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TITLE: **Evaluation of the Safety and Efficacy of the FAAH Inhibitor URB597**

PRINCIPAL INVESTIGATOR: **Alexander Neumeister**

CONTRACTING ORGANIZATION: **New York University**
New York, NY 10016

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
The award was to fund a 3-year program involving a phase I study to determine the safety, tolerability, and pharmacokinetics of orally administered URB597, the first potent and selective FAAH inhibitor, in healthy volunteers and a phase II study to determine the efficacy and safety of URB compared with placebo. Due to the Principal Investigator's leaving the institution in March of 2015 the study was discontinued prior to the preclinical evaluations for pharmacokinetics and toxicology. The supply of URB597 that had been produced was shipped to the Uniformed Services University (USU) as instructed by USAMRMC, August 2015.

15. SUBJECT TERMS
post traumatic stress disorder, OEF/OIF clinical trial, FAAH, CB1 receptor, brain imaging

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1. Introduction

The award was to fund a 3-year program involving a phase I study to determine the safety, tolerability, and pharmacokinetics of orally administered URB597, the first potent and selective FAAH inhibitor, in healthy volunteers and a phase II study to determine the efficacy and safety of URB compared with placebo. Due to the Principal Investigator's leaving the institution in March of 2015 the study was discontinued prior to the preclinical evaluations for pharmacokinetics and toxicology.

2. Keywords

Post traumatic stress disorder, OEF/OIF clinical trial, FAAH, CB1 receptor, brain imaging

3. Accomplishments

What were the major goals of the project?

Study 1 Specific Aims: The purpose of the study I is to demonstrate the safety and tolerability of URB597 as well as determine the optimal dose for the Phase II study. Individual steps involve (1) manufacturing of the drug substance to support the optimization of a formulation and later manufacture the clinical trial material, as well as implementation of bioanalytical methods to detect in plasma the drug substance and its main metabolites; (2) evaluation of pharmacokinetics of the drug formulations, and (3) evaluation of the safety/toxicology of the drug substance in preclinical models including rat and non-human primates, and (4) determination of the optimal dose for the Phase II study in single and repeated dose studies in humans.

Study 2 Specific Aim: To conduct a 4-week, randomized, placebo-controlled, double-blind, outpatient proof-of concept (POC) clinical trial to test the efficacy and tolerability of URB597 in OEF/OIF military personnel (N=46) with combat-related PTSD. In addition, we collect surrogate markers of treatment response (CB_1 receptor density and changes in fear processing), which are linked to both, the neurobiological underpinnings of PTSD and the mechanism of action of URB597.

What was accomplished under these goals?

OBJECTIVE 1: **Coordinate Study Staff for Study 2, POC Trial in OEF/OIF PTSD**.

Timeframe: Months 1-3
Tasks: hire and train study staff for the completion of Major Task 1 and 2.
Percentage of Completion: 100%

OBJECTIVE 2: **Conduct Phase I Safety Studies of Optimal Dosing for URB597**.

Tasks: (1) manufacturing of the drug substance to support the optimization of a formulation and later manufacture the clinical trial material, as well as implementation of bioanalytical methods to detect in plasma the drug substance and its main metabolites; (2) evaluation of pharmacokinetics of the drug formulations, and (3) evaluation of the safety/toxicology of the drug substance in preclinical models including rat and non-human primates, and (4) determination of the optimal dose for the Phase II study in single and repeated dose studies in humans.

Percentage of Completion: 25%

What opportunities for training and professional development has the project provided?
Nothing to Report

How were the results disseminated to the communities of interest?
Nothing to Report?

4. **Impact**

What was the impact on the development of the principal discipline(s) of the project?
Nothing to Report

What was the impact on other disciplines?
Nothing to Report

What was the impact on technology transfer?
Nothing to Report

What was the impact on society beyond science and technology?
Nothing to Report

5. **Changes/Problems**

The Principal Investigator for this study Alexander Neumeister resigned from the New York University School of Medicine March 12, 2015 and after a period of evaluating possible new leadership it was decided that the study should be closed June 25, 2015, future year funds were de-obligated and a final closeout of all contracts and business was initiated. As requested by USAMRAA the 1.5kg of URB597 that had produced by vendor STA Pharmaceutical Hong Kong Limited was shipped to Gary H. Wynn at the Uniform Services University (USU) August 11, 2015.

6. **Products**

Under a Service Agreement between STA Pharmaceutical Hong Kong Limited, and New York University School of Medicine, a contract was executed on September 26, 2014, and a Purchase Order was issued on October 6, 2014 to develop and manufacture the Active Pharmaceutical Ingredient (API) C13121804 (URB597). This material was to be used to carry out the above referenced animal studies, and the two human protocols, but the study was discontinued before the pharmacokinetic and toxicology studies commenced.

7. **Participants & Other Collaborating Organizations**

Name:	Alexander Neumeister
Project Role:	Principal Investigator
Nearest months worked:	3.00
Contribution to the Project:	He directed the contract work between NYU School of Medicine and the contractors. He communicated with the USAMRMC Animal Care and Use Review Office to obtain approval for the animal studies. He directed the regular team meetings.

8. Specialist Reporting Requirements

None

9. Appendices

None