

2012 REQUEST FOR PROPOSALS

NOVEL THERAPEUTIC DEVELOPMENT PROGRAMS FOR TREATMENT OF MULTIPLE SCLEROSIS

Issued By
Fast Forward, LLC with Leadership Funding from EMD Serono, Inc

Fast Forward, LLC announces the 2012 Request for Proposals (RFP) under a collaboration agreement between Fast Forward and EMD Serono. This RFP will:

- Support academic and early stage commercial development programs directed towards therapeutic approaches within the scope of this RFP as defined in **Section 3.0**.
- Fund two independent programs;
 - *Accelerating Innovation Program (academic and seed-stage companies);*
 - *Accelerating Commercial Development Program (early stage companies and/or commercial entities).*
- Support projects for a one-year period.

The scientific focus of this RFP is:

1. **Development of therapeutics that target B cell lineages involved in multiple sclerosis pathology**
2. **Identification of surrogate or endogenous ligands for Orphan G Protein-Coupled Receptors (GPCRs) expressed exclusively or primarily in the central nervous system (CNS) that relate to the pathology of multiple sclerosis**

To be considered for funding, proposals must meet the following guidelines:

- **Scope:** The proposal must address one or more of the above **two** areas of scientific focus.
- **Intellectual Property:** The proposed research must have existing intellectual property owned or exclusively licensed by the applicant or organization and/or will lead to new intellectual property.
- **Translational:** Proposed programs must have the potential to lead to the development of a small molecule or biologic drug through proposed target validation, lead generation, lead optimization, preclinical characterization, or entry into clinical trial.

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1.0 Program Timeline and Informational Overview

1.1 RFP Timeline

RFP Release	October 10, 2011
Informational Conference Calls	November 11, 2011
	January 23, 2012
	March 26, 2012
Full Proposals Due	May 1, 2012
Award Announcements	August 1, 2012

1.2 Informational Teleconferences

Fast Forward will hold informational teleconferences November 11th 2011, January 23rd 2012, and March 26th 2012 in order to answer specific questions and provide additional information to potential applicants. Interested applicants should RSVP by email to research@fastforward.org to receive conference call logistics. Participation in the informational teleconference is encouraged but is not a requirement.

2.0 Background

Fast Forward:

Fast Forward, LLC is a nonprofit organization established in 2007 by the National Multiple Sclerosis Society USA in order to accelerate the development of treatments for multiple sclerosis (MS). Fast Forward accomplishes its mission by connecting university-based MS research with private-sector drug development and by funding early stage biotechnology and pharmaceutical companies developing innovative new MS therapies. Fast Forward operates on a venture philanthropy model and seeks a financial return from companies or institutions in connection with its portion of its financial support of specific research programs.

EMD Serono:

EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany, a global pharmaceutical and chemical company, is a leading US biopharmaceutical company with significant market positions in MS through Rebif® (interferon beta-1a) in the neurological disease multiple sclerosis and has extensive programs in oncology and endocrinology. EMD Serono and its affiliates are committed to developing additional innovative therapies from MS.

Fast Forward and EMD Serono Collaboration:

In 2009, Fast Forward entered into a multi-year collaboration agreement with EMD Serono, Inc to fund innovative programs in academic institutions and early stage companies. Fast Forward and EMD Serono have agreed to fund MS drug discovery research and development programs. As part of this collaboration, EMD Serono will provide funding for the research programs selected through this RFP. In return, EMD Serono and its parent company, Merck KGaA, will have a first option for a right to negotiation for intellectual property arising from funded programs. Funded recipients in both academic and commercial organizations will have an opportunity for follow-on funding and collaboration with EMD Serono for further commercial development of their research programs.

3.0 Program Details

3.1 Scientific Priority Areas

The purpose of this RFP is to solicit proposals within the scientific focus. Fast Forward's process will review, evaluate, and recommend for funding those projects that have the potential to lead to novel therapeutic approaches to treat multiple sclerosis.

