Study Protocol
Interdisciplinary Study of A Novel Anticonvulsant in Alcoholism
NCT #: NCT02901041
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IRB Office use only Date submitted_____ FB_____ Exp. ____

BU Charles River IRB
Application Form (Full Board and Expedited Review)

SECTION A: PROTOCOL AND CONTACT INFORMATION

Protocol Number (To be assigned by IRB Office):	4299
Protocol Title:	Interdisciplinary Study of A Novel Anticonvulsant in Alcoholism
Principal Investigator (Name, degrees, licenses, etc.): ☒ Mr. ☐ Ms.	Todd Farchione, Ph.D.
Department/School:	Center for Anxiety and Related Disorders
BU Mailing Address:	900 Commonwealth Avenue, 2nd Fl, Boston, MA 02215
Email:	tfarchio@bu.edu
Telephone:	617-353-9610
Additional Contact Person:	
Email:	
Telephone:	

☒ YES **(REQUIRED)**	I confirm that I qualify to serve as the Principal Investigator of this study and am in compliance with the following policies: • http://www.bu.edu/orc/files/2015/05/PI_Resp_SOP_Final.pdf

SECTION B: FUNDING

Provide information regarding **ALL** funding sources in this section. This includes **ANY EXISTING FUNDING, PENDING FUNDING, OR FUNDING THAT HAS BEEN APPLIED FOR TO SUPPORT THIS RESEARCH**.

Please check all that apply:	
☒	This research is funded Have you received Just In Time (JIT) Notification? ☒ Yes ☐ No

☐	Funding has been requested Have you received Just In Time (JIT) Notification? ☐ Yes ☐ No NOTE: Once the funding has been awarded, submit an amendment to the IRB to add the funding source
☐	Research is not funded

If the research is funded or funding has been requested, it is REQUIRED that you complete the box below. The Sponsor Award # must be included in the box below. If you don't have an award #, please state that in the box below. If you have multiple funding sources, add additional boxes as necessary.

Sponsor Name		National Institute on Alcohol Abuse and Alcoholism (NIAAA)
Title of Grant/Proposal		Interdisciplinary Study of Two Novel Anticonvulsants in Alcoholism
Sponsor Award # **(REQUIRED)*** ***If Award # is pending, put pending. Once the funding has been awarded, submit an amendment to the IRB to add the funding source**		2R01AA015923-06
YES	**NO**	
☒	☐	Is Boston University the Prime Awardee of the grant?
☐	☒	Is Boston University receiving a sub-award? Name of Prime Recipient: N/A

***NOTE:** Provide a copy of the grant application, funding proposal, scope of work, or sub-award agreement. The University is required to verify that all funding proposals and grants have been reviewed by the IRB before funds are awarded.

If this research study is for your dissertation, provide a copy of your prospectus (if available).

SECTION C: CONFLICT OF INTEREST

☒ YES **(REQUIRED)**	I confirm that **all** those responsible for the design, conduct, or reporting of the proposed program, including at minimum, all Senior/key personnel in the grant application, have completed the financial interest disclosure forms, submitted them to the COI office, and completed training as dictated at: http://www.bu.edu/orc/programs-committees/coi/, and as provided under the Boston University Policy on Investigator's Conflicts of Interest.
Of the financial interest disclosure forms submitted, has anyone checked "yes" to any of the questions on either the FIND1 or NONFIND1 form?	

☐ Yes*	☒ No

***If anyone checked "yes" to any of the questions on either the FIND1 or NONFIND1 form, the IRB Director will contact the COI office to obtain the disclosure information.**

SECTION D: TYPE OF REVIEW

For Guidance regarding Type of Review please refer to the following website:
http://www.bu.edu/irb/guidance-and-faqs/submission-guidance/difference-between-exempt-expedited-and-full-board

I. **FULL BOARD** ☒

Please refer to the IRB website for Full Board submission deadlines and meeting dates:
http://www.bu.edu/irb/about-us/meeting-dates/

Note: The IRB will make the final determination on the Type of Review

***Minimal risk** means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Note: Section E of this application, which includes study team members, was removed from this document prior to submission to ClinicalTrials.gov. The names and training dates of study team members are not necessary to evaluate study procedures or methods.

SECTION F: LOCATION OF THE RESEARCH

YES*	NO	
☐	☒	Will this research take place at sites/locations other than Boston University? Note: If the research will take place at Boston University, state the location (Building and Room number): Center for Anxiety and Related Disorders at Boston University, 648 Beacon Street, Boston, MA 02215

*If **YES,** please complete the boxes below

NOTE: You are responsible for obtaining permission/letters of support for research conducted off-site. This may include locations such as schools, workplaces, community organizations, etc. You must submit the letters/documentation of support with this application.

Institution Name and Address (if known)	Describe Involvement (recruiting, consenting, data analysis, etc.) of the site. If the site or the site staff is not involved (engaged)[1] in research procedures, state NONE.	IRB/Ethics Approval/Site Permission Attached? If no[2], explain the plan to obtain this approval.

		If the site is not engaged in the research, you do not need to complete the box.

YES*	NO	
☐	☐	Is the off-site location requesting that the Boston University IRB review the protocol in place of local IRB review? *If **YES**, complete the Single IRB Review Form "Boston University is Institution A": http://www.bu.edu/irb/application-forms/.

YES*	NO	
☐	☐	Is the BU PI the lead investigator **OR** is BU the lead site for this research? **Note: This box only needs to be completed if the off-site location is engaged in the research.**
*If **YES**, provide the following information in this box: ○		

YES*	NO	
☐	☐	Will this research be conducted outside of the United States?*

*If **YES**, complete the International Research Form at http://www.bu.edu/irb/application-forms/

SECTION G: STUDY SUMMARY

Summarize the study in lay language (do not copy from the grant/scope of work/proposal, etc.). This summary should include the research design, purpose, objectives, research question, hypothesis, and any relevant background information. **Note: Do not include a list of citations in this section. Please limit this section to no more than 300 words.**
Alcoholism is the third leading cause of preventable death in the US, accounting for 80,000 deaths annually. Almost 18 million US adults have alcohol use disorder (AUD); however, approved medications for the treatment of AUD has shown limited effectiveness. Zonisamide (ZON), a broad spectrum anticonvulsant, has proven to be more effective than a placebo in reducing alcohol intake in individuals with alcohol dependence. ZON's mechanism of action seems to be quite distinct from currently approved anti-alcoholism medications, which holds promise for treatment of individuals who are not responsive to conventional medications.

However, much remains unknown about ZON's therapeutic mechanisms and ZON's efficacy in treating patients with a diagnosis of AUD.

To fill in these gaps, we will conduct a double-blind randomized controlled study that assesses ZON's treatment mechanisms and effectiveness in reducing alcohol consumption in patients with AUD. Participants will be randomized to one of two conditions: 1) treatment with ZON and a computerized alcohol reduction and medication compliance program called *Take Control* (TC); 2) treatment with a placebo (PLC) and TC. To understand the neurobiology behind ZON's potential therapeutic effects on AUD, fMRI will be acquired at baseline (pre-treatment) and near the end of study treatment and used to compare the brain activity of the ZON+TC versus PLC+TC group while they perform an alcohol and emotional-word Stroop task, as well as an alcohol related cues task.

Compared to the PLC+TC group, we hypothesize that the ZON+TC group will: 1) have significantly greater reductions in alcohol consumption by the end of a 12-week treatment period; 2) show enhanced midbrain-frontal connectivity while performing the Stroop task during an fMRI procedure; and 3) decreased limbic and prefrontal activity during an alcohol cues task.

SECTION H: RESEARCH METHODS AND ACTIVITIES (Check all that apply)

☒	Collection of audio, video, digital, or image recordings
☒	Biological samples → **Complete Biological Samples Form:** http://www.bu.edu/irb/application-forms/ Examples: blood, hair, cheek swab, urine, tears, saliva, etc.
☒	Collection of data that may be sensitive and if disclosed could put subjects at risk for legal or social harms. Examples: Illegal behaviors, HIV status, psychiatric illness, information related to sexual behaviors, etc.
☐	Coordinating Center/Lead Site
☐	Deception
☐	Devices → **Complete Devices Form:** http://www.bu.edu/irb/application-forms/
☒	Drugs → **Complete Drugs Form:** http://www.bu.edu/irb/application-forms/
☐	Ethnographic: The study of people in their own environment through the use of methods such as participant observation and face-to-face interviewing
☐	Focus Groups
☐	Genetics Testing → **Complete Genetics Form:** http://www.bu.edu/irb/application-forms/

☒	MRI
☒	Placebo
☒	Pregnancy Testing
☒	Randomization
☒	Surveys, interviews, questionnaires
☐	Secondary Data Analysis
☐	Other (please describe):

SECTION I: SUBJECT POPULATION

Number of Subjects to be Enrolled:
 	
If you have sub-groups or more than one arm, please separate out these enrollment numbers.
 	
Note: Please account for subjects who may drop out or be withdrawn from the study. Any subject who signs a consent form is considered to be enrolled regardless of whether they complete any study procedures
	Total of 180 Enrolled
	
	Total 100 Randomized:
	- Target Male:Female ratio 55:45
	- Target number per treatment arm:
	  - PLC+TC: 50
	  - ZON+TC: 50
	AUD is far more common in men than in women. Our proposed enrollment gender ratio reflects this difference in prevalence.

Check all categories that apply to your target population:	
☒	Adults
☐	Children (< 18 years of age)
☐	Cognitively-Impaired Adults
☐	Non-English Speaking

☐	Prisoners
☐	BU Employees
☐	BU Students
☐	Wards of the state
☐	Other (please describe):

If Categories other than 'Adult' are checked, describe the additional safeguards that have been put in place to protect that subject population. For Cognitively-Impaired Subjects, provide the rationale for including this population in this research study.
N/A

Eligibility Criteria
Inclusion Criteria: 1) DSM-5 diagnosis of an Alcohol Use Disorder (AUD) 2) Adults ages 21 to 65 years old 3) Expressed desire to stop drinking alcohol completely or to reduce alcohol consumption 4) Reported drinking an average of at least 14 standard drinks per week for males, or 7 for females occurring over a 28-consecutive day period during the 90 day-long time window that preceded the screening session 5) Must be willing to discontinue psychotherapy for substance use disorder (except A.A. session attendance)
Exclusion Criteria (exclusion criteria are the specific criteria which would disqualify an individual from participating in the study, not simply the opposite of the inclusion criteria): Exclusion from Recruitment: 1) Bipolar disorder, schizophrenia, current bulimia/anorexia, dementia, or other substance use disorder, with the exception of nicotine, marijuana, and caffeine. 2) Clear and current suicidal risk. Subjects who are determined by either the medical team or PI to be at moderate to high risk of suicide (as evidenced by reports of the following: persistent thoughts about how one might kill themselves, intentions of acting on thoughts of killing themselves, making plans to kill themselves, making preparations to kill themselves, a suicide attempt in the past year, or 2 or more hospitalizations due to depression within the past 5 years) will be excluded from recruitment. 3) Significant medical problem (e.g. uncontrolled diabetes, cancer, uncontrolled hypertension) or neurological conditions (e.g., seizures, dementia, PD) that in a clinical context would require prioritization for immediate treatment or simultaneous treatment that could interact with the study treatment in unknown ways.

4) Medical contraindication to the use of ZON, as indicated by the FDA Zonisamide medication guide. These include history of significant renal disease or current renal impairment (as indicated by creatinine levels greater than 2.0 mg per dL in females and 2.5 mg per dL in males), kidney stones, liver problems (as indicated by AST/ALT outside of normal limits), and evidence of metabolic acidosis (as indicated by serum or plasma bicarbonate < 22 mmol/L)

   Note: Following randomization, treatment will be discontinued under the authority of the study physician if there is evidence of metabolic acidosis, acute renal injury (>threefold increase in serum creatinine levels from baseline) or a significant change in liver function (AST or ALT > 3X UNL for more than two weeks).

