2019

RESEARCH GRANTS

FIGHT MND.

IT TAKES PEOPLE

CLINICAL TRIAL GRANTS

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INTRODUCTION

FightMND Call for Proposals:

Phase II/III Clinical trial applications for novel, high-potential treatments for people living with MND/ALS

Applications Open: November 1st 2018

Letter of Intent due: January 19th 2019

Submit Letter of Intent to: research@fightmnd.org.au

Invitation to submit full application: 9th February 2019

Full application due: April 1st 2019

Recipients Announced: Late June 2019

FightMND is pleased to announce a call for Phase II/III clinical trial applications for novel, high-potential treatments in Motor Neurone Disease/ Amyotrophic Lateral Sclerosis (MND/ALS) within the Australian Clinical Trials Consortium of hospitals.

The call for clinical study proposals is intended for academic-industry partnerships including but not limited to pharmaceutical, bio-therapeutic/biotechnology companies, academic institutions and universities, hospitals, and MND researchers throughout the world. Up to AUD $1,000,000 (Phase II) - AUD $1,500,000 (Phase III) in support from FightMND is available per grant.

Potential Phase II clinical trials should include therapeutic interventions that have:

I. a pharmacodynamic marker that can measure whether the targeted pathway of interest has been affected, and
II. a plan to collect samples for biomarker studies, and
III. shown promising efficacy in at least two (2) MND disease models, one of which must be a representative model of human sporadic MND

Industry partnership applications are strongly encouraged with shared funding proposals.

Note: it is NOT an Australian Regulatory requirement for drugs to have an IND submission prior to commencement of projects in Australia.

Since infrastructure support is provided by this grant, applicants are required to contact FightMND prior to their grant submission to collaborate on the budget portion.

RESEARCH OBJECTIVES

The following research objectives govern the parameters of the trials:

- This program is intended to enhance opportunities for translational research with the central emphasis on clinical studies/trials.
- Research conducted should lead to high quality data that form the basis of efficacy or Phase III trials.
- Clinical study proposals must include trials of novel drugs or drug combinations, devices, or management practices for the treatment of MND.
- Each application must propose one Phase II clinical treatment trial. In this context, Phase II trials may be proof-of-concept trials that will be carefully designed to establish the safety of drug candidates in the target MND population, and determine the relationship between the dose and desired activity. Applications for Phase II randomised placebo-controlled trials are welcomed.

Applications will be reviewed by the FightMND Scientific Advisory Panel (SAP). The following will be considered in making funding decisions (See "Selection Criteria" for further details):

- Scientific rationale and merit, novelty, and the value of the project
- Feasibility of the clinical trial
- Significance of the clinical question and potential to change clinical management to progress to Phase III testing.

The successful applicant will retain control of the trial as well as intellectual property relating to the therapeutic agent being investigated.

Applicants may request the full AUD $1,500,000 in research support or may request a smaller amount depending on the appropriate needs of the proposed study. A maximum of 10% indirect costs is allowable and should be included in the AUD $1,500,000 .

Industry partnership applications are strongly encouraged with shared funding proposals.

Trial logistic and infrastructure support can be provided through a FightMND approved Contract Research Organisation (CRO) and can be a combination of any or all of the following clinical research support services:

- Access to 10 Clinical sites across Australia with access to between 50 to 350 MND Patients at each site allowing for ease of enrolment
- Project Management
- Grants and Contracts Management
- Biomarkers and bio-banking
- Investigator brochure preparation or finalisation;
- Start-up activities: site selection and feasibility, preparation and submission of Institutional Review Board/Ethics applications, Investigator meetings, contract negotiation;
- Site Initiation, monitoring, site management and close-out activities;

RESEARCH OBJECTIVES

- Investigator meeting organisation, participation and close-out activities
- Third party vendor selection and management
- Study budget negotiation (sites and vendors) as well as budget management
- Data management expertise with internal and external vendor capabilities;
- Biostatistician who is a specialist in neuroscience projects;
- Medical Monitoring capabilities; utilising neurologists for this service as required;
- Data Safety Management Board selection, preparation of associated documentation, maintenance and assistance in report preparation;
- Regulatory: assistance in preparation of IND packages, attendance at pre-IND, End of Phase 2 meetings, pre-NDA meetings;
- Medical writing including Clinical Study Report preparation;
- Preparation of Standard Operating Procedures;
- Training of site and study personnel in Good Clinical Practice.