Fast Forward is currently seeking proposals limited to modulation of the following cells or targets involved in MS:

- 1. Development of therapeutics that target B cell lineages involved in multiple sclerosis pathology**
- 2. Identification of surrogate or endogenous ligands for Orphan G Protein-Coupled Receptors (GPCRs) expressed exclusively or primarily in the central nervous system (CNS) that relate to the pathology of multiple sclerosis**

3.2 Scientific Background & RFP Focus

B lymphocytes as MS therapeutic targets

Considerable therapeutic development for MS has focused on modulation of T cell responses. However, several lines of evidence point to an important pathogenic contribution from B cells. Oligoclonal antibody bands of unknown specificity in the cerebrospinal fluid are a hallmark of MS, evidence of somatic hypermutation and antigen-driven B-cell selection and expansion. B cells and plasma cells are detected in MS lesions, with the highest concentrations in active lesions and during the later stages of disease. Furthermore, ectopic B cell aggregates form in meningeal regions of the brain and spinal cord of progressive MS patients, and intrathecal levels of anti-myelin IgG and IgM correlate with rapidly progressing disease. Therefore, therapeutic strategies that target B cells may complement current immunosuppressive strategies that are more T cell focused.

B cells play many roles in normal immune function and in autoimmune diseases. Upon stimulation, naïve antigen-specific B cells can clonally expand and differentiate into plasma cells, secreting immunoglobulins that carry out effector functions including complement fixation, opsonization, and antibody-dependent cell-mediated cytotoxicity. A population of memory B cells persists following this initial expansion, enabling a more rapid and higher affinity antibody response to repeat antigen stimulation. B cells can also present antigen to T cells, forming the immunological synapse and secreting cytokines that contribute to T cell activation and influence T cell subtypes (e.g. TH1, TH2). In contrast, regulatory B cells (Bregs) may suppress T cell responses, including responses to autoantigens¹, by secreting IL1-10.

Several approaches to MS treatment point to the potential benefit of modulating B cells, but they also raise questions about the optimal target strategy. Plasmapheresis demonstrated the temporary benefits of removing autoreactive antibodies from the serum of MS patients, but since B cells are also capable of antigen presentation to T cells as well as the secretion of pro- and anti-inflammatory cytokines, modulating or eliminating these cells could have multiple effects on the autoimmune response. The successful trial and approval of rituximab

(Rituxan®)², a chimeric monoclonal antibody against CD20, validated the approach of targeting B cells in MS. Nevertheless, the positive effect of this molecule in the treatment of the disease cannot necessarily be attributed to reduction of autoantibodies *a priori* since the Ig levels did not change in the course of the treatment. This speaks to additional roles for B cells in pathology in MS. Additionally; some patients treated with rituximab have developed progressive multifocal leukoencephalopathy (PML). Similarly, Alemtuzumab, a monoclonal antibody targeting CD52 on lymphocytes and monocytes, induces a strong immunosuppression and yielded some clinical improvement in relapsing-remitting MS patients, but also produced serious adverse effects including immune thrombocytopenic purpura and anti-thyroid complications³. The fusion protein Atacept offered an alternative approach to B cell modulation, combining the extracellular domain of the receptor TACI (Transmembrane Activator and CAML-Interactor) with a modified Fc portion of human IgG to enhance stability. Because TACI is the common receptor for both BLYS (B-lymphocyte stimulator) and APRIL (a proliferation-inducing ligand), atacept was designed to bind two important regulators of B-cell maturation, function, and survival, reducing the signal to potentially autoreactive B cells⁴. Phase I studies in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) demonstrated safety and biological activity, but in Phase II studies of relapsing-remitting MS patients atacept treatment unexpectedly increased the incidence of relapse, prompting suspension of the trial.

