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FUNDING ANNOUNCEMENT REQUEST FOR APPLICATIONS

CHALLENGES IN PROGRESSIVE MS AWARDS

The International Progressive MS Alliance (Alliance) is pleased to announce a new funding initiative designed to accelerate research focused on the mechanisms underlying progressive MS through innovation and collaboration. Only research proposals that challenge current paradigms and/or traditional approaches used to investigate mechanisms of progressive MS to date will be considered. Applications that include investigators from multiple institutions are strongly encouraged. The Alliance anticipates that this award will expedite development of therapies for progressive MS.

WHAT IS THE ALLIANCE?

The International Progressive MS Alliance is an unprecedented global collaboration of MS organizations, researchers, healthcare professionals, the pharmaceutical industry, companies, trusts, foundations, donors and people affected by progressive MS, working together to address the unmet needs of people with progressive MS. Our promise is more than hope, it is progress. Learn more about the Alliance at www.progressivemsalliance.org.

OVERALL GOALS FOR THIS REQUEST FOR APPLICATIONS (RFA)

The Alliance has identified a number of key areas of significant unmet need that must be overcome before new treatments for progressive MS can be developed, one of which is a clear understanding of the mechanisms that lead to progression. (reference: "Setting a research agenda for progressive multiple sclerosis: The international collaborative on progressive MS". Multiple Sclerosis Journal 2012 Nov; 18(11):1534-40).

Progression in MS is thought to occur when the extent of axonal loss exceeds the compensatory capacity of the CNS. Numerous mechanisms leading to neurodegeneration and axonal dysfunction in MS, including CNS intrinsic immune responses, have been described; there is evidence that these mechanisms occur from disease onset. While targeting of some of these pathologic mechanisms has resulted in therapeutic effects in the EAE mouse model, studies in patients with progressive MS have been less promising (reviewed in "Progressive multiple sclerosis: from pathogenic mechanism to treatment". Brain 2017;140:527-546).

The goal of this RFA is to uncover new mechanisms driving progressive MS that may be used to identify therapeutic targets that will ultimately slow or stop disability progression. Research

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proposals should be innovative, and have the potential to fundamentally advance the understanding of the mechanisms underlying progressive MS. They should not be incremental advances that build on existing knowledge of progressive MS disease mechanisms, but rather should explore new avenues for understanding the key drivers of progressive MS. High risk proposals that have the potential to result in a paradigm shift in progressive MS will be prioritized. Preliminary data supporting the proposal are encouraged but not required.

Proposals should aim to achieve one of the following goals:

1. Identify novel insights into molecular pathways that contribute to axonal loss in progressive MS including but not limited to:
 - a. glial activation
 - b. neurodegeneration
 - c. compartmentalized/smoldering inflammation, including interactions among resident CNS cells and the innate immune system
2. Identify novel insights into molecular pathways that promote neuroprotection and/or repair including inhibitors and/or missing promoters of remyelination and myelin repair.

Proposals focused on the contribution of immune pathways to MS pathophysiology that are known to drive acute inflammatory responses in the relapsing forms/phases of MS, including the adaptive immune system, are out of scope for this RFA and will not be considered.

Support for each of these awards is limited to a maximum of €75,000 in total costs for 12 months.

This RFA is open to all international researchers in academic and other non-profit organizations, as well as to researchers in commercial organizations. Applications that include investigators from more than one institution will be given higher priority.

It is anticipated that as many as 15 grants may be awarded through this RFA. Awards will be contingent on the availability of funds and the receipt of a sufficient number of meritorious applications in one or more of the areas identified.

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ESTIMATED TIMELINE

Milestone	Date
RFA release date	December 2019
Informational call(s) for applicants	January 2020
Stage I: Application due	February 2020
Anticipated notification of Stage I approval	March 2020
Stage II: Application due	May 2020
Notification of funding decisions	October/November 2020
Public announcement of awards	November/December 2020
Anticipated start date of funding*	January 2021

*This will be the earliest possible date for funding. Release of funds will be contingent on successful execution of research agreements between the institutions and the Alliance. Thus funding dates may be later if considerable negotiation is required between the partners.