SELECTION CRITERIA

Reviewers will provide an overall impact/priority score to reflect their assessment of the likelihood for the project to exert a sustained and powerful influence on MND research and the potential for clinical impact on disease biology. This evaluation will be assessed based on the following five core criteria:

SIGNIFICANCE

- Does the proposed clinical study bring forward a new potential therapy for people with MND?
- Is there sufficient preclinical data (pharmacology, toxicology and efficacy) to support initiation of the proposed trial?
- Can the proposed clinical trial be initiated expeditiously?
- Does the study have a pharmacodynamics marker that can measure whether the targeted pathway of interest has been affected by the drug?
- Is there a proposed plan to collect, store, and analyse samples for biomarker or other patient characterisation studies?
- Does the proposed trial protocol, if completed successfully, provide a sound platform for efficacy and Phase III trials?

INNOVATION

- Does the proposed clinical trial employ novel concepts, approaches, and/or methods?

DESIGN

- Is the conceptual framework, design, methods, and proposed analyses adequately developed, well-integrated, and appropriate to the aims of the study?
- Have potential problems and alternative strategies been considered?
- Is/are the primary endpoint(s)meaningful?

ENVIRONMENT/COLLABORATIVE POTENTIAL

- Does the scientific environment in which the work will be done contribute to the probability of success?
- Does the proposed study take advantage of useful collaborative arrangements with other industry partners?

INVESTIGATOR(S)/SPONSOR(S)

- Is the Primary Investigator (PI) or sponsor appropriately trained/qualified to carry out the study?
- If the application includes Early Stage or New Investigators, do they have appropriate experience, training and support?

SUBMISSION GUIDELINES

LETTER OF INTENT

Please use the template below as an example of the format required in submission of your letter of intent. Lettor of intent submissions should be submitted with a minimum size 12 font, 1 cm margins and must not exceed 3 pages.

Principal Investigator:	Institution:
Biostatistician:	Institution:
Pharmacologist (if applicable):	Institution:
Estimated direct costs for the first year of funding:	

Please note that a maximum of 10% indirect costs may be included. The total budget including indirect costs cannot exceed AUD $1,500,000 (unless additional funding sources are available outside of these grants)

Primary Study aims:		
Secondary aims (if any):		
Briefly describe any relevant pre-clinical or clinical evidence that supports the study rationale:		
Briefly describe the study design:		
Indicate how the primary aims of this preliminary study will help optimise the design of the eventual definitive phase III trial:		
Number of subjects to be enrolled: ~		
Number of Australian Clinical Sites :		
Describe how the intervention will be administered, including dose and duration as applicable. Do you have drug and placebo in hand for the study?		
Does this preliminary study include placebo or control groups? If “yes” provide applicable rationale	YES	NO
Does the trial drug have preclinical efficacy data in at least 2 MND disease models - one of which MUST be a representative model of sporadic disease	YES	NO

SUBMISSION GUIDELINES

Describe the plan for sample collections and willingness to share samples with the MND research community:		
Describe the pharmacodynamic markers that will be used in the trial:		
Describe ethical and consent considerations of the proposed protocol:		
Participating pharmaceutical or device manufacturing company (if any):		
Do you hold or have you applied for an IND/IDE for this protocol? (Please note: it is NOT a requirement for trials in Australia)	YES	NO
List all cores that you are interested in utilising from a FightMND approved contract research organisation (CRO) - see "Research Objective" page 4 for details		

SUBMISSION GUIDELINES

Should you be invited to submit a full application, submissions must include the following:

SUMMARY/OVERVIEW (1 PAGE MAXIMUM)

- The summary should be a succinct and accurate description of the proposed work when separated from the application.
- State the project application's broad, long-term objectives and specific aims making relevance to FightMND's mission of discovering effective treatments and ultimately a cure for MND/ALS.
- Describe concisely the research design and methods for achieving the stated goals.
- This section should be informative to other persons working within MND/ALS research and/or clinical trials, and understandable to a scientifically or technically literate non-expert.