These recent clinical trials highlight the opportunities and challenges in targeting B cells for MS. As mentioned above, B cells have multiple functions. B cells are the key contributor to humoral immunity, and therefore complete ablation of all B cells, including Bregs and pathogen-specific B cells, may not be an ideal therapeutic goal. Recent trials in MS have targeted different B cell subsets with varying success. By targeting CD20, rituximab eliminates early pre-B cells but does not affect differentiated plasma cells. In contrast, atacept likely impairs mature B cells and plasma cells, sparing progenitor cells and memory B cells. The results of rituximab, alemtuzumab, atacept, and other recent B cell-directed therapies suggest that targeting certain B cell lineages or subsets while sparing others may be a key to successful treatment of MS.

In this RFP, we seek proposals with an identified B cell molecular target and a rationale, based on published literature and/or preliminary data, supporting its potential as a therapeutic target in multiple sclerosis. We are not soliciting projects that block or eliminate B cells producing antibodies against individual myelin components. Broadly immunosuppressive approaches that affect most T cells or innate immune cells in addition to B cells are also outside the scope of this RFP. Rather, applicants are encouraged to propose approaches that would modulate defined B cell subsets or lineages. Proposals that seek to identify new molecular targets in B cell subsets or lineages are considered too early for this program. The target of the therapy should be validated, i.e. of known composition with an established role in B cell development or function, preferably with a demonstrated role in autoimmune disease. Projects can include high throughput screening to generate leads against a validated B cell target, optimization of a lead, or testing in an appropriate B cell-dependent animal model of MS.

Applicants must discuss in advance potential projects with Fast Forward staff to ensure that the developmental goals are within the scope of the RFP. This will determine your

candidacy for submitting a full proposal. Only complete proposals received by the designated deadline from qualified applicants will be reviewed.

References:

1. Ray A. et al. A case for regulatory B cells in controlling the severity of autoimmune-mediated inflammation in experimental autoimmune encephalomyelitis and multiple sclerosis. *J. Neuroimmunol.* 230:1-9, 2011.
2. Hauser SL et al. B cell depletion with rituximab in relapsing-remitting multiple sclerosis. *N. Eng. J. Med.* 358:676-88, 2008.
3. Coles AJ et al. Alemtuzumab vs interferon beta-1a in early multiple sclerosis. *N. Eng. J. Med.* 359:1786-801, 2008.
4. Hartung H-P, Kieseier BC. Atacicept: targeting B cells in multiple sclerosis. *Ther. Adv. Neurol. Disord.* 3:205-16, 2010.

Orphan GPCRs in the CNS

To date, G protein-coupled receptors as major therapeutic targets represent 30% of all approved drugs¹. Nearly 800 genes (~4% of the human genome) encode members of the GPCR superfamily. Several classes of GPCRs with identified ligands (e.g. sphingosine-1-phosphate receptors, chemokine receptors) have demonstrated roles in MS and are targets of drugs that are approved or in clinical trial.

Roughly 500 of these GPCRs are chemosensory, including chemokines and chemoattractant GPCRs. Their ligands are generally well characterized. In contrast, approximately a third of identified transmitter GPCRs have no known cognate ligands² and are termed orphan GPCRs^{3,4}. Based on expression patterns, certain orphan GPCRs are likely drug targets, but lacking identified ligands they are not amenable to traditional screening for agonists or antagonists. However, recent advances in reverse pharmacology are identifying endogenous ligands, “de-orphaning” these GPCR receptors and opening them to traditional drug development approaches such as high throughput screening⁵.

Fast Forward is currently seeking proposals that aim to de-orphan GPCRs with no known cognate ligands. Specifically, we wish to support identification of endogenous or surrogate ligands for GPCRs which are highly enriched or unique to the CNS and involved in MS-associated neurodegeneration and demyelination. The association of an orphan GPCR and MS may be validated based on experiments that exacerbate or ameliorate disease, for example RNA interference or targeted knockouts that affect the clinical severity and/or pathohistology associated with EAE. Alternatively, changes in expression of a GPCR associated with developing lesions or progressive disease may mark it as a gene of interest. GPCRs associated with other neurodegenerative diseases, neuronal repair, or oligodendrocyte differentiation may also qualify within the scope of this RFP.

