Request for Applications: Development of Biomarkers for Myotonic Dystrophy Studies

Solicitation Name: 2016-MDF Myotonic Dystrophy Biomarker Development
Contracting Office Address:

Myotonic Dystrophy Foundation (MDF)
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Contracting Officer: John Porter, Ph.D., Interim Chief Science Officer, MDF
Date Issued: 4 April 2016
Proposals Due: 27 June 2016, 5 PM Pacific
Notification of Selection: 30 September 2016
Period of Award: 1 October 2016 – 29 September 2017
Anticipated overall award: $150,000
Number of awards to be issued: One

Synopsis

Through this Request for Applications (RFA), MDF recognizes an urgent need to develop or refine biomarkers for use in myotonic dystrophy studies and trials. MDF will issue one $150,000 award for a one-year project that addresses the development of a biomarker in the context of a particular therapeutic development program or the qualification of a biomarker across multiple therapeutic development programs.

Background

Myotonic dystrophy is an autosomal dominant, variable, multi-systemic repeat expansion disorder characterized by muscle weakness, fatigue, myotonia, cataracts, cardiac conduction defects and endocrine and gut motility dysfunction. The two forms, DM1 and DM2, are caused by expansions in two unrelated genes, which result in different, but related clinical phenotypes. DM1 is generally more severe and has a very severe congenital form and a juvenile form, while DM2 is usually milder and adult onset. Only palliative therapies are currently available for this progressive and life-threatening disease, although experimental treatments are starting to progress to the clinical testing stage.

As potential new therapies for myotonic dystrophy are developed, there is an ever increasing need for tools to aid in the conduct of clinical trials. Biomarkers, “indications of medical state observed from outside the patient, which can be measured accurately and reproducibly”¹ have many uses in therapy development including diagnosis, determining if a therapeutic is reliably affecting its target, tracking the progression of a condition, or monitoring changes in a condition...
due to a therapeutic effect. More specifically, in clinical trials, biomarkers are frequently used for safety assessment, dose selection, stratification, and patient selection/enrichment\(^2\). When enough evidence links a biomarker to a change that is clinically meaningful to a patient, a biomarker may even be used as an approvable endpoint for a new therapeutic, although this is an extremely high hurdle\(^3\).

Biomarkers can be integrated into drug development through either of two pathways: (1) regulatory submissions for drug approval in the context of a single drug development program; or (2) establishment of the biomarker for use in multiple drug development programs. The latter path is known as “biomarker qualification” and is a voluntary process overseen by the FDA’s Center for Drug Evaluation and Research (CDER) Biomarker Qualification Program [http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284076.htm]. Investigators developing biomarkers through either route should seek early guidance from the FDA. Note that there is no formal meaning of the term “validated” in the context of the FDA and biomarkers. Informally, a “validated biomarker” may be one that has been used successfully in a past drug development program in a specific context.

There are currently no qualified biomarkers for myotonic dystrophy and no single use biomarkers have yet had a successful track record given that no therapeutics have ever been approved for myotonic dystrophy; however, investigators in the field have given considerable thought to what types of biomarkers may be useful for therapeutic development in myotonic dystrophy. At an MDF-sponsored meeting on endpoints and biomarkers held in Washington D.C. in 2014, investigators discussed the potential for using patterns of splicing changes, myotonia, CNS changes and protein serum changes to monitor the effect of a potential therapeutic for myotonic dystrophy [http://www.myotonic.org/experts-participate-dm-regulatory-workshop].

**Important References:**


**Study Requirements**

Projects may focus either on the development of a biomarker for a particular myotonic dystrophy therapeutic development program or on the qualification of a biomarker that may be used in multiple drug development programs. Investigators should describe how the FDA will be
consulted in the development plans and should identify at least two milestones to which grant payments will be linked (typically MDF allows a start-up payment of no more than 33% of the total budget that is not milestone-linked).

Due to the size and duration of this award, it is not anticipated that investigators seeking to qualify a biomarker will be able to do so without additional outside funds or the need for additional future funding. Applicants are encouraged to consider ways to leverage funds by engaging in collaborations or piggy-backing on existing projects; if this is not possible, goals should be realistic about what can be accomplished in this time span with this amount of funding.