5) History of anticonvulsant-induced rash
6) Currently taking:
   a. acamprosate, naltrexone, topiramate, disulfiram, or benzodiazepines
   b. a medication that is a moderate or major inducer of cytochrome P450 3A4 enzymes
   c. an amphetamine or other psychomotor stimulant
   d. opioids or have been treated chronically with opioids
   e. antipsychotic agents, anticonvulsants, or sedative hypnotics
   f. drugs with "sulfa" moiety (e.g. sulfonamides, sulfonylureas, carbonic anhydrase inhibitors, thiazides, and loop diuretics), except ethacrynic acid
7) Previously received ZON for the treatment of an AUD
8) Known allergy to sulfonamides
9) Implantation of anything containing magnetically sensitive material including metal plates, aneurysm clips, and cardiac pacemakers, stents; history of sheet metal work, claustrophobia
10) Non-English speakers
11) Women who are trying to become pregnant, pregnant women or women who are lactating (breastfeeding)

    Note: Women of child bearing potential (not postmenopausal for at least one year) will only be admitted into this study if they are found to have a negative HCG test during screening and agree to use of an effective means of contraception during the course of the study. Acceptable forms of birth control include one or more of the following: tubal sterilization, partner's vasectomy, intrauterine device, hormonal birth control pills, hormonal skin patch, hormonal vaginal ring, hormonal under-the-skin implants, and hormone shots. Condoms, considered a less reliable method of birth control, must be paired with one of the above reliable forms.

Exclusion from Participating in the Active Treatment:

12) Reduction in the mean number of drinks consumed per week by 50% or more between the phone screen and the in-person screening or report of average drinks per day falling within safe levels of alcohol consumption (i.e. 2 drinks/day for males and 1 drink/day for females by the HHS standard) two weeks prior to screening.

SECTION J: RECRUITMENT

Provide a summary of the recruitment process, including who will recruit, when and where recruitment will occur, and how subjects will be identified

Note: Submit any recruitment materials such as advertisements, brochures, flyers, letters/e-mails, scripts, etc. Please submit these materials as separate documents in either Word or PDF format.

A recruitment team of a 3-4 approved study staff will be responsible for recruiting participants for this study. The recruitment team will use the IRB approved flyers to advertise across multiple recruitment sources. Participants will be recruited via web, radio, newspaper, digital billboard, movie theaters, and Massachusetts Bay Transportation Authority (MBTA) advertisements:

Web Ads:
Online advertisements will be placed on several recruitment platforms (e.g., Facebook, Craigslist).

Radio Ads:
Advertisements will be submitted to local radio stations.

Newspaper Ads:
Advertisements will be put in local area newspapers.

MBTA Ads:
Advertisements will be placed on MBTA trains, buses, and stations.

Digital Billboard Ads:
Digital advertisements (e.g., the study flyer) will be used for recruitment.

Movie Theater Ads:
Advertisements will be played on screens in movie theaters.

The recruitment team will also liaise with colleagues in local area hospitals to make the study known to fellow professionals in the Boston area.

A telephone screening will be conducted to determine the initial eligibility of people who are interested in participating in the study. Potential participants who pass the telephone screening will be identified by their name and phone number, which will be kept in a password-protected database as outlined in Sections M, P, and Q of this application. Following the telephone screening, potential participants will be invited to the Center for Anxiety and Related Disorders at Boston University for an in-clinic screening session to further assess their eligibility for this study. Only those who pass this in-clinic screening will be included in the study and assigned participant numbers, which will be kept separate from any identifiable information.

Timeline:
Recruitment will begin approximately 3 months after obtaining IRB approval, during Year 1 of the study. Approximately 3-4 new participants will be recruited per month. We anticipate recruiting 5 participants in Year 1, 25 participants in Years 2 and 3, 30 participants in year 4, and 15 participants in Year 5.

SECTION K: CONSENT AND ASSENT

NOTE: Please refer to the consent and assent form templates on the IRB website when creating your consent/assent documents. The templates include the required elements of consent and will help to ensure that your consent/assent form meets the requirements of the federal regulations and the BU CRC IRB. The consent templates can be located at: http://www.bu.edu/orc/forms/human-subjects/.

Provide a summary of the consent process, including who will consent, and when and where consent will occur. The summary should include, as appropriate, any waiting period between informing the prospective participant and obtaining consent, that the prospective participant or the legally authorized representative has sufficient opportunity to consider whether to participate, and steps taken to minimize coercion or undue influence.

Note: Submit copies of all consent forms and scripts. Please submit these materials as separate documents in Word format.

Potential participants who meet eligibility criteria for this study following the telephone screening will be invited to the Center for Anxiety and Related Disorders at Boston University for an in-clinic screening to further assess their eligibility for the study. At the screening, participants will be provided an informed consent form to read over. However, the information in the informed consent should not be entirely foreign to them, as they will be given general information about the study at the initial telephone screening. All areas of the consent form will be verbally reviewed with the patient prior to obtaining written consent:
1) The purpose and duration of the study
2) Assessment and treatment procedures
3) Risks and benefits
4) Issues related to confidentiality

Participants will be informed that participation in the study is voluntary and that they have the right to withdraw from the study at any time without penalty.

Before a participant signs the informed consent, study staff will:
1) Answer any questions/concerns raised by the participant; and
2) Measure the participant's blood alcohol concentration (BAC) using a breathalyzer, to ensure that the participant provides written informed consent while sober (BAC=0.00%).

- If the participant's BAC is greater than 0.00% before signing the informed consent, he/she would have to reschedule the screening, which can be a few hours later or another day. If asked to reschedule, the participant will be asked not to drive home and

to make other transportation arrangements. If no one is available to take the participant home, a study staff member may call a taxi or car service. CARD will cover transportation expenses in this circumstance.

After the participant signs the consent form, they will receive a copy of it. Prior to conducting the first neuroimaging procedure at BU CILSE, study staff will also review the imaging procedures with the participant.

The consent form also specifies that data from the present study (#4299) will be combined with data from the supplemental study (#4890E) if participants sign consent for both studies.

For all other study sessions, participants with BAC levels greater than 0.02% will be asked to remain at the center until their levels reach below 0.02, or reschedule if necessary. Again, if a participant is drunk and is asked to reschedule the appointment, the participant will be asked not to drive home and to make other transportation arrangements. If no one is available to take the participant home, a study staff member may call a taxi or car service.

The first study session will be scheduled within 4-weeks after their in-clinic screening. If the one-month window expires before the participant can come in to CARD again, then the in-clinic screening session will have to be repeated to assess the participant's eligibility for the study.

Participants who meet eligibility for the study following the telephone and in-clinic screening will be notified of their eligibility to participate in our study via telephone by our study staff. Potential participants will be told that they can take up to two weeks to notify us of whether they would like to participate in this study or whether they need more time to decide. Potential participants who need more time to decide, will be told that they can contact us again whenever they're ready, as long as the study hasn't ended. However, as noted above, if there has been more than one-month between the screening and the participant's first treatment session, we may have to repeat the screening process to ensure eligibility for enrollment at that point in time.

Indicate the consent and/or assent process and document(s) to be used in this study. Check all that apply

Consent: Adults (≥21 years of age) N/A ☐ **One of the following MUST apply**	
☒	Consent Form/Information Sheet
☐	Verbal Consent (Script) **Note: If written consent will not be obtained, complete the 'Waiver of Written Documentation Consent' box (Box 1) located further down in this section**
☐	Consent will not be obtained **Note: If consent will not be obtained, complete the 'Waiver or Alteration of Consent' box (Box 2) located further down in this section**

Assent of Children (≤ 18 years of age) N/A ☒

One of the following MUST apply	
☐	Assent Form OR Parent Consent Form/Information Sheet (older children may sign the parent consent form along with their parents as long as the consent form is written at the grade level of the subjects)
☐	Verbal Assent (Script)
☐	Assent will not be obtained **If assent will not be obtained, one of the following conditions must exist:** 1. ☐ The capability of some or all of the children is so limited that they cannot reasonably be consulted 2. ☐ The children are too young to provide assent 3. ☐ The intervention or procedure involved in the research holds out the prospect of direct benefit to the health or well-being of the children and is available only in the context of the research 4. ☐ The research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at 45 CFR 46.116(d)*. **(Complete the 'Waiver or Alteration of Consent' box (Box 2) located further down in this section)** ***45 CFR 46.116(d):** **http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html**
Guidance on age requirements for obtaining assent: ● **Parental Permission for minors under 6 years of age** ● **Verbal assent for minors 6-11 years of age** ● **Written assent from minors ages 12-17 (unless verbal consent is approved for the parents/adult subjects**	
Parental Permission **N/A ☒** **One of the following MUST apply**	
☐	Parental Consent Form
☐	Parental Verbal Consent (Script) **Note: If written consent will not be obtained, complete the 'Waiver of Written Documentation of Consent' box (Box 1) located further down in this section**
☐	Parental permission will not be obtained **If parental permission will not be obtained, one of the following conditions must exist:**

	1. ☐ The research protocol is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children). **2.** ☐ The research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at 45 CFR 46.116(d)*. **(Complete the 'Waiver or Alteration of Consent' box (Box 2) located further down in this section)** ***45 CFR 46.116(d):** **http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html**

Consent: Cognitively Impaired Adults (≥18 years of age) N/A ☒ **Describe the process for the consent and/or assent process for enrolling cognitively impaired adult subjects including how capacity to consent is determined and if there is continual assessment of capacity**	
N/A	
Assent will be obtained from: ☐ All Subjects ☐ Some Subjects, specify: ☐ No Subjects	
☐	Consent will be obtained from the subject's Legally Authorized Representative **(REQUIRED)**

CONSENT OF NON-ENGLISH SPEAKING SUBJECTS N/A ☒ **Describe the process for obtaining consent from non-English speaking subjects. List the individual who will serve as the interpreter and his/her qualifications.** **NOTE: A copy of the translated consent along with the Attestation Form for Translation of Consent must be submitted. The Attestation Form can be located at:** http://www.bu.edu/irb/application-forms/
N/A

BOX 1—WAIVER OF WRITTEN DOCUMENTATION OF CONSENT

WAIVER OF WRITTEN DOCUMENTATION OF CONSENT N/A ☒ **Either Criteria 1 or 2 must be met in order to qualify**	**Yes**	**No**
☐ **Criteria 1**		
The research is **NOT** FDA Regulated	☐	☐

The only record linking the subject and the research would be the consent document	☐	☐
The principal risk would be potential harm resulting from a breach of confidentiality	☐	☐
Each subject will be asked whether the subject wants documentation linking the subject to the research and the subject's wishes will govern	☐	☐
A written statement/information sheet will be provided to subjects. If **NO**, provide rationale for not providing this information	☐	☐
☐ **Criteria 2**		
The research is **NOT** FDA Regulated	☐	☐
The research presents no more than minimal risk of harm to subjects	☐	☐
The research involves no procedures for which written consent is normally required outside of the research context	☐	☐
A written statement/information sheet will be provided to subjects. If **NO**, provide rationale for not providing this information	☐	☐

BOX 2—WAIVE OR ALTERATION OF CONSENT

WAIVER OR ALTERATION OF CONSENT N/A ☒ **All of the criteria below must be met in order to qualify**	**Yes**	**No**
The research is **NOT** FDA Regulated	☐	☐
The research involves no more than minimal risk to the subjects	☐	☐
The waiver or alteration will not adversely affect the rights and welfare of the subjects	☐	☐
The research could not practicably be carried out without the waiver or alteration	☐	☐
Whenever appropriate, the subjects will be provided with additional pertinent information after participation. If **NO**, provide rationale for not providing this information:	☐	☐
Provide the justification/rationale for why this study meets the above criteria for waiving or altering consent (REQUIRED):		

SECTION L: STUDY PROCEDURES

In the box below provide a detailed description of the study procedures to be performed (preferably in sequential order). Be sure to specify which procedures are for research purposes versus which procedures are part of standard of care, if applicable. Be sure to include the following information:

- **Methods of data collection**
- **Details regarding research activities/procedures/interventions**
- **Number, frequency, duration and types of subject contacts (visits, phone calls, internet surveys, mailings, etc.)**
- **Time required from each subject**

- **Use of equipment (eye-tracker, treadmill, sensors, etc.). Provide a brief description of equipment that will be used in the study.***

***Note: The IRB may request more information about the equipment (including equipment manuals) and/or request that you submit Appendix C: Device Form.**

Submit copies of all surveys, interview questions, assessments, screening scripts, etc. that will be used during the conduct of this study. Please submit these materials as separate documents in either Word or PDF format.