As an example, the previously orphan GPCR GPR17 has close structural relationships to P2Y and CysLT receptors, and screening with endogenous ligands from both receptor families

revealed that uracil nucleotides and cysteinyl-leukotrienes are cognate ligands for GPR17⁶. Levels of GPR17 are markedly increased at the site of brain injury, an *in vivo* indication of a potential role in damage and/or repair⁷. Genetic, pharmacological, and small interference RNA-mediated inhibition of GPR17 impaired oligodendrocyte precursor differentiation, suggesting a potential role in myelin repair⁸. *In silico* modeling and virtual screening, followed by functional and pharmacological *in vitro* confirmation, have identified additional agonists or partial agonists which may be tested for efficacy in neurodegenerative diseases including MS⁹. Thus, phylogenetic and expression analysis combined with a set of functional experiments resulted in the identification of small molecule agonists after *in silico* and more traditional chemical libraries screening, making these agonists potential drug leads.

For this RFP, proposals should cite evidence for CNS expression and role in neurodegenerative diseases, and outline a process to identify endogenous ligand(s) of the validated GPCR. Proposals should identify tissues or compound sets and assays for de-orphaning defined GPCRs. For recently de-orphaned CNS GPCRs, a high throughput screening may be proposed to identify hits that can help establish structure-activity relationships and lay the groundwork for lead optimization.

Applicants must discuss in advance potential projects with Fast Forward staff to ensure that the developmental goals are within the scope of the RFP. This will determine your candidacy for submitting a full proposal. Only complete proposals received by the designated deadline from qualified applicants will be reviewed.

References:

1. Hopkins AL, Groom CR. The druggable genome. *Nat. Rev. Drug Discov.* 1:727-30, 2002.
2. Vassilatis DK, et al. The G protein-coupled receptor repertoires of human and mouse. *Proc. Natl. Acad. Sci. USA* 100:4903-4908, 2003.
3. Libert F, Vassart G, Parmentier M. Current developments in G-protein-coupled receptors. *Curr. Opin. Cell Biol.* 3:218-223, 1991.
4. Howard AD et al. Orphan G-protein-coupled receptors and natural ligand discovery. *Trends Pharmacol. Sci.* 22:132-40, 2001.
5. Chung S, Funakoshi T, Civelli O. Orphan GPCR research. *Br. J. Pharmacol.* 153:S339-46, 2008.
6. Ciana P et al. The orphan receptor GPR17 identified as a new dual uracil nucleotides/cysteinyl-leukotrienes receptor. *EMBO J.* 25:4615-27, 2006.
7. Lecca D et al. The recently identified P2Y-like receptor GPR17 is a sensor of brain damage and a new target for brain repair. *PLoS One* 3:1-15, 2008.
8. Fumagalli M et al. Phenotypic changes, signaling pathway, and functional correlates of GPR17-expressing neural precursor cells during oligodendrocyte differentiation. *J. Biol. Chem.* 286:10593-604, 2011.

9. Eberini I et al. In silico identification of new ligands for GPR17: a promising therapeutic target for neurodegenerative diseases. *J. Comput. Aided Mol. Des.* 2011 (epub head of print).

Please note that the following program areas are **NOT** appropriate for this RFP and will not be considered:

- Proposals that do not directly address one or more of the scientific focus areas of this RFP
- Development of compounds for which the patent has expired or owned by third parties not involved in the proposal
- Lead molecules and drug-like compounds for which there is no clear path to patentability and/or exclusive ownership as a result of the funded research program
- Development of devices, diagnostics, assays, or animal models
- Gene therapy or related DNA- or RNA-based therapeutic approaches
- Exogenous stem cell-based therapies
- Autologous cell-based therapies
- Exclusive modulation of T cell activity (e.g. activation, trafficking) without effect on B cells
- Antibody or other macromolecular drug candidates to cellular or molecular targets in the CNS, unless there is PK/PD evidence of penetrance across the blood brain barrier
- Research projects to identify new GPCRs in the CNS