ELIGIBILITY

Principal Investigator: It is expected that the person designated as the principal investigator (PI) for this funding program is a scientist focused on basic, clinical or rehabilitation research that is considered eligible by his or her institution to apply for a research grant.

Organization: Organizations are the official recipients of grants and may be in any country. Eligible organizations include public research institutions, non-profit research organizations and commercial organizations (e.g. pharmaceutical or biotechnology companies, and contract research organizations) with a medical research focus and mission.

Commercial organizations are invited to participate in this RFA as collaborators when their particular skills and capabilities in drug discovery and development come to bear on the Alliance goals. The Alliance also appreciates willingness to co-fund important projects by commercial organizations.

Proposals that include commercial organizations must incorporate cross-sector collaboration (e.g. academic-industry collaboration) as part of the research plan. At least 50% effort of the partnership must be performed in a public (e.g. academic) institution or non-profit research organization and all funds will flow through the academic/non-profit organizations (with sub-awards to other investigators in the network). In addition, applicants will be expected to describe any intellectual property arrangements between the commercial organization and the academic collaborators related to the application.

The Alliance is unable to provide funding to countries currently subject to United States Department of State sanctions, United Nations Security Council sanctions or any sanctions in place by Alliance member countries.

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CONDITIONS

Awarded projects will be administered by the Alliance and will be subject to the Alliance's policies and procedures for funding programs. Support for proposals submitted in response to this RFA is limited to a maximum of €75,000 in total costs for a period of 12 months. Purchase of major items of equipment and use of funds for travel will not be permitted. The Alliance will support research costs that have been fully justified in the application and not normally paid for by the host institution. The Alliance will not provide funds for indirect cost recovery. The Alliance recognizes that in some cases certain administrative costs associated with an Alliance-funded program will not be borne by the institution. In such cases applicants will be permitted to allocate Alliance funds to defray these expenses, provided that the applicant and host institution certify that these funds are required for execution of the project and that institutional or other funds are not available to cover these costs. These costs should be listed on the "Other Expenses" line item of the application. Proposals from commercial organizations may not request support for administrative costs.

The proposal should include a project timeline. The organization will be required to provide a research progress report 6 months after the project begins and a final narrative report of the work accomplished. In addition, the grantee will be required to participate in an investigator meeting in 2022. An accounting of expenditures will be required within 30 days after the project ends. The grantee organization will also be required to comply with the Alliance's invention policy and other Alliance policies and procedures.

PREPARATION OF APPLICATION - SUBMISSION

The Alliance will use the National MS Society's (USA) application interface for this RFA. The Society employs a Web-based utility for the submission of grant applications. Investigators must first register with the online application site (nmss.fluxx.io) and complete a short Stage I application. Full grant applications can be submitted only after the applying investigator receives approval of the Stage I application. **Any full proposals submitted without prior approval will not be considered.** Questions regarding alignment and eligibility can be addressed to the contacts listed at the end of this RFA.

The final application should be concise, with the research Proposal Narrative strictly limited to three (3) pages. The application should consist of:

- a. Research Proposal Narrative. Provide a concise description of the research proposal not exceeding 3 single-spaced pages. 12-point font size must be used.
- b. Summary of research proposal that is accessible to the lay-person MS community, including how the work may benefit people with progressive MS.
- c. Statement of Expected Outcomes and Deliverables: As part of the Research Proposal Narrative, describe in 200 words or less the results and deliverables you expect, the importance of your research proposal to progressive MS, and the relevance to the mission of the Alliance and to the goals outlined in this RFA.