Note: If subjects will have standard of care procedures in addition to research procedures, clearly state which procedures are standard of care and which are for research purposes only

Overview

Potential participants will complete a telephone and an in-clinic screening to determine eligibility for this study. Eligible participants will be randomized to receive one of two treatment conditions: 1) Zonisamide plus *Take Control* (a computerized alcohol reduction and medication compliance program developed by the National Institute on Alcohol Abuse and Alcoholism (NIAAA)); 2) a placebo plus *Take Control*. For both conditions, participants will receive 12 treatment sessions. Participants will receive medication at each session, and they should have two weeks worth of medication on hand at any given time. Participants will take the medication as prescribed at home. The first 11 treatment sessions will include Take Control. The 12 treatment sessions will be followed by two drug dose taper sessions, and a follow up phone interview immediately following the final session.

Participants will also undergo two scans of less than 2 hours duration, one before they begin study sessions and the second near the end of the study (12th study week and before the medication taper). At the in-clinic screening session, participants will receive a "MRI Information for Research Participants" handout that answers some commonly asked questions about MRI and tells participants what they can expect while undergoing an MRI scan. Both scans will be conducted at BU CILSE. Participants will be screened before each scan session for pregnancy (urine sample, women of childbearing potential only), recent smoking or alcohol use (breathalyzers), and illicit substance use (urine sample). Participants will be asked to complete the Alcohol Urge Questionnaire (AUQ) before and after the scan. Participants will also be asked to complete item #8 from the AUQ before and after the Alcohol Cues Task. Eligible participants will complete a 1-hour 3 Tesla MRI scan involving structural imaging (MRI) and functional imaging (fMRI). The fMRI scans include a resting-state scan (no task involved) a cognitive (Stroop) task, and an alcohol cue reactivity task. The latter two scans involve presentation of visual images to participants while they are in the scanner. No contrast agent or invasive procedures are used. Only personnel trained in working in high magnetic field environments will work on this project. Imaging data will be analyzed on secure networks using only encrypted files. All data obtained will be coded to protect participant privacy and confidentiality.

One month following completion of study treatment (study week 16), participants will be asked to complete a follow-up telephone assessment.

The entire study is estimated to be completed in five years. The first six months to nine months of the project will be dedicated to hiring, training and certifying staff. Recruitment will begin within three months of obtaining IRB approval, during Year 1 of the study. Approximately 3-4 new participants will be recruited per month. We anticipate recruiting a total of 5 participants in Year 1, 25 participants in Years 2 and 3, 30 participants in year 4, and 15 participants in Year 5. The last third of Year 5 will be devoted to completion of data entry and data management procedures, preliminary analyses, and the preparation of manuscripts.

Screening Procedures

I. Telephone Screening

Individuals interested in participating in our study will be evaluated for initial eligibility by a telephone screening lasting 15-20 minutes in duration. This will be conducted by trained study staff that will follow the attached telephone screening script. The Alcohol Use Disorders Identification Test (AUDIT) will be used to help determine eligibility. If initial study eligibility is met, potential participants will be contacted via telephone to schedule a date for an in-clinic screening session. General information about the study will also be provided during this telephone screening.

II. In-clinic Screening

If a participant is eligible to complete the in-clinic screening session following the telephone screening, the in-clinic screening session will be conducted to ensure his/her eligibility for enrollment in the study. This 4-hour session will be conducted at the Center for Anxiety and Related Disorders at Boston University. Screening may be completed in a single visit or over multiple visits (e.g. a hematology or chemistry test needs to be repeated). If the participant completed a screening session for study #4617 within a 1-month window of their scheduled screening session for this study, the results from the duplicate assessments can be transferred to this study without being repeated.

The following procedures will be conducted during the in-clinic screening:

A. Questionnaires/Interviews (see below for detailed descriptions for each measure):

1) Demographic Information
2) Medical History (including information about prior/concomitant medications)
3) Anxiety and Related Disorders Interview Schedule
4) MINI Suicidality
5) Alcohol Timeline Follow-Back (TLFB)
6) Alcohol Dependence Scale (ADS)
7) Obsessive Compulsive Drinking Scale (OCDS) and the Alcohol Urge Questionnaire (AUQ)
8) Clinical Institute Withdrawal Assessment for Alcohol-Alcohol Revised
9) Clinical Global Impression Severity (CGI-S) and Improvement (CGI-I) Scales
10) Depression Anxiety Stress Scales (DASS)
11) Beliefs about Emotions Scale (BES)
12) Multidimensional Experiential Avoidance Questionnaire (MEAQ)
13) Anxiety Sensitivity Index (ASI)
14) Readiness to Change Questionnaire (RTCQ)
15) The Personality Inventory for DSM-5 – Brief Form (PID-5-BF)

16) Personality Assessment Inventory – Borderline Features Scale (PAI-BOR)
17) Inventory of Statements About Self-Injury (ISAS)

B. Biological/Medical Assessments

1) Vital signs (i.e. body temperature, pulse rate, respiration rate, and blood pressure)
2) Weight
3) Physical Exam
4) Urine Drug Screen (A general toxicology screen will be done on-site to identify substances that may be affecting the patient and to ensure subject safety. A list of drugs and/or metabolites analyzed and their corresponding limits of detection is provided in the appendix attached).
5) Ethyl Glucuronide (EtG) tests
6) Urine HCG test (for women of child-bearing potential only)
7) Alcohol Breathalyzer
8) Clinical Laboratory assessments (from blood sample by venipuncture; LAB):
    i. Comprehensive Metabolic Panel
    ii. Bicarbonate
    iii. Liver Function Tests (LFTs): Bilirubin Direct, Bilirubin Total, ALT, AST, Alkaline Phosphate, Protein Total and Albumin
    iv. Gamma-glutamyl transpeptidase (GGT)
    v. Phosphatidylethanol Alcohol Test (PEth)
    vi. LDH
    vii. Creatinine
9) Complete Blood Count with Differential (CBC with diff)
10) Birth Control Assessment (for women of child-bearing potential only)
11) Portland Neurotoxicity Scale (to assess side effects commonly experienced by individuals on antiepileptic drugs)

C. Neurocognitive Assessments (see below for detailed descriptions for each measure)

1) Hopkins Verbal Learning Test (HVLT)
2) Wechsler Adult Intelligence Scale-IV (WAIS-IV): Letter-Number Sequencing and Digit Span
3) WMS-IV Symbol Span
4) Delis-Kaplan Executive Function System (D-KEFS)
5) Letter Fluency and the Wide Range Achievement Test-IV (WRAT-IV)
6) Continuous Performance Test
7) Go/No-Go
8) Balloon Analogue Risk Task
9) Rogers Risk Task
10) Stroop Task
11) Alcohol Cues Task

III. Alcohol Use Related Assessments

A) **Alcohol Dependence Scale (ADS)** - Alcohol dependence will be assessed using the ADS. This 25-item scale has an internal consistency reliability estimate of 0.92 (Skinner & Allen 1982).

B) **Beck Depression Inventory II (BDI-II)** - BDI II will be used to detect depression in participants. The 21-item assessment encompasses all DSM-based depressive symptoms.

The BDI-II has been found to be reliable among medical samples (and it has demonstrated stability among psychiatric (r = 0.92) and student (r = 0.93) samples (Beck et al., 1996).

C) **Alcohol Timeline Follow-Back (TLFB)** - TLFB will be used to estimate participants' daily drinking. In this assessment, participants are presented with a calendar and asked to provide retrospective estimates of their daily alcohol consumption over a specified time period. It takes approximately 25-30 minutes to gather 12 months of data, and approximately 10 minutes to gather 90 days of data. The TLFB has a high test-retest reliability and correlates with other established measures of alcohol use (Sobell & Sobell, 1992).

D) **Clinical Institute Withdrawal Assessment for Alcohol Scale, Revised (CIWA-A**) - CIWA-A will be used to evaluate the severity of withdrawal symptoms. This 10-item scale, shortened from the 15-item CIWA-A scale, retains significant accuracy when compared to the original CIWA-A (r=0.99; Sullivan, Sykora, Schneiderman, Naranjo & Sellers, 1989).

E) **Obsessive Compulsive Drinking Scale (OCDS)** - OCDS will be used to assess alcohol craving and the urge to drink. The OCDS is a 14-item self-report questionnaire developed based on the Yale-Brown Obsessive Compulsive Scale, an interview-based rating scale. It takes approximately 5-10 minutes to complete. The OCDS is significantly correlated with independent measures of alcohol craving and with the amount of alcohol consumed, and has a positive relationship with independent measures of the severity of alcoholism (Anton, Moak, & Latham, 1995).

F) **Alcohol Use Questionnaire (AUQ)** - AUQ will be used to assess alcohol craving and the urge to drink. The AUQ is an 8-item self-report questionnaire, in which participants rate their agreement or disagreement to statements on a Likert-type scale. AUQ scores are strongly correlated to the severity of alcohol dependence and to cognitive preoccupation with alcohol, and decline with prolonged abstinence from alcohol (Bohn, Krahn, Staehler, 1995)

G) **Alcohol Use Disorders Identification Test (AUDIT)** - AUDIT will be used to screen for hazardous and harmful alcohol consumption. The AUDIT is a 10-item questionnaire assessing alcohol consumption and alcohol-related problems. Each response is scored from 0-4, giving a maximum possible score of 40. In a study of participants in 6 countries, the overall sensitivity of the AUDIT for hazardous and harmful alcohol use was 92% and the overall specificity was 94%, when a lower cut-off point of 8 was used (Saunders, Aasland, Babor, De La Fuente & Grant, 1993).

H) **Anxiety and Related Disorders Interview Schedule for DSM-5 (ADIS-5)** – This semi-structured, diagnostic clinical interview focuses on DSM-5 diagnoses of anxiety disorders and their accompanying mood states, somatoform disorders, and substance and alcohol use. The information derived from the interview using the ADIS allows clinicians to determine differential diagnoses and gain a clear understanding of the level and severity of each diagnosis. Principal and additional diagnoses are assigned a clinical severity rating (CSR) on a scale from 0 (no symptoms) to 8 (extremely severe symptoms), with a rating of 4 or above (definitely disturbing/disabling) passing the clinical threshold for DSM diagnostic criteria. Inquiries about suicidal ideation are part of this interview. This measure has demonstrated excellent to acceptable interrater reliability for the anxiety and mood disorders (Brown, Di Nardo, et al., 2001).

I) **MINI Suicidality -** The Mini International Neuropsychiatric Interview (MINI) for Suicidality Disorders Studies (MINI-SD) is a short structured diagnostic interview that appends a series of modules for suicidality disorder phenotypes at the end of the standard MINI (for more information about these suicidality disorders phenotypes, click here). This suicidality disorder module asks about the 12 different suicidality disorders phenotypes described by Sheehan & Giddens (in Suicidality: A Roadmap for Assessment and Treatment). These suicidality disorder phenotypes may have a different age of onset, natural history, clinical course, set of biomarkers, prognosis, and response to treatment (Lecrubier et al., 1997).