3.3 Expected Deliverables

Successful proposals will describe a development path to achieving agreed-to scientific milestones. Achieving such milestones will trigger financial payments to the organization. Examples of such milestones are:

- Identification of a novel small molecule or biologic lead with activity in the nM range against a defined target
- Optimization, preclinical characterization (e.g. pharmacokinetics, pharmacodynamics, stability, safety, process development), and/or advancement into clinical trial of a drug candidate that promotes activities within the scientific scope of this RFP
- Identification of an endogenous or surrogate ligand for a GPCR in the CNS

3.4 Proposal Process and Expectations

Applicants seeking funding through this RFP are expected to submit a proposal through Fast Forward's online application process. The proposal must include:

- A defined development plan outlining the optimization, preclinical testing, and/or clinical trial of promising therapeutic compounds with a mechanism of action within the scope of this RFP
- Clearly defined go/no-go decision points
- Description of a value adding milestone (e.g. optimized lead compound, completion of safety testing, IND submission, initiation or completion of a clinical trial)
- A summary of existing and expected intellectual property
- A summary of other third-party funds and obligations that result from any data or intellectual property generated from supported program within the scope of this RFP
- Approaches for optimization of therapeutic compounds (within the scope of this RFP), including chemical optimization, *in vivo* biology, pharmacology, toxicology, manufacturing optimization and formulation chemistry

Applications are encouraged from academic investigators and companies working on therapeutic strategies in other neurodegenerative diseases or CNS injury as well as from those focused on multiple sclerosis.

Applicants whose programs do not fall within the scope of this RFP should contact Fast Forward staff to determine if their project is suitable for funding by other Fast Forward programs.

Prior to receipt of funding through this RFP, each recipient organization shall enter into a written Sponsored Research Agreement with Fast Forward that will describe the recipient's responsibilities, milestones and deliverables associated with the funded program. This agreement will also describe the form and amount of the financial return that Fast Forward will receive from the recipient of the funding (See Section 10.3 Fast Forward Financial Return). In addition, prior to receipt of funding, each recipient will be required to enter into a Third-Party Agreement with Merck KGaA, which will grant Merck KGaA the right to negotiate an exclusive license to any intellectual property relating to the funded research (Section 10.0)

4.0 AVAILABLE FUNDS

- EMD Serono will commit up to \$3,000,000 annually for distribution by Fast Forward through programs described in this RFP. Subject to the availability of funds, Fast Forward has also committed to provide up to 10% of supplemental funding to each project funded through this RFP. Disbursement of actual funds will be contingent on the receipt of sufficient proposals of scientific and commercial merit

- Fast Forward intends to fund multiple proposals through both the Accelerating Innovation Program and the Accelerating Commercial Development Program
- Applicants for the *Accelerating Innovation Program* may request funding for a project period of up to one year and an annual budget of **direct and indirect costs totaling \$250,000**
- Applicants for the *Accelerating Commercial Development Program* may request funding for a project period of up to one year and an annual budget of **direct and indirect costs totaling \$500,000**
- Detailed budget justifications and updated workplans will be required of all applicants' budgets (including salary requests)

5.0 ELIGIBILITY REQUIREMENTS

5.1 Accelerating Innovation Program

Proposals for the *Accelerating Innovation Program* may be submitted by U.S. and non-U.S. entities, public and private universities, non-profit research organizations, and seed stage for-profit commercial organizations. The planning, direction, and execution of the proposed project will be the responsibility of the applicant and their organization.

5.2 Accelerating Commercial Development Program

Proposals for the *Accelerating Commercial Development Program* may be submitted by U.S. and non-U.S. commercial organizations. Responsibility for the planning, direction, and execution of the proposed project will be the responsibility of the applicant and their organization. In addition to information required of all applicants, applicants' companies are required to include financial statements (income statement and balance sheet) and documentation that the company has established sources of financing or funding throughout the period for which funding is requested under the submitted proposal.

