will be administered to the Canadian institutions where the PI and Co-I's are affiliated/employed.

The teams are encouraged to include researchers at all academic levels, as well as researchers within and outside the neuroscience field who wish to apply their expertise to the scope of this project in the area of MS.

B. Study Sites

The study must include at least three Canadian academic research centers that will recruit participants, ideally from at least two provinces. A ministry within the Alberta government has expressed interest in contributing to funding this initiative and the applicants are encouraged to include investigators and/or study sites from Alberta.

To address any questions concerning eligibility, investigators are encouraged to contact Dr. Karen Lee (msresearchgrants@mssociety.ca) before submitting their application.

THE LETTER OF INTENT FOR PLANNING GRANT

The objective of the planning grant is to:

- Provide start-up funds to plan and develop a competitive strategy and produce a collaborative research proposal for the full application
- Support the formation and planning activities of the newly-configured investigative team

A successful letter of intent will include the following elements as part of the proposal:

- Assembling the multidisciplinary investigative team, including in-person planning sessions
- Hiring/funding a temporary research coordinator/project manager to manage the planning and execution processes
- Developing a feasibility and execution plan (e.g. resources and competencies; timeline and deliverables, contingency plan if falling behind scheduled deliverables or if some event alters the plan and impacts ability to execute)
- Identifying currently existing infrastructures for data platforms, bio repositories and others opportunities that could be used and leveraged in the development of the cohort
- Provide full research concept outline and how one question from each research domain will be addressed

The Letter of Intent will include the following components (for a detailed list and description of **ALL** the required components for the Letter of Intent, please consult the Application Guidelines):

- **Scientific Plan:**
  - Background stating the objective of the overall research project including hypothesis and the scientific questions that will be addressed specifically related to the three research domains
  - The team will provide an outline of the feasibility assessment which will ultimately inform type and timing of data collection as well as effect sizes, and reliability and validity of such data to address the broader research question. The team will design ***the*** overall research concept and will define the measures/endpoints to be evaluate during the study. Data collected may include imaging, immunological assessments, genetic analysis, patient reported outcomes and other biomarkers. Applicants need to consider both available retrospective data and a prospective design. The retrospective data should inform the prospective research design. It is not expected that the study will be able to identify all clinical, imaging, immunologic and genetic biomarkers for disease progression; however,

the applicants need to consider the approach that is likely to yield a sustainable model. Only by following people with MS over a longer time period will we be able to define variables that are associated with progression.
    - An overall strategy as to how the collaborative team will look to define, identify and assemble a sufficiently large cohort of people with MS that will be followed long term and best address the research questions raised in this RFA.

- **Data Integration:**
    - A preliminary outline of how this study will leverage but not duplicate existing platforms and infrastructure, including current national and international cohort studies, or make use of existing data platforms and biosamples from other studies or leverage other funds, or align with other efforts to sustain the proposed cohort is required. Also important, this outline should address how key lessons from other research efforts will be incorporated.
    - An outline of how data collection will be streamlined across study sites, including standardization of the MRI data to be collected
    - Outline considerations regarding infrastructure for collecting data, data integrations, streamlining IT systems and privacy.

- **Administration, Governance and Timelines:**
    - An initial description of the structure of the project to support the scientific plan Research team structure, list of team members and anticipated roles of individual members
    - A preliminary description of the centers that will be involved and the consideration of how other centers may be included over time
    - A description of comprehensive communications and information-sharing plans among team members and centers.
    - A list of key milestones and timelines for the work that is anticipated over the period of the planning grant
    - A description of the incorporation of people living with MS in the design, input and/or governance structure of the team.

- **Budget:**
  A budget description of how the team will spend the available planning grant funding to complete a full application submission.

CRITERIA FOR ASSESSMENT OF THE PLANNING GRANT

Scientific Plan: the impact and importance of the long-term endeavor

- Did the proposal demonstrate originality, relevance and potential to advance knowledge on progression?
- What are the strengths and weaknesses of the proposed scientific plan and are the objectives and methods, end points aligned with the aims of this RFA?
- Did the applicants propose to answer the specific questions relating to disease progression posed in this RFA?

- Is the theoretical approach or framework of the scientific plan appropriate and have the applicants demonstrated that they can establish a sound research model during the planning stages?
- Did the applicants consider the potential design of the cohort, including type of data and methods for data collection and sample population description?
- Has the retrospective, as well as, the prospective data collection been considered within the design of the research concept ?
- Is the budget appropriate and has an adequate description of how funds will be allocated during the planning phase been provided?

Governance and Administration: the feasibility and capability of the team

- Did the applicants provide detailed information about the team members and the organizational structure of the network, including breakdown of responsibilities, involvement of collaborators, and how each team member will contribute towards the planning activities?
- What is the caliber and capacity of the team members? Do they have the appropriate knowledge, experience and technical expertise to carry out their roles in the cohort?
- Does the team possess experience in large scale, multi-site collaborative studies and prospective and/or retrospective data collection?
- What is the quality, quantity and significance of past experiences among the team members, including published and/or creative outputs and ability to support the lead investigator?

Planning and Development: foresight in to the future of the cohort

- Has sufficient engagement of people affected by MS proposed in the planning stage? Are the insights that will be gained useful to developing the cohort?
- Has data integration across multi-sites been considered and do they intend to develop this further during the planning stage?
- Is there clear demonstration of a plan/consideration of the use of existing platforms?
- Did the applicants provide a thoughtful and thorough landscape analysis of existing cohorts that may be considered for potential integration? Will their proposed model duplicate existing efforts?
- Have the applicants considered the long-term sustainability of the cohort?

Execution : ability to meet milestones

- Is there a general idea of how recruitment of patients will be handled? Are the timelines sufficient?
- Have the applicants included buffers and contingency planning?

TIMELINE

- **March 15, 2017**: Launch of RFA & Letter of Intent submission opens
- **May 8, 2017**: Letter of Intent submission closes
- **June 1, 2017**: Announcement of Letter of Intent planning grant
- **November 1, 2017**: Full application submission closes
- **December 2017**: Review with comments sent to applicants
- **January 2018**: Announcement of full grant
- **February 2018**: Funding begins (at the earliest)

CONTACT INFORMATION

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