J) **Clinical Global Impression Severity (CGI-S) and Improvement Scales (CGI-I;** Guy, 1976**)** – These widely used clinican-rated instruments assess global severity and improvement from pre-treatment baseline on 7-point scales. The CGI-I and CGI-S will be used to define clinical response. The CGI has good reliability and validity (Zaider et al., 2003; Lenze et al., 2009).

K) **Depression Anxiety Stress Scales (DASS;** Lovibond & Lovibond, 1995) – The DASS will be used to measure three related negative emotional states of depression, anxiety, and tension/stress. Participants rate the degree to which a series of statements apply to them on a scale from 0 "Never" to 3 "Almost Always."

L) **Beliefs about Emotions Scale (BES;** Rimes & Chadler, 2009**)** – This measure consists of 12 items and is designed to assess negative beliefs about emotions. Responses are rated on a scale from 0 (totally disagree) to 6 (totally agree). There is empirical support for its validity, reliability, and sensitivity to change.

M) **Multidimensional Experiential Avoidance Questionnaire (MEAQ;** Gamez et al., 2011**)** – The MEAQ is a 62-item scale designed to assess experiential avoidance, which is defined as the tendency to avoid negative internal experience (thoughts, emotions, physical sensations). The measure is comprised of six subscales: behavioral avoidance, distress aversion, procrastination, distraction and suppression, repression and denial, and distress endurance. The measure has exhibited good internal consistency and a high degree of convergent and discriminant validity.

N) **Anxiety Sensitivity Index (ASI;** Reiss et al., 1986**)** – The ASI is a 16-item questionnaire designed to assess fear of anxiety related symptoms. The ASI has a high degree of internal consistency and stable test–retest reliability over a three-year period (Maller & Reiss, 1992).

O) **Readiness to Change Questionnaire (RTCQ;** Rollnick et al., 1992**)** – The RTCQ is based on Prochsaka & DiClemente's (1986) stages of change model that is commonly utilized to resolve addictive tendencies, and is comprised of three stages: precontemplation, contemplation, and action. This questionnaire is therefore commonly used with excessive drinkers to measure their readiness to change. The RTCQ shows good validity and reliability.

P) **The Personality Inventory for DSM-5 – Brief Form (PID-5-BF;** Krueger et al., 2011**)** – The PID-5-BF is a 25-item personality trait assessment scale for adults age 18 or older. This measure assesses five personality trait domains: negative affect, detachment, antagonism, disinhibition, and psychoticism.

Q) **Personality Assessment Inventory – Borderline Features Scale (PAI-BOR;** Morey, 1991**)** – The PAI-BOR is a 24-item measure that is based off a 4-factor model of

borderline personality disorder. These factors are affective instability, identity disturbance, negative relationships, and self-harm (Jackson & Trull, 2001).

R) **Inventory of Statements about Self-Injury (ISAS;** Klonsky & Glenn, 2008**)** – The ISAS was designed to measure the frequency of 12 non-suicidal self-injury (NSSI) behaviors (Section I. Behaviors), as well as assessing 13 functions of NSSI (Section II. Functions). In the present study, we are only utilizing Section I to determine frequency of NSSI behaviors among participants. The ISAS has shown good validity and reliability.

S) **Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q;** Endicott, Nee, Harrison, & Blumenthal, 1993) – The Q-LES-Q is a self-report measure that assesses the degree of satisfaction and enjoyment experienced over the past week. The measure consists of 14 items and assesses satisfaction across the following domains: physical health, mood, work, household activities, social relationships, family relationships, leisure activities, daily functioning, sexual drive and interest, economic status, living situation, physical stability, vision, and overall sense of well-being. The Q-LES-Q has demonstrated high internal consistency and good construct validity (Ritsner et al., 2002).

T) **Work and Social Adjustment Scale (WSAS;** Marks, Connolly, & Hallam, 1973) – The WSAS is a five-item measure asking participants to rate the degree of interference caused by their symptoms in work, home management, private leisure, social leisure, and family relationships. Interference is rated over the past week on a 0 to 8 scale (0 = not at all interfering to 8 = severe interference). The WSAS is a descriptive measure of subjective interference in various domains of living.

IV. Biological Assessments

To assess safety-related issues the following will be obtained from subjects: BAC (with alcohol breathalyzer), adverse events, concomitant medication, urine drug screens, urine pregnancy tests for all females of child bearing potential weeks, birth control assessments, blood chemistries and hematology (CMP, CBC, creatinine, LDH, Bicarbonate, liver panel: Bilirubin Direct, Bilirubin Total, ALT, AST, Protin total and Albumin, and Alkaline Phosphate), body weight, Portland Neurotoxicity Scale, Pill Count Compliance, and GGT (as putative biomarker of alcohol use). We will be collecting 1-2 mL of blood from each participant for both the screening session and session 4. We will be collecting 1.5-3 mL of blood from each participant at the screening session and roughly every other week during the acute treatment phase . Overall, we will be collecting between 6.5-13 mL of blood per participant over the duration of their time in the study. The total amount of blood to be drawn overall for the study will therefore be 650-1,300 mL. The Phosphatidylethanol Alcohol Test (PEth) is a blood test that is used to detect prolonged or heavy alcohol consumption within the past 2-3 weeks. The Ethyl Glucuronide (EtG) test indicates the level of ethanol in urine up to 80 hours after ingestion. Zonisamide (the study drug) will be tested for on study week 8. This test will determine levels of Zonisamide in each participant to ensure that they are metabolizing the medication properly. Assessments will be obtained on the first day of study medication administration in the first treatment week and following the schedule appearing in Table 1, thereafter.

V. Neuropsychological Assessments

Neuropsychological function will be assessed using Hopkins Verbal Learning Test (HVLT), Wechsler Adult Intelligence Scale-IV's (WAIS-IV) Letter-Number Sequencing and Digit Span, WMS-IV Symbol Span, Delis-Kaplan Executive Function System (D-

KEFS) Letter Fluency and the Wide Range Achievement Test-IV (WRAT-IV). Impulsivity will be evaluated using the CPT and the Go/No Go task. Risk taking behaviors will be measured with the Balloon Analog Risk Task and the Rogers Risk task during weeks 1 and 12. Functional and structural images will be acquired during the Stroop test and Alcohol Cues task during fMRI imaging sessions, which will be administered at study weeks 1 and 12.

A. **Hopkins Verbal Learning Test-Revised (HLVT-R;** Brandt & Benedict, 2001**)** – The HVLT-R is a brief assessment of verbal learning and memory (recognition and recall) for individuals 16 years and older. The HVLT-R requires recall of a series of 12 words over three learning trials, free recall after a delay, and a recognition trial. The assessment takes approximately 5-10 minutes, with a 25-minute delay, to complete.
B. **Wide Range Achievement Test-IV (WRAT-IV;** Wilkinson, G. S., & Robertson, G. J., 2006**)** – The WRAT-IV is a norm-referenced test that measures the basic academic skills of word reading, sentence comprehension, spelling, and math computation.
C. **Symbol Span: Wechsler Memory Scale (WMS-IV;** Wechsler, 2009**)** – The WMS-IV is a neuropsychological test designed to measure the various memory functions of a person. The measure includes 7 subsets and A person's performance is reported as five Index Scores: Auditory Memory, Visual Memory, Visual Working Memory, Immediate Memory, and Delayed Memory.
D. **Delis-Kaplan Executive Function System-Letter Fluency (D-KEFS;** Delis, Kaplan, & Kramer, 2001**)** – D-KEFS is a neuropsychological test used to measure a variety of verbal and nonverbal executive functions (reasoning, planning, problem solving, etc.) for both children and adults (ages 8-89 years).
E. **Digit Span and Letter Number Sequencing: Wechsler Adult Intelligence Scale (WAIS-IV;** Weschler, 2008**)** - The WAIS-IV is a neurological test developed to assess cognitive ability in adults. This instruments aids in examining the relationship between intellectual function and memory. The test includes 11 subtests of various formats. Approximately 60 to 90 minutes is required for completion.
F. **Continuous Performance Test (CPT)** - The CPT measures brain damage. The CPT includes two attention tasks, the second one being more difficult than the first. In the first task, participants are presented a series of 31 letters, one letter by one letter, and are asked to click on a button when the letter X appears. In the second task, participants are presented with a series of 31 letters, and are instructed to click on the button only when the letter X appears directly after the letter A appears. The letters appear at approximately 0.92s intervals, and responses are scored correctly if the button is clicked within 0.69s after the letter appears. In both tasks, participants received 2 trial runs before being given either a 5-minute test or a 10-minute test. Participants are scored in two ways, by dividing the number of correct responses given by the number of correct responses possible, and by dividing the number of correct responses given by the total number of responses given (how many times s/he clicked the button (Rosvold et al, 1956).
G. **Go/No Go task** - In this online task, participants are first presented with a go or a no-go cue, and then presented with a go or no-go target. Participants are instructed to respond to a go target by clicking on a button, and not to respond to a no-go target. The cues have a high probability of signaling a correct target (valid cues), and a low probability of signaling an incorrect target (invalid cues). Incorrect responses to the no-go target are

used to assess inhibitory control, which reflect impulse control. A test includes 250 trials and takes approximately 15 minutes to complete (Fillmore 2003**)** (http://www.impulsivity.org/measurement/cued_Go_NoGo).

H. **Balloon Analogue Risk Task** - In this online task, participants are presented with a balloon. Clicking a button will pump the balloon, causing it to inflate and the participant to be awarded a certain amount of money. This happens until a threshold when a pump will cause the balloon to explode and all money would be lost. At any point in time, participants can choose between pumping the balloon further and risking it exploding, or not pumping the balloon and collecting the money they have already earned. 90 trials are conducted and the average number of pumps delivered are used to measure levels of risk-taking (Lejuez et al., 2002).

I. **Rogers Risk Task** - In this online task, participants are assigned a certain number of points to begin with and are instructed to make decisions that will increase their total score. They are then presented with tasks that involve gambling their points. For example, they are presented with red and blue boxes and told that one box contains a yellow ticket. If they choose a red box that has a yellow ticket, they will gain 30 points, but if they choose a red box that does not have the yellow ticket, they will lose 30 points. If they choose a blue box that has the yellow ticket, they will gain 70 point, but if they choose a blue box that does not have the yellow ticket, they will lose 70 points. Participants' speed of decision-making and choice are used to measure their willingness to take risks (Rogers, 1999).

J. **Stroop Task** - The Stroop tasks will be shown to subjects using a behavioral experiment software called E-Prime. During the task, neutral words and alcohol-related words will be projected on the screen in different color fonts. Participants will be instructed to press a color button on a button box that correspond to the color of the font of the word on the screen. There are four colors on the button box, which are red, blue, yellow, and green. Four blocks of stimuli all of which include alcohol related (e.g. bar, vodka) words, color (e.g. blue, green) words and neutral words (e.g. years, minute). There is a practice run of the stroop task to get participants used to using the button box, which takes about 2 minutes. Then there goes the actual stroop task, which takes about 7 minutes.

K. **Alcohol Cues Task** - The Alcohol Cues Task entails the presentation of five sets of images, with both neutral and alcohol-related images. These cues will be shown to subjects using a behavioral experiment software called E-Prime. Subjects will be instructed to look at the images on the screen in the MRI scanner. There are five runs of the task. In the beginning of each run, participant will see "Get Ready" on the screen. There are 22 pictures in each run. In each run, participant will see a fixation cross for a varied amount of time from 6000 milliseconds to 14000 milliseconds followed by the presentation of an alcohol image or a neutral image for 4000 milliseconds. In each run there are 2 images with animals in it. Participants are instructed to press a red button on a button box each time they see an animal that is not a human on the screen. The entire task takes approximately 40 minutes to complete.