6.0 Application and Review Process

Potential applicants should note the following:

- Applicants from academic institutions **may not** submit dual applications to this RFP and the National MS Society's research programs.
- Applicants **may not** submit simultaneous proposals to the *Accelerating Innovation and Accelerating Commercial Development Programs*.

6.1 RFP Timeline

The application and review process for this RFP will adhere to the following timeline:

RFP Release	October 10, 2011
Informational Conference Calls	November 11, 2011
	January 23, 2012
	March 26, 2012
Full Proposals Due	May 1, 2012
Award Announcements	August 1, 2012

7.0 FULL PROPOSAL

7.1 Full Proposal Submission and Review

All proposals will be treated with confidentiality by Fast Forward and its reviewers as described in Section 8.0. Upon receipt, all proposals will be reviewed for completeness by Fast Forward. Proposals must contain sufficient specific information to allow adequate scientific and commercial potential review of the proposed research. Incomplete proposals will not be reviewed. As part of its due diligence process, Fast Forward reserves the right to request additional information after submission of the full proposal. Full proposals will be evaluated by a PRC (Program Review Committee) which will be comprised of scientific and business experts drawn from Fast Forward's Scientific and Business Advisory Committee. All applicants chosen for the full proposal review will receive summaries of the PRC's deliberations. All recommendations of the PRC are final and may not be appealed.

Final funding decisions will be made by the Fast Forward Board of Managers and will be based on the recommendations of the PRC. Each award will be provided pursuant to a Sponsored Research Agreement between the recipient and Fast Forward with Merck KGaA as a potential intended third-party beneficiary.

7.2 Full Proposal Review Criteria

The intent of this RFP is to support innovative translational programs including, but not limited to preclinical and clinical development programs. Full proposals will be evaluated against the following criteria:

Scientific Merit:

- **Rationale:** Does the proposal address an important aspect of the RFP and does it have compelling commercial potential to lead to a marketable product?
- **Innovation:** Is the proposal original and innovative? Does the project challenge existing paradigms or clinical practice or address an innovative hypothesis, novel target or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area? Does the proposal address an unmet medical need?
- **Research Team:** Are the lead investigator and collaborators qualified and well-suited to carry out the proposed research program?
- **Scientific Plan:** Is there proof of concept for the proposed hypothesis? If not, what is the rationale for successful outcome? Is the plan sufficiently developed and appropriate to the project? Are the specific aims clearly defined? Are milestones and go-no decision points articulated? Are the milestones and timeline realistic for the one-year funding period?
- **Environment:** Is the research environment appropriate and likely to contribute to the success of the proposed research program? Does the environment foster collaborative arrangements that may support the proposed research activities? Is the research environment compliant with appropriate rules and regulations for conducting animal studies?
- **Budget:** Is the proposed budget reasonable and justified relative to the proposed research?

Commercial Considerations:

- **Commercial Feasibility:** Does the proposal define a potential path from lab to clinic? What are key milestones that would support the proposed path?
- **Therapeutic Strategy:** Does the proposed therapeutic approach address unmet needs relative to existing alternatives/therapies for treatment of MS? Is the strategy feasible and appropriate to MS? Are tools such as in vitro assays and in vivo models available to facilitate proof of proposed hypothesis?
- **Development Potential:** Is there a development path that enables the drug candidate to advance through preclinical and/or clinical development?
- **Intellectual Property:** Has the applicant or organization secured its intellectual property? If not, is it in the process of securing its intellectual property?
- **Third Party Obligations:** Has the proposed program been funded by other parties that may limit the freedom to operate (e.g. required cross-licensing, blocking patents, prior art, limited patent life)?
- **Future Development:** Are there any known limitations to advance this program from the laboratory to the clinic? If so, please define the technical or business considerations?
- **Subcontracting:** Does applicant plan to subcontract any of the research program with a third party?