RESEARCH PLAN (MAXIMUM 7 PAGES)

- Background data and significance.
- Preliminary Studies.
- Research design and methods (study design; participant description; data to be collected; plan of analysis).
- Supportive documentation including a proposed timeline (e.g. Gantt chart) demonstrating that the trial will be conducted expeditiously.
- References .
- Appendix materials are allowed, including material to demonstrate that the treatment is ready for testing in humans. Please note: it is NOT a regulatory requirement for drugs to have an IND submission prior to human trials in Australia.

BUDGET

- Applicants are strongly encouraged to contact FightMND in regards to budgeting and use of the Foundation approved contract research organisation (CRO).
- Provide a full budget and budget justification.
- Budgets must include costs to cover clinical trial/research nurses at trial sites.

RULES AND REQUIREMENTS

- The application deadlines are described in this guideline.
- All applicants are asked to submit their applications electronically (file size not to exceed 5MB) in Word doc or PDF format (size 12 font, minimum 1 cm margins).
- The research project grant application should be forwarded via email to Dr Rebecca Sheean, Research Manager, at research@fightmnd.org.au

GRANT CONDITIONS

PROPRIETARY RIGHTS

The Principal Investigator/Sponsor will maintain full control of scientific work and all corresponding responsibilities. A scope of work will be agreed upon by all parties prior to initiation of funding. If necessary, confidentiality agreements will be incorporated.

REPORTING REQUIREMENTS

Funding recipients will be required to submit reports on a regular basis. The reporting schedule is outlined in the following table.

REPORT	REPORTING FREQUENCY	DUE
Progress against pre-determined milestones and/or targets*	6-monthly	Every 6 months from receipt of funds
Financial Reports (to be included in progress report)	Annually	Every 12 months from the receipt of funds
Final Report	Once Only	At project completion
Ad hoc reports	As requested by FightMND	On request with a negotiable time frame not greater than six weeks
FightMND Research Symposium Presentation (Melbourne, Vic)	Annually	At commencement of funding and every 12 months from receipt of funds.

PRIVACY AND CONFIDENTIALITY

All information contained in applications forwarded to FightMND will be regarded as confidential. Documents containing personal information will be handled and protected in accordance with the provisions of the *Privacy and Data Protection Act 2014* (Vic). Personal information will only be disclosed with the permission of the individual to whom it relates, or where the Act allows.

Applicants consent to the information supplied as part of their application being disclosed for the purposes of the evaluation and administration of the grant. Such disclosure includes but is not limited to members of the FightMND Scientific Advisory Panel (SAP), independent readers/assessors requested by the SAP to provide advice on the applications, the FightMND Board, and relevant employees of FightMND involved in the research grant process. Applicants acknowledge that announcement of the funded grants will involve a dissemination of information to the public about the general nature of the funded grants.

GRANT CONDITIONS

PUBLICATIONS, PRESENTATIONS, ACKNOWLEDGMENTS AND PUBLICITY

- Grantees are expected to seek publication of findings in refereed journals during and as soon as possible after conclusion of the project (subject to condition 18). FightMND and the grantee jointly undertake to notify each other before published reference is made to the findings of the project and to reach agreement on the form of publication wherever possible.
- Grantees must inform FightMND immediately when results from FightMND funded research are accepted for publication or presentation. The grantee must provide FightMND with reprints, photocopies or electronic copies of the final version of any such publications.
- **Open Access Policy:** Grantees of awards from FightMND are mandated to make their peer reviewed papers, directly arising from the grant, available through open access. These research papers should be available within the PubMed Central repository as soon as possible, but definitely within six months of publication of the paper. Publication costs can be included in the project budget.
- **Posters: costs and accessibility:** If FightMND funded research is accepted for presentation as a poster, the costs of poster production may be claimed as part of the consumables budget (to a maximum of $250 per project grant).The poster must acknowledge FightMND as a source of funding and should include FightMND's logo. FightMND should be provided with an electronic copy of the poster for use on our website and social media.
- To ensure the long-term sustainability of income for research and to reflect and maintain our reputation for funding research of the highest scientific excellence and of greatest relevance to MND, all opportunities to promote FightMND must be pursued. The grantee and the host institution are obliged to co-operate with FightMND over any publicity or fundraising activity arising from research funded by FightMND. Where it is the main funder of the research, FightMND reserves the right to lead on publicity.
- Grantees and the host institution must notify FightMND's Research Manager Dr Bec Sheean at research@fightmnd.org.au and Communication Manager Andrew Holmes andrew@fightmnd.org.au, at least five working days in advance of any publicity arising from research wholly or co-funded by a FightMND grant. Any press release or other material including reference to FightMND funded research must be approved by our team before it is released to the media. In any oral or written report or poster presentation relating to FightMND funded research, the author must acknowledge our support and display our logo where practical. All references to FightMND funded work placed on websites, electronic bulletin boards and similar must state clearly that the work is funded by "FightMND" and ideally a link should be included to the charity's website: www.fightmnd.org.au
- Grantees must ensure that the FightMND's support is acknowledged in all publications, presentations and similar. It is essential for grantees to acknowledge that their research has been supported wholly or in part by FightMND, either in the text or in a footnote. The grant reference must also be provided to FightMND.