Table 1. *Schedule for assessments and interventions for the Screening Period, Treatment Weeks 1-12, Dose Taper weeks 13 and 14, Follow-Up week 16.*

Assessments for week 1 occur prior to the start of treatments.
Cmeds/AE=Concomitant Medications /Adverse Events, CIWA-AR=Clinical Institute Withdrawal Assessment for Alcohol Use

Assessment	SC	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Medical /Biological Assessment																	
Medical History	X																X
Birth Control	X	X			X				X				X				
Vitals/Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
BAC	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Pregnancy Test HCG	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Urine Drug Screen	X	X			X				X				X				
Urine EtG		X											X				
Blood Lab Tests	X	X		X	X		X		X		X		X				
Pill Count			X	X	X	X	X	X	X	X	X	X	X		X		
Portland Neurotoxicity Scale		X	X		X		X		X				X				
CMeds/AE	X	X	X	X	X	X	X	X	X	X	X	X	X		X		
CIWA-AR	X	X	X		X		X		X				X		X		
Zonisamide									X								
Clinician Interviews																	
ADIS-5	X														X		
MINI Suicidality	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
TLFB	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Questionnaires																	
Demographic	X																
BDI-II		X											X				
ADS	X																
OCDS		X			X				X				X				X
AUQ		X			X				X				X				X
CGI-S & CGI-I		X	X	X	X	X	X	X	X	X	X	X	X	X	X		
DASS	X												X				
BES	X												X				
MEAQ	X												X				

ASI	X											X				
RTCQ	X											X				
PID-5-BF	X											X				
PAI-BOR	X											X				
ISAS	X															
Q-LES-Q	X											X				
WSAS	X											X				
Neurocognitive																
WRAT-IV		X										X				
D-KEFS		X										X				
WMS-III Symbol Span		X										X				
WAIS Digit Span & Letter Number Sequencing		X										X				
HVLT		X										X				
CPT		X										X				
Go/No-Go		X										X				
BART		X										X				
Rogers Risk Task		X										X				
Imaging Session																
Stroop Task		X										X				
Alcohol Cues Task		X										X				
Intervention																
Medication Sessions		X	X	X	X	X	X	X	X	X	X	X	X	X		
Take Control		X	X	X	X	X	X	X	X	X	X					

Randomization

Participants who continue to be eligible for the study following the in-clinic screening will be randomized to one of two treatment conditions: 1) Zonisimaide and *Take Control* (TC) computerized program; 2) a placebo and TC. An adaptive randomization will be used, where gender, heavy drinking, handedness, and smoking status will be variable levels.

Study Sessions

All participants will be required to have a BAC of 0.02% or less to complete study sessions. Following screening, subjects will receive either ZON or drug placebo (and TC) for 12 weeks, followed by a 2 week taper off medication. Most weekly study sessions will be approximately 45-60 minutes in duration. Session 1 will be approximately 3 hours, while session 12 will be approximately 2 hours in duration. Follow-up data will be collected at the end of the drug taper (week 14) and then again two weeks later (at study week 16). We will allow up to four weeks for completion of this week 16 follow-up phone assessment. Therefore, participants will have a 20-

week window to complete all study procedures before their participation is considered complete. Assessments that will be obtained during the course of the study are shown in Table 1.

We will ask participants to schedule a standing appointment for each week of the 14-week study, with each appointment scheduled 7 days apart. However, we will allow participants to reschedule an appointment between 7-10 days after their previous session if necessary. The length of time until the subsequent session would then be modified in an attempt to re-establish the original schedule. If a session is scheduled beyond this 7-10 day window (i.e., days 11-14), the session will still be conducted but will be considered the next session. The prior session will be considered "missed." Participants who miss two consecutive sessions during any 14-day period will be tapered off the study medication and withdrawn from the trial for safety reasons. Participants who are withdrawn will be asked to return weekly to complete the medication taper.

Interventions:
Medication treatment (Zonisamide vs. placebo) and Take Control will be administered using a double-blind procedure to subjects during scheduled visits over a period of 14 weeks.

I. Zonisamide (ZON):
All medication records and dispensing will be managed by the nurse administrator. Pills will match the placebo. Based on previous findings (Knapp et al., 2015), ZON dose of 400 mg daily will be used as the target maintenance dose in this study. A final target maintenance ZON dose of 400 mg will be given after a seven week long titration period. Based on the known half-life of ZON, it is expected that it will take approximately 2 weeks to reach steady state for a given dose of ZON. Participants will begin the medication taper schedule at week 12. According to this schedule, participants will be reduced to a dosage of 300 mg for the entirety of week 12, reduced to a dosage of 200 mg for the first three days of week 13, reduced to a dosage of 100 mg for the next three days, and then the participant will be done taking the medication. Therefore, the participant will be completely off of the medication by the day before the week 14 session. Pill placebo will be administered according to the Zonisamide schedule.

Dosage escalation and maintenance regimen

Week 1 + 2	Week 3 + 4	Week 5 + 6	Week 7 – 12 Maintenance
100 mg/day (once a day)	200 mg/day (once a day)	300 mg/day (once a day)	400 mg/day (once a day or two divided doses)

Dosing will be modified, if needed, to adjust for subject tolerance of drug dosing or to reduce adverse drug effects. Verification of medication adherence compliance will entail comparing the patient's self-report against the number of pills remaining in the medication vial. Pill counts will be conducted at each visit to encourage medication adherence.

Medication will be dispensed according to a two-week dosing schedule by medical personnel at weekly study sessions. Participants will be supplied with two medication bottles at each study visit, containing between 4-7 days of medication in one bottle and 7 days of medication in the other. At any given time, participants may have between 10-17 days of medication in two or three medication bottles. Patients will self-administer medications daily, as directed.

Patients who have to discontinue medication will be permitted to remain in the study and participate in study assessments and will be allowed to continue to receive TC. Participants who are withdrawn from the study will be tapered off the medication. Any unused medication can be returned during the taper period, either in person or by a postage-paid return envelope we will supply them with.

II. Take Control:

Subjects in all groups will be asked to view *Take Control* (TC)—a novel computerized alcohol reduction and medication compliance program derived from the National Institute on Alcohol Abuse and Alcoholism's (NIAAA's) self-help approach, *Rethinking Drinking*. *Take Control* consists of 11 motivational and educational modules, which will take around 1.5 hours in total.

All subjects will receive standard medication management during each visit, with additional adherence counseling, when needed.

Assessments:

I. Medical Assessments:

a. Vital signs (i.e. body temperature, pulse rate, respiration rate, and blood pressure)
b. Weight
c. Urine Drug Screen (A general toxicology screen will be done to identify substances that may be affecting the patient and to ensure subject safety. A list of drugs and/or metabolites analyzed and their corresponding limits of detection is provided in the appendix attached).
d. Urine HCG test (for women of child-bearing potential only)
e. Alcohol Breathalyzer
f. Clinical Laboratory assessments (from blood sample by venipuncture):
    1. Comprehensive Metabolic Panel
    2. Bicarbonate
    3. Liver Function Tests (LFTs)
    4. Gamma-glutamyl transpeptidase (GGT)
    5. Complete Blood Count with Differential (CBC with diff)
g. Birth Control Assessment (for women of child-bearing potential only)

II. Clinical Administered Assessments/Self-Report Measures:

Clinician administered assessments and self-report measures will be completed at various treatment sessions. See Table 1 for detailed information on the timing and assessment schedule.

Post-Treatment Period

Follow-up assessments will be obtained at the end of the final week of drug treatment, i.e. study week 14, and a phone interview at study week 16. During the follow-up interview, the subject will provide data for the TLFB and for reports on adverse events (AEs), and concomitant medications.

Digital Recordings

Recordings of the clinical interview portion of the in-clinic screening session will be digitally recorded to ensure adherence to the screening protocol and inter-rater reliability for the administration of the clinical assessments. In addition, digital recordings will be collected during the assessments occurring throughout treatment. In particular, the neuropsychological evaluation portion will be recorded to determine adherence and reliability of the study procedures.

The digital recordings will be stored using a highly secure, password protected drive. We will label these files with a code. The digital recordings will be destroyed along with the other study data, after 7 years following the end of the study.

Data Analysis

1. Demonstrate that ZON will attenuate changes resulting from performance on alcohol-word and negative-word Stroop tasks in the activity of frontal-parietal and midbrain regions and the connectivity to networks associated with these regions in AUD subjects. Our working hypothesis is that midbrain activity will be lower in ZON treated subjects than in placebo subjects following performance on alcohol and negative emotion Stroop task, which will occur in association with enhanced mid-brain-frontal connectivity and increased synchrony.

Fixed effects models will be used to analyze data for brain activation in regions of interest, with treatment group as a between group factor and Stroop task type and order of stimuli presentation will be within subject factors. Regions of interest will include parahippocampal gyri, midbrain substantia nigra and red nucleus, dorso-lateral prefrontal cortex, and cerebellum.

Connectivity will be assessed using the Free Surfer analysis described below. Seeds will be used for the dorsolateral prefrontal cortex and the midbrain (substantia nigra) following Muller-Oehring et al. (2013).

2. Demonstrate that ZON administration attenuates the enhanced regional brain activity and craving- induced by exposure to alcohol related cues in AUD subjects. Our hypothesis is that exposure to alcohol-related cues will increase brain activity in select limbic and prefrontal areas to a lesser degree in ZON as compared to placebo treated AUD subjects.

Fixed effects models will be used to analyze data for brain activation in regions of interest, with treatment group as a between group factor and stimulus type and order of stimuli presentation was within subject factors. Regions of interest, based on the meta-analysis of Schacht et al. (2013), will include the ventral striatum, medial prefrontal cortex, and the anterior cingulate cortex.

3. Demonstrate that the ZON induced changes in brain activity are predictive of reduced ethanol consumption.

Logistic regression analysis will be used to evaluate zonisamide-induced decreases in the BOLD response in the ventral striatum and the medial prefrontal cortex as predictors of complete abstinence or reduction to safe drinking levels (defined as consumption of no more than more than 2 standard drinks per day) during study weeks 10 to 12.

4. Replicate the finding that ZON will reduce alcohol consumption in AUD subjects.
Our working hypothesis is that the drinks consumed per day and percent days drinking will be significantly lower in AUD subjects receiving ZON than in those treated with placebo. Drinking measures derived from the TLFB data will include the percent days drinking, the number of drinks consumed per day, and the percent days heavy drinking. Heavy drinking will be defined as 4 or more drinks per day for women and 5 or more drinks per day for men. Alcohol consumption measures will be analyzed using repeated measures mixed models analysis using SAS PROC MIXED (ver 9.3, SAS Institute, Cary, NC) with baseline values for these measures used as covariates. Comparisons will be made for data obtained for the 12 week treatment period for the two conditions.

5. Demonstrate that ZON administration will reduce impulsive and risk taking behaviors.
Our working hypothesis is that the ZON will decrease risk taking behavior as assessed using the Rogers Risk Task and the Balloon Analog Risk Task and impulsivity as measured using the Go/NoGo and the Continuous Performance Test (CPT).

Repeated measures mixed models analysis will be used to analyze data obtained for pre-randomization and week 12 data for the Rogers Risk Task, the Balloon Analog Risk Task, the Go/NoGoTask, the CPT, and Go/No Go. Model generated group least square means values for week 12 will be compared using student t-tests.

Matthew W. Gallagher will provide statistical consultation. He will not have access to identifiable information and will not have any contact with study participants.

<u>Imaging Acquisition and Processing:</u>

BOLD RESPONSE- Image Acquisition
Functional images will be acquired on a Siemens Prisma 3T scanner using a 64-channel phased array headcoil. Blood oxygenation level-dependent (BOLD) contrast will be measured using a gradient echo-planar T2* weighted imaging sequence (TR = 2000 ms, TE = 28 ms, EPI factor = 47). The images will contain 36 axial slices and each slice will be 64 x 64 pixels. The voxel size will be 3 mm x 3 mm x 3 mm. T1-weighted structural images will also be obtained in the same session along with a brief EPI sequence acquired with oblique slices to ensure the integrity of right and left throughout image format conversion. All images will be converted to FSL-NIfTI format prior to our model-based analysis and the integrity of left and right for each subject will be confirmed.