**Eligibility**

Proposals are welcome from academic institutions and/or biotechnology or pharmaceutical companies. Collaborative projects are encouraged.

- Applicants or teams of applicants must have access to the knowledge, resources and skills necessary to carry out the proposed research
- Submitting PIs and Co-PIs must:
  - Be a professional or faculty member at an appropriate educational, medical or research institution, or company and be qualified to conduct and supervise a program of original research;
  - Have both administrative and financial responsibility for the grant;
  - Have access to organizational resources necessary to conduct the proposed research project; and
  - Hold a Doctor of Medicine, Doctor of Philosophy, Doctor of Science or equivalent degree.

Applicants from foreign academic institutions or companies are permitted

**Submission Process and Requirements**

Proposals cannot exceed 10 pages in length, and must be submitted in 11-point font. Proposals should be submitted via email to MDF Grants Manager Elizabeth Habeeb-Louks (elizabeth.habeeb-louks@myotonic.org) no later than 27 June 2016, 5 PM Pacific.

The proposal must include the following (within 10 pages):

1. Brief lay abstract, no more than four sentences
2. Technical abstract of no more than two paragraphs
3. Description of the background and rationale for project
4. Detailed description of the research plan. Be sure to address caveats, contingencies, and appropriateness of methods
5. Explanation of how project input from the FDA will be sought (you may include, outside of the ten-page limit, examples of existing communications with the FDA if available)
6. If the application involves a collaboration, description of the rationale for, and logistics of the collaboration, including contributions of all parties, plan for communication and sharing of equipment and/or team members
7. Figures (may be embedded in text or included at the end)

In addition, (not included in the 10-page count) proposals must include:

8. References
9. Detailed budget in spreadsheet or table format (see “Other Requirements” for instructions on dividing the budget between collaborators)
10. Accompanying budget description and justification (one paragraph)
11. Description of facility(ies) and equipment, if any, that will be used for the project (one paragraph)
12. Very brief: Names, degrees, training/qualifications, experience, role in project and percent effort for team members from both groups in the collaboration (may be submitted as a table)
13. CVs of all participating team members;
14. Letters from collaborators and/or in support of the application
15. Face page provided by MDF for this RFP (see attached)

Submit proposals as a single PDF file, including the signed face page, and all supporting documents to MDF Grants Manager Elizabeth Habeeb-Louks (elizabeth.habeeb-louks@myotonic.org) by the designated deadline with the subject line “RFP: 2016 Myotonic Dystrophy Biomarker Development.”

Review and Selection
Projects will be reviewed by an ad hoc committee composed of individuals with expertise in one or more areas relevant to this project including clinical aspects of the disease, biomarker development and regulatory compliance. All reviewers will sign confidentiality agreements and conflict of interest statements. Applicants may request that particular reviewers or reviewers from particular organizations not be considered.

Review criteria:
- Experience and expertise of applicants
- Facilities and resources
- Feasibility of research plan
- Feasibility of collaboration, if applicable, including balance of responsibilities and intellectual contribution
- Regulatory compliance plan
- Relevance to therapy development for myotonic dystrophy (big picture)

Other Award Conditions
Budget: If the project involves a collaboration, one collaborator should be the submitting PI and the other should be the Co-PI. The award will be made to the organization of the submitting PI and the organization of the Co-PI will be considered a subcontractor. It will be the responsibility of the submitting PIs organization to manage the agreement with the subcontractor.

Applicants must confirm that the funds awarded will be used only for the research project described in the application; indirect costs and overhead charges are not allowed for these proposals. Equipment charges are allowed upon written approval from the Wyck Foundation and/or MDF.

We request that any biomarkers for DM developed or refined with our funds will be made available promptly to the DM research and drug development communities at large, either free-of-charge or through reasonable licensing fees.

The Wyck Foundation and/or MDF may request a proportionate return on its investment, to be negotiated at the time the award is made.
References