GRANT CONDITIONS

- When speaking publicly and to representatives of the media about FightMND funded research, grantees and researchers should ensure they make it clear to the media and others that they should be presented as a "FightMND-funded scientist". Please note that researchers should consult our Research Manager and Communications Manager at research@fightmnd.org.au and andrew@fightmnd.org.au respectively, before speaking to the media.
- There is a subtle but important difference between speaking as a "FightMND-funded scientist" and acting as a spokesperson for the FightMND. Representatives of the media may not always be aware of this difference. Researchers who speak to the media must ensure that their personal views are not misrepresented as being attributable to FightMND.

CHANGE OF TERMS OF AWARD

- Reallocation of funds from one expense heading to another, as detailed in the grant award letter, requires written permission from FightMND.
- Grantees will be required to complete an Award Amendment Application detailing any and all proposed changes to the project. Applications must be submitted (where possible) at least eight weeks prior to the changes taking place, and submitted to FightMND Research Manager Dr Bec Sheean at research@fightmnd.org.au. FightMND must be kept informed at all time of any changes to the original grant.
- Any request for major changes in the terms of the award, e.g. for additional staff or equipment, must be made in the form of a new and separate grant application, which will be considered in competition with all other new applications.

CHANGES TO CONDITIONS OF AWARD

- FightMND reserves the right to change the Terms and Conditions of these Clinical Trial Grants at any time. If this occurs during the lifetime of an award, the revised Terms and Conditions may be applied in place of those issued at the time of the original award.
- Successful applicants will be given at least 8-weeks notice of any change to conditions of the grant.

EARLY TERMINATION OF AN AWARD

- FightMND reserves the right to terminate an award at any time. Circumstances which might lead to termination include:
  - Any breach in the Terms and Conditions under which the award was made.
  - If the project has not started within three months of the agreed start date.
  - The work is diverging markedly from the original approved project. Grant holders must inform FightMND immediately when they are aware of a change of direction. There may, however, be circumstances in which the change is acceptable on scientific grounds.
  - Failure to submit adequate progress reports, or serious and unresolvable problems identified by a site visit.

GRANT CONDITIONS

- Work has stopped on the trial, or the principal investigator has ceased to be actively involved in the project. FightMND must be informed immediately if the situation arises.
- FightMND will endeavour to give 60 days prior notice before termination of an award.
- If an award is terminated, FightMND will meet costs properly and necessarily incurred under the award up to the termination date. However, payments will not, in aggregate, exceed the amount of the grant remaining to be paid at the time of termination of the award.
- In the event of work being discontinued by the host institution, written notification must be sent to FightMND, together with a report on the work carried out to date, setting out reasons for the termination.

SCIENTIFIC INTEGRITY

In the rare event of scientific fraud occurring, FightMND wishes to make it clear that it is the responsibility of the employing authority to investigate any suspected case of fraudulent activity. FightMND agrees to provide funding providing the employing authority can produce evidence of a procedure for dealing with scientific fraud. If fraud should be proven the grant must be repaid in full to FightMND forthwith.

INDEMNITY

FightMND does not provide cover for negligent or non-negligent harm for participants in FightMND funded studies. The host institution should ensure that local arrangements are in place should claims arise.