Analysis
The images will be analyzed using FSL 4.1.1 with the FMRI Expert Analysis Tool (FEAT) v5.98 (Smith et al., 2004; Jenkinson et al., 2012). FSL's general linear model will be used to

model each subject's BOLD response to each explanatory variable (EV). The fMRI data will be co-registered to MNI space and regions of significant activation will be determined through using the Harvard-Oxford Structural Atlas included with FSL (Makris et al., 2006; Frazier et al., 2005; Desikan et al., 2006; Goldstein et al., 2007). In second and third level analyses, we will use cluster thresholding with a Z threshold of 2.3 and a cluster p threshold of 0.05. We will use a fixed effects model for these analyses. All analyses of the fMRI data will include active task > control condition contrasts as well as control > active task contrasts as a reality check.

CONNECTIVITY

FreeSurfer Analysis

All of the subject's MRI scans will be processed using FreeSurfer. FreeSurfer is a software application developed by the Martinos Center for Biomedical Imaging by the Laboratory for Computational Neuroimaging (*FreeSurfer Wiki*, 2014). FreeSurfer's package of tools for visualization of structural and functional brain data will be used to analyze this data set. The FreeSurfer 'recon-all' tool, which is a fully automated structural imaging stream that runs 30 steps will be used to execute all of the volumes and surface processing pipelines (*FreeSurfer Wiki*, 2014). The FreeSurfer recon-all pipeline contains steps for: motion correction, intensity normalization, talairach transformation, skull stripping, segmentation of the cortex, subcortex and white matter, to generate surfaces and create spherical and flattened representations. There are three automated atlases in FreeSurfer's recon-all script for cortical segmentation and labeling: Desikan-Killiany, Destrieux and DKT40 atlas. In this study we will use the Desikan-Killiany atlas.

The Freesurfer GUI Freeview will be used to model the subject's brain scans in 2 dimensional and 3 dimensional space in order to inspect the recon-all processing output. The topical defects that occur and need to be fixed with Freeview are white matter and gray matter subcortical segmentation, and the corresponding processing step in the recon-all pipeline is re-run for correction.

Resting state DICOM scans will be converted to Nifti files with MRIcron's *dcm2nii* in order to be processed in The Functional Connectivity Toolbox 2014 (CONN). CONN is a Matlab-based cross-platform software that will be used to compute, analyze the functional connectivity of fMRI (Whitfield-Grabrielli and Nieto-Castanon, 2012). The CONN toolbox uses Matlab version 2012 and SPM8 to process the resting-state fMRI scans into ROI-to-ROI connectivity matrices, test hypotheses and visualize data (Whitfield-Grabrielli and Nieto-Castanon, 2012). CONN uses a seed-driven RSFC analysis strategy, where the pearson's correlation coefficient is calculated between the seed time course and the time course of all other voxels (Whitfield-Grabrielli and Nieto-Castanon, 2012). The correlation coefficients are converted to normally distributed scores using Fisher's transformation to allow for second-level General Linear Model analysis (Whitfield-Grabrielli and Nieto-Castanon, 2012). The correlation maps depend on the specific location of the seed so that functionally and anatomically heterogenous ROI are dissociated in order to delineate functional anatomy in the brain by sharp transitions in correlation patterns that signal functional boundaries across the cortex (Whitfield-Grabrielli and Nieto-Castanon, 2012).

The subject's processed MPRAGE scans are imported into CONN, and used alongside the resting state scans. CONN uses CompCor strategy for spatial and temporal preprocessing to

define and remove confounds in the BOLD signal to prevent the impact of physiological noise factors and motion in the data (Behzadi et al., 2007). The CompCor strategy is unique because it is more flexible in its characterization of noise (Behzadi et al., 2007). CompCor models the influence of noise as a voxel-specific linear combination of multiple empirically estimated noise sources, which are estimated from the variability in the BOLD responses within noise ROIs (Behzadi et al., 2007). This is important for the removal of fMRI noise because cardiac and respiratory effects do not have a common spatial distribution in their effects. The removal of this richer characterization of the range of voxel-specific noise effects and additional movement along with temporal filtering and windowing the BOLD signal at each voxel protects against confounds in RS-FC without introducting artifactual biases in connectivity measures.

CONN creates subject-specific ROI files and registers them to the subject space. 99 ROIs will be used as the seeds of interest for whole-brain subject-specific ROI-ROI connectivity analyses.

Power Analysis: Power analysis for drinks consumed per day during the last three weeks of treatment were determined using data for the placebo and zonisamide groups from our previous study (Knapp et al., 2015). A power value of 0.9 was found for a group size of 40, with alpha=0.05, and with an effect size of 0.74. In our previous study of ZON approximately 20% of subjects dropped out before week 12 of the study. Consequently, we will randomize 50 subjects per group to reach a target of 40 subjects in week 12 of the present study. Based on data reported by Rubio et al. (2009) for errors of commission on the CPT, a measure of impulsivity, a power value of 0.97 would be obtained for an alpha value of 0.05 for a group size of 40. Based on the findings of Myrick et al., (2008) for the difference between the activation of the ventral striatum for placebo and naltrexone groups a power of 0.88 was seen for an effect size of 0.7 for a group size of 40.

Safety Analysis: For safety, subjects will be assessed as having had any serious adverse event during the treatment period or not, and additional analyses will be done by separate types of adverse events. Tolerability will be assessed as a subject being able to continue on the study drug for the entire study duration without requiring discontinuation. The safety and tolerability of the study medications will be first assessed using contingency tables and chi-square tests. Fisher's exact test will be employed for rare adverse events. The chi-square analysis will be followed by logistic regression analyses, adjusting for the stratification factor. Time to drug discontinuation for serious adverse events and time to withdrawal from the study for any reason will be assessed using Kaplan-Meier survival curves and compared between study treatments using the log rank test. Poisson regression will be used to evaluate the rate of serious adverse events by arm stratified by the time periods of dosage escalation, dosage maintenance, and dosage taper.

Covid-19 Protocols: Since the beginning of the pandemic in April, 2019 we have modified our protocol in order to minimize the risk of participants contracting and/or spreading Covid-19. Study procedures are no longer taking place at CARD. Instead, all study sessions are being conducted remotely via a HIPAA-compliant Zoom platform. There is no physical contact between study personnel and study participants. The following changes have been made to the protocol described above to preserve study integrity while also reducing participant risk:

- No study procedures, including medical procedures, take place at CARD.
- Participants are required to visit Quest Diagnostic Centers upon screening and roughly every other week during the acute treatment phase. During these sessions participants have their blood drawn and their urine sampled.
- Prior to their screening sessions, participants are mailed a breathalyzer that is used to measure their blood alcohol content, as well as a blood pressure cuff which they use at every visit. They use the breathalyzer prior to signing consent and prior to every study session. The breathalyzer reading is shown to study personnel via Zoom.

SECTION M: RISKS

Describe any expected risks to subjects. Consider physical, psychological, social, political, legal, economic, or other risks that are related to the study.

The primary risks involved in this study are those associated with alcohol withdrawal, and the use of ZON as monotherapy. The primary risks to the patient are deterioration of symptoms if subjects are receiving placebo.

Alcohol Withdrawal

Subjects may experience symptoms associated with alcohol withdrawal. Approximately 1.2% (1 out of 85) of subjects in a recent alcohol dependence treatment study (Interdisciplinary Study of Two Novel Anticonvulsants in Alcoholism, 2013), in which anticonvulsants were being evaluated, had experienced withdrawal symptoms severe enough to require in-patient detoxification. Subjects requiring treatment for withdrawal in the present study will be referred for detoxification at other treatment sites and will not be readmitted into this study. The risk of

severe withdrawal is minimized by the requirement that subjects must be sober when they provide informed consent.

Persons drinking at the level required for entry may experience moderate to severe withdrawal symptoms if they stop drinking abruptly or if they attempt to taper their drinking, including shakes or tremors, chills, nausea and/or vomiting, agitation, sleeplessness, seizures, and delirium (disorientation, altered sensorium, and hallucinations).

Potential side effects of Zonisamide

The most common adverse reactions associated with ZON administration in seizure patients include: somnolence (17%), dizziness (13%), and anorexia (13%). Less common adverse effects include: agitation (9%), irritability (9%), depression (6%), speech abnormalities (5%), confusion (6%), difficulty with concentration (6%), difficulty with memory (6%), fatigue (8%), insomnia (6%), nausea (9%), and headache (10%). In some patients, ZON can contribute to problems with concentration, attention, memory, mood, thinking, speech, or language. ZON may produce urinary lithiasis [Kubota et al., 2000]. The incidence of this is reported to be 1.9% in clinical trials in the United States and 0.2% in Japanese clinical trials. The risk of urinary stone formation may be higher in dehydrated and bedridden patients.

Acute myopia and secondary angle closure glaucoma have been reported in patients receiving ZON. Symptoms in reported cases have included acute onset of decreased visual acuity and/or ocular pain. Symptoms typically occur within one month after initiating ZON therapy.

Zonisimaide can cause metabolic acidosis, which results in high levels of acid in the body. If untreated, metabolic acidosis can lead to kidney stones or soft bones. Kidney stones can also occur while taking ZON in the absence of metabolic acidosis. The rate of occurrence for kidney stones is 28.7 per 1000 patient-years of exposure in the first six months, 62.6 per 1000 patient-years of exposure between 6 and 12 months, and 24.3 per 1000 patient years of exposure after 12 months of use (Food & Drug Administration (FDA), 2020).

Other rare but potentially life threatening side effects include allergic reactions that may affect different parts of the body, cause blood cell changes such as reduced white blood cells counts, or lead to a serious skin rash such as Stevens-Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN). SJS and TEN are two forms of the same life-threatening skin disease that cause rash, skin peeling, and sores on the mucous membranes.

Finally, psychotic episodes have occurred in patients being treated with ZON with the risk being higher in younger patients (Miyamoto et al., 2000). One case of ZON-induced systemic lupus erythematosus has been reported in a child being treated with ZON and the anticonvulsant agent ethosuximide (Mutoh et al., 2001). This child improved after discontinuation of ZON. Renal tubular acidosis associated with ZON has been reported (Inoue et al., 2000; Mirza et al., 2011). This problem is reversed with the discontinuation of ZON administration.

Risks of MRI

There are risks associated with undergoing MRI assessments for people with contraindications to MRI scans (e.g., those with pacemakers or other metallic implants, with a history of sheet metal work, women who are pregnant, and people with claustrophobia. Additionally, subjects may be at risk if unauthorized metallic items, which can fly into the magnet, are brought into the scan room.

Risks of phlebotomy
Risks associated with having blood drawn are slight, but may include: excessive bleeding, fainting or feeling lightheaded, hematoma (blood accumulating under the skin) and infection (a slight risk any time the skin is broken). The likelihood of these risks will be minimized by having blood drawn by a trained phlebotomist, nurse, or physician.

Risks related to disclosing personal information:
Subjects may experience discomfort and anxiety when answering questionnaires and when responding to tests evaluating their mood states and alcohol cravings. During assessment, subjects may experience some discomfort or anxiety from discussion of personal information. In addition, subjects may experience some interference with daily activities due to scheduling of assessment and treatment sessions.
Subjects may find questions about their history distressing or uncomfortable. They may feel nervous when answering psychological questions.

Risk of loss of confidentiality
The investigator and his staff will take every precaution to maintain subject confidentiality; however, there is always the possibility that confidentiality may be broken.

Describe the plan to minimize risks. Include in the description the availability of any medical or psychological resources.

The overriding concern of the investigators is the safety of the subjects who participate in this study. Participants will be informed about all risks and told that they may withdraw from the study at any time and may refuse to complete any treatment procedures. Study personnel will be monitoring the patients' clinical condition carefully and constantly and will withdraw patients from the study if their clinical condition warrants.

