The Academic Medical Organization of Southwestern Ontario (AMOSO)

December 1, 2010

Dr. M. Beaton
Department of Medicine
London Health Sciences Centre
UH, Room ALL-132

RE: Application to the AMOSO Opportunities Fund – "Evaluation of Therapy and the Quantification of Hepatic Steatosis and Liver Disease using Magnetic Resonance Imaging in Non-alcoholic Fatty Liver Disease"

Dear Dr. Beaton:

The Opportunities Fund Sub-Committee of the AMOSO Governing Committee has completed its deliberations, and the recommendations for funding of the September 30, 2010 Call for Proposals were approved at the November 26, 2010 Governing Committee meeting. As part of the deliberations, the budget request was also evaluated.

The AMOSO Governing Committee is pleased to advise, that for your project they have approved one-time total funding of $97,500 which includes Year 1 funding in the amount of $32,500 for AFP physician compensation for one day per week. The release of Year 2 and Year 3 funding will be contingent on an annual review process to ensure the project is achieving its stated objectives. To support the success of your project, reviewers' feedback and comments are provided with this letter for your consideration. It is noted that ethics approval from the Office of Research Ethics has been included with your proposal.

The allotted one-time funding for this proposal aligns with the compensation guidelines for Opportunities Fund applications as approved by the AMOSO Governing Committee. It is at the discretion of the Practice Plan(s) if they wish to provide any incremental funding.

In order to secure Year 2 funding, an annual report will be required for review by the Opportunities Fund Sub-Committee. The AMOSO office will notify you when your annual report will be due. As indicated in your proposal, the intended start date of your project was October 2010. Please confirm this start date with the AMOSO office or advise if you would like to consider the option of a new start date to align with the flow of funding for your project. **Please advise AMOSO no later than December 13, 2010 if a decision is made to <u>not</u> proceed with this project.**

On behalf of AMOSO, I would like to thank you for your application to the Opportunities Fund, created through AFP Funding for London.

Sincerely,

Patricia M Telfer

Patricia Telfer
Executive Director, AMOSO
On behalf of:
John Denstedt, MD FRCSC FACS
Chair, AMOSO Opportunities Fund Sub-Committee; and
John Sangster, MD MCISc(FM) CCFP FCFP
Chair, AMOSO Governing Committee

CC: Dr. J. Brown, Chair of the AFP FMC
Ms. S. Thomsen, AFP Practice Plan Administrator
Dr. D. Hollomby, City-Wide Department Chief/UWO Chair

REVIEWERS' COMMENTS

Please note: Reviewer comments are not intended as an assurance of future funding, but are provided as feedback for consideration and guidance in achieving the goals and objectives of the project for Year 1, Year 2 and Year 3.

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- the Project Lead has excellent potential and is very committed.
- concern that the Project Lead would not be able to get enough pilot data out of the number of sample sizes.
- concern that with two main projects, as well as other projects, could end up with data which is not analyzable and which won't help the Lead for the next step.
- has good collaboration.
- the Project Lead took the past comments to heart and made a good attempt to answer the criticisms, including the provision of critical support letters which were missing in the last submission.
- the Project Lead is enthusiastic and overall the project is good with ethics approval obtained and peer review funding, notably PSI, achieved.
- keen and well trained person.
- (likely due to setting up the clinic), productivity is modest.
- sample sizes have been done but are likely overly optimistic – how can you find 15% less fibrosis – on bx or 15% fewer patients, is it reasonable to find this result in a short period of time, esp as there is bx error – will it be on imaging, etc? Will biopsies be read blinded. Phlebotomy trial: likely more feasible to have a surrogate outcome.
- the Project Lead is doing the metabolic liver clinic but doesn't seem to have aid in trial design (or it is not provided) so there is concern there will be many negative studies as all will be small (Type II error). Similarly for the incretin study, 20 individuals seems very small.
- expertise might be needed in helping to suggest the primary outcomes and what analyses are needed for each study.
- the resubmission has substantively addressed the comments from the reviewers related to the initial submission. Specifically, a more detailed description of the statistical analysis and sample size calculations has been provided for both portions of the study. The calculations are partially based on pilot data that have now been produced.
- this proposal is very clinically relevant.
- the Project Lead should have no difficulty recruiting patient subjects.
- this proposal, although ambitious, is very impressive.
- the therapeutic role of phlebotomy is very intriguing and has not yet been studied, although the theoretical basis for suggesting a trial is well-articulated by the Project Lead.

- studying the pharmaceutical agent, stigalipin, is very interesting and exciting as insulin-resistance is well recognized to have a role in the disease process. Currently, stigalipin is licensed for diabetes mellitus and clinicians should not use it for this indication, outside of a formal clinical trial, given the lack of published pilot studies. The Project Lead's study with this medication would therefore be unique and would greatly contribute to the pharmacotherapeutic knowledge in this area. Importantly, the outcome of the Lead's single arm study of this drug for NAFLD/NASH should encourage the pharmaceutical manufacturer to consider a formal clinical trial for this indication.

- the bench research component of this project is interesting and will undoubtedly generate many published papers in both the proteonomic and genomic fields.

- in terms of originality, this proposal incorporates all of the current clinical issues with regards to this disease process and constitutes a comprehensive multidisciplinary programmatic approach to this disease entity.

- the feasibility of this project appears to be certain and will utilize resources, both material and intellectual, that are already present at The University of Western Ontario.

- this proposal should generate many peer-review papers, will lead to further research in this area and most likely will translate into improvements in clinical practice.

- all of the objectives of this proposal are easily achievable and the timelines proposed are feasible.

BUDGET: Recommended funding: one day per week per year for three years = total funding of $97,500.