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- d. **Work Plan and Timeline.** Provide a concise list of steps, outcomes, deliverables and milestones, not exceeding 2 single-spaced pages.
- e. **Budget and Budget Justification.** Details and justification of all budget items relative to the proposed research should be provided. Applicants may request funds for a maximum of 12 months of support, not exceeding €75,000. The Alliance will support research costs that have been fully justified in the application and not normally paid for by the host institution. The Alliance will not provide funds for indirect cost recovery. The Alliance recognizes that in some cases certain administrative costs associated with an Alliance-funded program will not be borne by the institution. In such cases applicants will be permitted to allocate Alliance funds to defray these expenses, provided that the applicant and host institution certify that these funds are required for execution of the project and that institutional or other funds are not available to cover these costs. These costs should be listed on the “Other Expenses” line item of the application. The budget is part of the research Proposal section that is uploaded from the MSGrants site. Investigators may request the funds in the following categories: salaries for personnel, patient costs, consumable supplies, and other expenditures. Applicants should highlight any potential to leverage funding from other sources in their budget request.
- f. **Biographical Sketches.** Brief 1-2 page biosketch of the PI and key co-investigators must be included. This should include a summary list of relevant publications.

REVIEW

Stage I applications will be reviewed by the Alliance scientific staff and Scientific Steering Committee members to determine a) whether the research proposal is appropriate and aligned with this RFA; and b) whether the PI meets the eligibility criteria.

Full applications will be reviewed by a panel of subject matter experts convened by the Alliance, which will include people affected by progressive MS. The scientific review criteria for the application include the following, in order of importance:

- Adherence to the specific objective of the RFA and alignment and relevance to the mission and goals of the Alliance
- Extent of collaboration between institutions, including the potential for novelty and innovation resulting from the collaboration
- Importance of research contribution to address knowledge gaps in progressive MS
- Scientific potential and scientific critique of the proposed work plan
- Resources requested: are the funds requested essential for the work, and do the importance and scientific potential justify funding on the scale requested?
- Expertise of the investigators
- Appropriateness of the resources and environment

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In addition to the scientific review, the proposal will be evaluated by members of the MS community, selected for their personal experience or knowledge of multiple sclerosis. Their input will be combined with the assessments of professional scientific reviewers. Because of this review process, it is important that the community summary be relevant, accurate and intelligible to that audience and consistent with rest of the technical content of the proposal. It is recommended that applicants test their community summary on an intelligent member of the public. As appropriate, we suggest involving members of the MS community in the preparation of the proposal and demonstrating how this input impacted the application. Finally, it is important that the community summary and the main proposal are consistent with regards to the objectives of the program and its benefit for the MS community.

The Alliance Scientific Steering Committee will consider the expert scientific reviews for each proposal and develop a recommended portfolio of projects for funding. The Steering Committee will refer its recommendations to the Alliance Executive Committee for approval. The decision of the Executive Committee is final.

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CONTACT INFORMATION

ITALIAN MS SOCIETY	Gabriele Dati, Ph.D. Biomedical Research and Grant Office Coordinator Email: Gabriele.Dati@aism.it Tel: +39 010 271 3259
MULTIPLE SCLEROSIS INTERNATIONAL FEDERATION	Clare Walton, Ph.D. Head of Research and Access Email: clare@msif.org Tel: +44 (0) 20 7620 1911
MS SOCIETY OF CANADA	Pamela Kanellis, Ph.D. Assistant Vice-President, Research Managing Director, endMS research and Training Network Email: Pamela.Kanellis@mssociety.ca Tel: +1 416-967-3024
MS SOCIETY, UNITED KINGDOM	Susan Kohlhaas, Ph.D. Executive Director of Research Email: Susan.Kohlhaas@mssociety.org.uk Tel: +44 (0) 20 8827 0220
NATIONAL MULTIPLE SCLEROSIS SOCIETY USA	Douglas Landsman, Ph.D. Vice President, Research Email: Douglas.Landsman@nmss.org Tel: +1 212.476.0536
MS RESEARCH AUSTRALIA	Julia Morahan, Ph.D. Head of Research Tel: +61 02 8413 7921 Email: jmorahan@msra.org.au