In order to minimize risks, patients with prominent suicidal ideation (assessed as part of the clinical interviews, including the MINI, and with the self-monitoring forms) will be excluded. Treatment will be closely monitored by the PI in weekly supervision meetings. The MINI Suicidality interview will be used to measure participants' suicidality scores during the screening session, and will be administered to measure suicidality at every session during clinic visits, and at follow up by phone. A significant increase in depression is defined by scoring at least 10 points higher than baseline on the BDI-II, and getting a total scoring of at least 17. Clinical judgement by the study physician or associated licensed psychologist will be used to decide whether a suicidal potential has developed. The clinical case of any patient showing significant increases in depression symptoms or developing suicidal potential will be reviewed by the PI. These patients will be asked to withdraw from the protocol and given or referred to immediate clinical intervention. Appropriate protective factors and safety plan will be followed based on the attached document, if the patient reports suicidal thoughts with high levels of intent

with a specific plan/access, or regardless of plan. Additionally, all patients will be clearly informed of their right to withdraw from the study at any point.

Alcohol Withdrawal

In order to minimize the possibility of hospitalization during withdrawal, subjects who meet eligibility criteria at the first screening visit will be told that it is unsafe to stop drinking abruptly. They will be educated with respect to symptoms of early and late withdrawal, and be advised to contact the clinic in the event that medically-managed withdrawal may be indicated. A study physician is available by telephone at all times to advise patients concerning withdrawal symptoms or other matters concerning the study. If it is suspected at any time during the study that the subject may be going through withdrawal after a period of heavy drinking and is experiencing withdrawal symptoms that greater than a 10 on the CIWA-AR scale, they will be advised to come to the clinical site for further evaluation, or go directly to an emergency department.

The blind for medication will be kept by the PI and can be accessed 24 hours in case of emergency.

Zonisamide

In order to minimize potential side effects of ZON, subjects who can be expected to experience any severe side effects will be excluded from the study by the screening procedures. Laboratory values for relevant blood chemistry will be collected at screening and approximately every two weeks during the acute treatment period. Treatment will be discontinued under the authority of the study physician if there is evidence of metabolic acidosis, acute renal injury (>threefold increase in serum creatinine levels from baseline) or a significant change in liver function (AST or ALT > 3X UNL for more than two weeks). A physician will be available on-call at all times to answer medical questions or to assess subjects for potential medical problems or untoward effects due to their participation in the study. In addition, participants will carry an alert card on their person, explaining the effects of the study medications and a 24-hour phone number to call, in case of emergency. Should a subject experience a severe adverse drug reaction, they will receive an evaluation by a physician. Symptoms may become severe enough to require hospitalization in order to be managed safely and assistance with withdrawal will be readily available during all phases of treatment. If management of withdrawal is necessary, subjects will be evaluated and treated at a local emergency facility. However, no special provision will be made for compensation or for payment for treatment solely because of their participation in this study.

The dosage regimen selected for the administration of Zonisamide in this study (target maintenance dose of 400 mg per day) was selected based on our experience with this drug in treating alcohol-dependent subjects. The Take Control alcohol reduction and medication compliance program has been tested in one of our completed multisite clinical trial and is currently being used in a second NIAAA sponsored multisite medication trial.

MRI

These risks are minimized by following standard guidelines including staff training on what materials are not allowed in the scanner suite. The proposed neuroimaging procedures are done

on a routine basis but only by qualified personnel who have undergone MRI safety certification. Accordingly, only trained and certified personnel are eligible to assist in imaging procedures. In addition, we utilize an extensive screening protocol to ensure that persons with metallic objects (including pacemakers) in their body are excluded from participation. This includes careful screening of welders or individuals who work with sheet metal who might have very small metal fragments in their eyes. Participants must not only have no metal appliances in their body but must also have no history of claustrophobia, and also be able to lay flat in the scanner for an hour. To date, we have not observed any adverse reactions to MRI imaging other than mild claustrophobia that resolved by immediate removal of these individuals from the MRI scanner.

Disclosing Personal Information

A member of the research team will be with the subject at all times during the study sessions and will be able to answer questions concerning procedures and psychological tests. Subjects do not need to answer questions if they do not want to.

Confidentiality

In order to maintain confidentiality, data with participants' identification information will be stored in an encrypted volume on a server within a secure data center created by BU CAS Information Technology, which is only accessible to study personnel. Access is controlled via Active Directory groups, utilizing Kerberos authentication for individual access. Access audits will be scheduled to keep the list up to date, and to remove users that no longer require access to this dataset. Other study data, without any identifiable information of the participants will be stored online in Google sheets, under a Google account specially created for this study, which is only accessible to study personnel.

A certificate of confidentiality has been obtained for this study from NIAAA, to further protect the privacy of subjects' records.

Confidentiality will be maintained by keeping research data from this study in a secure file cabinet, separate from any clinical data about the subjects. Particular attention is drawn to the regulations promulgated by the FDA under the Freedom of Information Act providing, in part, that proprietary information furnished to clinical investigators and Institutional Review Boards will be kept confidential by the FDA only if maintained in confidence by the clinical investigator and IRB. To maintain subject confidentiality, all laboratory specimens, CRFs, reports and other records will be identified by a coded study subject number only. Research and clinical records will be stored in a locked cabinet. Only research staff will have access to the records. Subject information will not be released without written permission, except as necessary for monitoring by the FDA and the IRB. Subjects will be interviewed in private. Data analysis will be performed on coded data and will not refer to the participants' names. Access to data will be available only to investigators involved in this study.

SECTION N: BENEFITS

Describe the potential benefits to subjects related to the study. State if there are no direct benefits.

NOTE: Compensation and/or course credit are not considered benefits.
Results from a recently completed clinical trial of the effects of Zonisamide on alcohol consumption by alcohol-dependent subjects (see Preliminary Data Section) and from a previous placebo-controlled clinical trial (Arias et al., 2010) indicate that this drug may reduce ethanol intake in individuals with AUD. Take Control computerized program, which all subjects will be asked to complete, should also help subjects in learning how to reduce their consumption of alcohol. Subjects who participate in this study may benefit from the close monitoring and interventions provided to treat their AUD. These potential benefits are provided without charge.

Describe the potential benefits to society and/or others related to the study
This study promises to provide important information about the relative efficacy and safety of a novel treatment strategy to improve outcome for patients with AUD. The results of this study should provide information on the neurobehavioral mechanisms through which Zonisamide may act to facilitate the reduction of drinking in AUD. These findings may be of value in helping to differentiate individuals with AUD who fail to respond to the effects of Zonisamide administration on subjects from those who do not based on their reactivity on alcohol cue tasks. This would provide a basis for identifying subjects who would expect to benefit from treatment from Zonisamide. It could also be of value in the screening of newly synthesized broad spectrum anticonvulsant medications that are structurally related to Zonisamide for their potential efficacy as medications for the treatment of AUD. Also, the results of this study should provide further evidence regarding the usefulness of Take Control computerized alcohol reduction and medication compliance program for use in alcohol treatment clinical trials. Information obtained regarding the neurobehavioral mechanisms that mediate Zonisamide's effects on alcohol consumption will provide a basis for determining which patients might be most responsive to Zonisamide's therapeutic effects on AUD. They, also, may help in the development of procedures for assessing whether newly synthesized drugs that chemically related to Zonisamide may be of potential use in the treatment of AUD. A potential benefit of undergoing MRI scans is the discovery of previously undiagnosed structural brain abnormalities. If there are possible brain abnormalities, MRI examinations and results can be forwarded to Primary Care Physicians if subjects complete a Medical Records Release Form.

SECTION O: COSTS/PAYMENTS

YES*	NO	
☐	☒	Are there any costs to subjects as a result of participating in this study? *If YES, provide a description of the costs: N/A

☒	☐	Will subjects be compensated for participating in the study? Compensation may include cash, checks, gift cards, lotteries, course credit, etc. *If YES, provide a description of the compensation: $100 for completion of scan 1; $100 for completion of scan 2. $50 for session 4, $50 for session 8, $100 for session 12, and $50 for the one month follow-up. Participants can earn up to $450 for completion of all study procedures in this trial. **NOTE:** Payments should be prorated to compensate subjects for time and procedures completed
☒	☐	Will identifiable information be sent to Central University departments (Accounts Payable, Post Award Financial Operations, etc) for payment purposes? *If YES, this information must be disclosed in the consent form.

SECTION P: CONFIDENTIALITY OF DATA

Describe how data will be stored (e.g. paper, electronic database, etc.)
Participants will be referred to by participant numbers from the moment they are recruited. Consent form: Participants' signed consent forms will be kept in a locked cabinet at the Center of Anxiety and Related Disorders at Boston University, to which only the staff of this experiment can access. The participant's study ID number will not be associated in any way with their signed consent form. The consent forms will be stored for at least 7 years after the completion of this research. Data: Data stored for each participant will be de-identified, containing only participant numbers. All data will be stored electronically in one place. Most assessments/questionnaires will be conducting electronically using the Qualtrics online data collection platform, but any physical copies of data will be stored in one locked cabinet accessible only by experimenters. Participant numbers will not be associated to any identifiable information in any dataset. This data will be stored for at least 7 years after the completion of this research.

Per Boston University (BU) Record Retention Policy, records concerning human subjects must be retained for 7 years. Please refer to the policy at: http://www.bu.edu/policies/finance/record-retention/. As the investigator, you must also adhere to all applicable requirements as defined by regulatory agencies (e.g. FDA, etc.) or Sponsors.

YES*	**NO**	
☒	☐	Will you collect identifiable information? (e.g. names, social security numbers, addresses, telephone numbers, etc.) *If YES, complete the box below
Describe the coding system* that will be used to protect the information including who will have access to the code		

***Coding system: Coding systems are used to: 1) protect the confidentiality of the research data and 2) allow the investigator to link subjects to their responses. Each subject is assigned a unique study ID at the beginning of the study. A separate document (key) should be maintained that links the names of the subjects to the study ID numbers.**		
Participant records are coded with an alpha-numeric code that cannot be linked back to them without access to the participant ID key file. The ID key file is maintained in an encrypted volume on a server within a secure data center to store this information created by BU CAS Information Technology, which is only accessible to the study personnel. Access is controlled via Active Directory groups, utilizing Kerberos authentication for individual access. Access audits will be scheduled to keep the list up to date, and to remove users that no longer require access to this dataset. Participant information sharing between study personnel will occur only via secure networks. Only approved study staff will be able to assess the ID key file.		
YES*	**NO**	
☐	☒	Will you share data with others outside of the study? *If YES, complete the box below
Describe how data will be transferred and how confidentiality will be maintained (e.g. identifying information will not be sent outside, etc.)		
N/A		

Describe how you will maintain the confidentiality of the data (e.g. locked cabinet, password-protected files, encryption, etc.) **Note: Confidentiality refers to the researcher's agreement with the participant about how the subject's identifiable private information will be handled, managed, and disseminated** **For further assistance and/or access to resources regarding information security, please refer to the BU Information Security website:** http://www.bu.edu/tech/security/
An encrypted volume will be created by the BU CAS Information Services & Technology (IS&T) on a server within a secure data center to store this information. Access is controlled via Active Directory groups, utilizing Kerberos authentication for individual access. Access audits will be scheduled to keep the list up to date, and to remove users that no longer require access to this dataset. Access is controlled via Active Directory groups, utilizing Kerberos authentication for individual access. Access audits will be scheduled to keep the list up to date, and to remove users that no longer require access to this dataset. Participant records are coded with an alpha-numeric code that cannot be linked back to any identifiable information without access to the participant ID key file. No records will ever contain a participant ID and identifiable information at the same time except the ID key file. The ID key file is maintained in a separate folder on the encrypted volume to which only the study PI has access through Kerberos login. Any electronic copies of other study data without identifiable information will be stored on this encrypted volume, too, accessible to only study personnel. Physical copies of records containing identifiable information (e.g., signed informed consent form), will be stored in locked drawers at CARD, separate from the participant's study ID.