Additional Considerations for Accelerating Commercial Development Applicants:

- **Management Team:** Does the management team of the commercial organization have the requisite qualifications and expertise to direct the activities of the program?
- **Independent Funding:** Has the company received prior funding to support the organization's activities? Does the company have sufficient funds to operate independent of funding provided via this RFP?

8.0 Confidentiality

Companies or institutions acknowledge that Fast Forward and EMD Serono may receive Confidential Information of the company or institution in response to this RFP. Fast Forward and EMD Serono may provide such Confidential Information on a "need to know" basis to its affiliates, employees, consultants, contractors and advisors; provided, that Fast Forward and/or EMD Serono shall cause recipients of Confidential Information to hold as confidential and not, directly or indirectly, disclose, publish or use for the benefit of any third-party or itself, except in carrying out Fast Forward and EMD Serono's obligations under this RFP, any Confidential Information of the other Party or such other Persons, without first having obtained the company's or institution's written consent to such disclosure or use. "Confidential Information" shall include, but not be limited to confidential and proprietary information, know-how, scientific information, clinical data, efficacy and safety data, adverse event information, formulas, methods and processes, specifications, pricing information, customer information, business plans, trade secrets and all other similar information. Confidential treatment of information shall apply only to those portions of a proposal which are clearly marked as containing Confidential Information. Applicants are instructed to identify which portions contain Confidential Information and may not label their entire proposal as confidential. This foregoing shall not apply to any information which:

- (a) is or becomes public through no unauthorized action of Fast Forward, EMD Serono or their affiliates;
- (b) was already in the possession of the Fast Forward, EMD Serono or their affiliates;
- (c) was independently developed by the Fast Forward, EMD Serono or their affiliates;
- (d) is disclosed by the receiving Party pursuant to interrogatories, subpoena, or a civil investigative demand of a court or governmental agency; or
- (e) is required to be disclosed by Fast Forward or EMD Serono under any statutory, regulatory or similar legislative requirement or any rule of any stock exchange to which it or any Affiliate is subject.

9.0 Conflicts of Interest

Investigators and collaborators submitting proposals in response to this RFP will be excluded from serving on the PRC. Fast Forward acknowledges that individuals invited to serve on a PRC may have an actual or perceived conflict of interest that arises during the proposal review

process. A PRC member will be considered to have a conflict of interest if they are a collaborator, sub-contractor, and/or consultant with an investigator that has a proposal before Fast Forward in response to this RFP; if the proposal has been submitted by another individual within the reviewer's institution or company regardless of whether or not reviewer has had any involvement in preparing the application; if the reviewer, his/her immediate family, or professional associate(s) has a financial or vested interest in the outcome of the proposed research (even if no significant involvement is apparent in the proposal being considered); or the PRC member has been involved in discussions regarding the application, is a provider of services, cell lines, reagents, or other materials, or writer of a letter of reference for the applicant.

When a conflict of interest is deemed to be present, the PRC member will be ineligible to review the proposal and will be asked to recuse themselves when the proposal is discussed during the review process, including when it is scored. Results of the review will not be made known to the conflicted reviewer until after the entire review process is complete. PRC members will also be urged to avoid any actions that might give the appearance that a conflict of interest exists, even though they may believe there may not be an actual conflict of interest.

10.0 ADDITIONAL REQUIREMENTS

10.1 Merck KGaA Right to First Negotiation

As a condition to accept funding under the Research Program the recipient will undertake certain obligations as outlined below:

- Among the rights granted to Merck KGaA is an option to enter into exclusive negotiations with the funded recipient regarding any intellectual property derived from the Research Program.
- Merck KGaA will have 90 days from the completion of the research to exercise its option.
- If Merck KGaA does not exercise its option then the funded recipient shall have no further obligations to Merck KGaA. If Merck KGaA chooses to exercise its option then it shall enter into a 6 month exclusive negotiation period with funded recipient with respect to a license or further development of the intellectual property relating to the Research Program.
- The scope and terms of such potential agreement shall be reached upon mutual agreement by both parties. Such agreement may include but not be limited to an exclusive license or other arrangements representing a co-development and commercialization relationship with Merck KGaA based upon the Research Program and resulting intellectual property. Acceptance of funding does not limit, or aim to define, either the scope or the terms of such future agreements between Merck KGaA and funded recipient and funded recipient has no obligations beyond good faith negotiations to reach mutually agreed terms. If Merck KGaA exercises its option to enter into negotiations but the parties are not able to reach an agreement, then the funded recipient may enter into discussions with other third parties. However, recipient will be prohibited for a period of one year from entering into a bona fide agreement of any nature on terms that taken as a whole are more favorable to the third party than the terms offered by Merck KGaA. For clarity, such restriction only pertains to the intellectual property resulting from the funded Research Program.

- In order to protect Merck KGaA's right of first negotiation, the recipient will be prohibited from transferring, licensing or otherwise encumbering the relevant intellectual property at any time during the term of the funded Research Program and for the subsequent option period, until Merck KGaA provides notice with respect to its intent to exercise its option and right for first negotiation. Furthermore, until Merck KGaA exercises its option, funded recipient will be prohibited from entering into any collaborations or similar agreements that would interfere with Merck KGaA's exercise of its rights. These restrictions will lapse when either Merck KGaA chooses not to exercise its right of first negotiation or upon the expiration of the negotiation period.

10.2 Fast Forward Financial Return

Fast Forward seeks to participate in the success of the research programs that it funds with corporate entities. As such, the Sponsored Research Agreement shall grant Fast Forward an option to purchase some form of equity shares in the company. Alternatively, Fast Forward may receive a financial return on its funding based on royalties received by the company in the form of upfront or milestone payments from their corporate partners or the commercialization of products resulting from the funding research. In connection with the negotiation of the Sponsored Research Agreement, the parties shall negotiate in good faith any equity grant to Fast Forward and/or royalty and milestone payments to be agreed by the parties and other reasonable and customary terms for agreements of this type. With respect to academic institutions, the financial return to Fast Forward will be determined on a case-by-case basis.

10.3 Publicity

Recipients of funding through this RFP acknowledge that Fast Forward has the right to disclose the existence of a funding relationship and include a non-confidential summary of the research being funded at the initiation of the program in any descriptions of its research portfolio, fundraising activities, and reporting requirements.

Recipients of funding through this RFP also agree to acknowledge financial contribution of Fast Forward and Merck KGaA in any announcement or publications describing a therapeutic or diagnostic for multiple sclerosis utilizing information developed in whole or in part from the funded program.

10.4 Reporting Requirements

- **Progress Reports:** Progress reports are due every three months. Reports will be submitted online via the Fast Forward online reporting system. Progress report instructions will be provided by Fast Forward approximately two months before they are due. Funded investigators are expected to provide a comprehensive final report to Fast Forward within one month of a project's completion. Successful achievement of milestones will be used to determine continued funding. Funded investigators are

expected to meet scheduled milestones and provide deliverables on time. Failure to meet milestones, furnish scheduled deliverables, including any reports, or to comply with the terms of a sponsored research agreement may serve as a basis for termination of funding by Fast Forward at any time during the funded research term.

- **Financial Reporting:** Investigators' organizations are expected to account for the funds expended under any Fast Forward sponsored research agreement; any funds spent either not in accordance with the approved research project or prior to pre-approval of any material change in the project are both (i) recoverable by and subject to restitution by the investigator's organization to Fast Forward and (ii) may be cause for immediate termination of funding by Fast Forward.

11.0 INQUIRIES

Applicants are encouraged to contact Fast Forward for clarification of any issues or questions regarding this RFP. Any questions should be presented well in advance of the application deadline. Please direct inquiries regarding programmatic, fiscal and administrative issues to Maya Merrell, Senior Manager, at maya.merrell@fastforward.org, or at 212-476-0443.