Physical copies of data that are distinguished by participant ID will be stored in a locked cabinet at CARD, separate from any identifiable information, only accessible to study personnel.
Data collected from online assessments, interviews and questionnaires using Qualtrics, a password-protected online survey-administration and data-collection tool, will be de-identified, only distinguishable by study ID. Recruitment and progress tracking data will be collected and maintained in Google Sheets on Google Drive created with a BU Google account, since BU Google Drive (NOT the consumer version of Google Drive) is approved for confidential data and FERPA data (but not restricted/HIPAA data). Study data collected and maintained online including but not restricted to assessments, interviews, progress tracking will be de-identified, only distinguishable by study ID.
Participant information sharing between study personnel will occur only via secure networks.

YES	NO	
☒	☐	Will you obtain a Certificate of Confidentiality? Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. For more information about a Certificate of Confidentiality, please review the NIH website at: http://grants.nih.gov/grants/policy/coc/

SECTION Q: PRIVACY

Describe how you will protect the privacy of subjects. Include the following information: location of data storage, who will have access to study information, and location of study visits

Note: Privacy can be defined in terms of having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others

All study procedures and sessions will be conducted in locations where the subject's privacy can be maintained.

An encrypted volume will be created by the BU CAS Information Services & Technology (IS&T) on a server within a secure data center to store this information. Access is controlled via Active Directory groups, utilizing Kerberos authentication for individual access. Access audits will be scheduled to keep the list up to date, and to remove users that no longer require access to this dataset. Access is controlled via Active Directory groups, utilizing Kerberos authentication for individual access. Access audits will be scheduled to keep the list up to date, and to remove users that no longer require access to this dataset.
Participant records are coded with an alpha-numeric code that cannot be linked back to any identifiable information without access to the participant ID key file. No records will ever contain a participant ID and identifiable information at the same time except the ID key file. The

ID key file is maintained in a separate folder on the encrypted volume to which only the study PI has access through Kerberos login.
Any electronic copies of other study data without identifiable information will be stored on this encrypted volume, too, accessible to only study personnel.
Physical copies of records containing identifiable information (e.g., signed informed consent form), will be stored in locked drawers at CARD, separate from the participant's study ID.
Physical copies of data that are distinguished by participant ID will be stored in a locked cabinet at CARD, separate from any identifiable information, only accessible to study personnel.
Data collected from online assessments, interviews and questionnaires using Qualtrics, a password-protected online survey-administration and data-collection tool, will be de-identified, only distinguishable by study ID. Recruitment and progress tracking data will be collected and maintained in Google Sheets on Google Drive created with a BU Google account, since BU Google Drive (NOT the consumer version of Google Drive) is approved for confidential data and FERPA data (but not restricted/HIPAA data). Study data collected and maintained online including but not restricted to assessments, interviews, progress tracking will be de-identified, only distinguishable by study ID.

Participant information sharing between study personnel will occur only via secure networks.
All participant records and data will be stored at least 7 years after the completion of this research.

Only approved study staff will be able to make any contact with participants and/or have access to study data. Study staff are not allowed to disclose any participant's personal information to anyone outside of the study without permission from the participant. This study will only be conducted at CARD and at BU CILSE. Participants will only be required to make 15 study visits, each ranging from 1-2 hours, unless additional study procedures are required. Participants will be told from the very beginning of the study that they can withdraw from the study anytime without penalty, and that they do not have to disclose any information that they are not comfortable with sharing.

SECTION R: MONITORING STUDY DATA

How will data be monitored?: **Note: The Data and Safety Monitoring Plan should be tailored to the nature, size, and complexity of the research protocol, the expected risks of the research, and the type of subject population being studied**	
☐	Principal Investigator
☐	Monitor/Monitoring Group
☒	Data and Safety Monitoring Board (DSMB) Note: The DSMB Charter must be submitted with this Application For more information regarding a DSMB, please refer to the following website: http://www.nidcr.nih.gov/Research/ToolsforResearchers/Toolkit/DSMBGuidelines.htm

Describe the plan for monitoring study data. This should include a description of how data will be collected and analyzed as the project progresses to assure the appropriateness of the research, its design, and subject protections.

Functional Organization of the DSMB
The Chairperson of the DSMB will communicate by e-mail and telephone conference with the other members. Communication pertaining to review of serious adverse events (SAEs) will occur within a week of receiving any new SAE report. Reporting and communication about other matters will occur on a yearly basis, for the duration of the study. Decisions of the DSMB will be made based on a majority vote of the members. Meetings of the DSMB will be held at least one time a year at the call of the Chairperson and /or NIAAA Program Official.

Monitoring of Safety Data by the DSMB
1. Unblinded Reporting – Safety information for this study will be reported to the DSMB in an unblended manner. A statistical penalty will not be assessed for the ongoing unblinded review of safety by the DSMB. Unblinded data will not be released to the investigators unless necessary for safety reasons.
2. Range of Safety Reporting to the DSMB – It is considered necessary for the purpose of monitoring the safety of the study that the DSMB review not only adverse events (AEs) and serious adverse events (SAEs), but also other data that may reflect differences in safety between treatment groups. This includes treatment retention rates and reasons for dropout.
3. Serious Adverse Events – Expedited review will occur for all events meeting the FDA definition of Serious Adverse Events (SAEs) – i.e., any fatal event, immediately life-threatening event, permanently or substantially disabling event, event requiring or prolonging inpatient hospitalization, or any congenital anomaly. This also includes any event that a study investigator or the DSMB judges to impose a significant hazard, contraindication, side effect, or precaution. All relevant information will be reported to the DSMB for each SAE including information about the event and its outcome, concomitant medications, and the subject's medical history and current conditions. Reporting to local IRBs will be completed within 24 hours of the SAE. Notification by e-mail shall be made to the DSMB within 7 days of the occurrence of any SAE.
4. Non-Serious Adverse Events - A non-serious adverse event is any untoward or unfavorable medical occurrence in a study participant, including any abnormal sign (e.g. lab results, physical exam findings, symptom or disease associated with the participant's involvement in the study, regardless of whether or not the cause is related to participation in the study, that are do not meet criteria for being a serious adverse event. At yearly intervals during the course of the study and then again at its completion, the DSMB will be provided with unblinded summaries of the numbers and rates of adverse events by treatment group. These reports will include types of events, severity, and treatment phase. Data on individual non-serious adverse events is not expected to be needed for this review.
5. Other Safety-Related Reports – At yearly intervals throughout the course of the study, the DSMB will also receive unblinded summary reports of treatment retention and reasons for dropout, by treatment arm and study phase.

6. Study Stopping Rules – If at any time during the course of the study, the DSMB judges that risk to subjects outweighs the potential benefits, the DSMB shall have the discretion and responsibility to recommend that the study be terminated.

Monitoring of Data Quality by the DSMB
At least on an annual basis during the course of the study, the DSMB will receive a report on data quality and completeness. At a minimum, this will include an overview of the progress of patient intake and retention; summary reports describing patient compliance with visits, evaluations, and dosing as described in the protocol; and a summary of the completeness and quality of key data elements needed to characterize patients, their dosing, and their primary and secondary outcomes. These reports will be used by the DSMB to evaluate the capacity of the data capture and processing to support scientifically valid analyses.

Data Safety Monitoring Plan
Because all BU CILSE procedures are nonsignificant risk in nature, the co-investigator at BU CILSE will execute a Data Safety Monitoring Plan (DSMP) covering BU CILSE procedures. This DSMP includes monitoring and regular reporting of accumulated study data to Dr. Farchione. DSMP procedures covering subject safety will be executed if necessary to protect the safety of human subjects. Subject safety and adverse events will be monitored and assessed by study staff during each study visit. If any adverse events should occur, the subject can withdraw voluntarily or, if a contraindication to MRI scans or other disqualification from study eligibility becomes apparent, at the discretion of the BU CILSE co-investigator.

Adverse events related to BU CILSE study procedures will be reported to Dr. Farchione. Serious adverse events, non-serious unexpected adverse events that are related or possibly related to the study, and unanticipated problems involving subjects or others will be reported to Dr. Farchione as soon as possible and within 5 working days/7 calendar days. Within 10 working days of this notification, a full written report regarding events will be submitted to Dr. Farchione. Events that do not fall into the above categories will be reported to Dr. Farchione in summary format for inclusion into the annual IRB continuing review report.

Annual DSMB Report to NIAAA
Annually during the course of the study the DSMB will prepare a summary report of its findings regarding safety and quality based on data received to that point in the study. This report will include a summary of all safety findings, as well as an assessment of protocol compliance and data quality. Any recommendations to improve patient safety, protocol adherence, or data quality will be made in the annual DSMB report. A copy of the annual DSMB report will be sent to the local IRBs along with the annual renewal report.

SECTION S: HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA)

YES*	NO	
☐	☒	Is this research being conducted in a covered entity? The following components have been determined to be covered entities on the Boston University Charles River Campus:

		• Sargent College Rehabilitation Services
		  ○ Physical Therapy Center at the Ryan Center for Sports Medicine and Rehabilitation
		  ○ Sargent Choice Nutrition Center
		• The Danielsen Institute
		• Boston University Health Plan
		*If YES, contact the IRB office for assistance.

SECTION T: FAMILY EDUCATIONAL RIGHTS AND PRIVACY ACT (FERPA):
FERPA is the federal law that protects the privacy of student education records. Research funded by the Department of Education or research conducted in educational institutions that receive funds from the Department of Education (for research or other purposes) must comply with FERPA.

YES *	NO	
☐	☒	Does this study involve collection of information from student school/university records? *If YES, refer to the following websites for guidance on FERPA: • http://www.bu.edu/orc/files/2015/11/Fed_Agency_SOP_Nov_2015_Final.pdf • http://www.bu.edu/reg/general-information/ferpa/ • http://www2.ed.gov/policy/gen/guid/fpco/ferpa/index.html **If FERPA applies, you must complete the box below:**
In accordance with FERPA, written consent must be obtained to access student records. The consent must: • Specify the records that may be disclosed • State the purpose of the disclosure • Identify the person or class of parties to whom the disclosure can be made		
☒ YES **(REQUIRED)**	I confirm that I will comply with the FERPA policy that is in place at the educational institution where I am conducting my research. This includes, if applicable, the requirements for written agreement when requesting a waiver of consent for personally identifiable information. **If an agreement is required, this agreement must be submitted to the IRB.**	

SECTION U: PROTECTION OF PUPIL RIGHTS AMENDMENT (PPRA):
PPRA is a federal law that affords certain rights to parents of minor students with regard to surveys that ask questions of a personal nature. Research funded by the Department of Education or research conducted in educational institutions that receive funds (for research or other purposes) from the Department of Education must comply with the PPRA.

YES *	NO	
☐	☒	Does PPRA apply to this study? *If YES, refer to the following websites for guidance:

		• http://www2.ed.gov/policy/gen/guid/fpco/ppra/index.html • http://www.bu.edu/orc/files/2015/11/Fed_Agency_SOP_Nov_2015_Final.pdf **If PPRA applies, you must complete the box below:**
In accordance with PPRA, written parental consent must be obtained prior to subjects participation in the study.		
☒ YES **(REQUIRED)**	I confirm that I will comply with the PPRA policy that is in place at the educational institution where I am conducting my research.	

SECTION V: CLINICAL TRIALS REGISTRATION:

The Food Drug and Administration Amendments Act (known as FDAAA 801) requires that "applicable clinical trials" be registered and have results reported on clinicaltrials.gov. The Responsible Party for a clinical trial must register the trial and submit results information. In addition, the International Committee of Medical Journal Editors (ICJME) also have requirements for registration. Please see box below to determine if your study requires registration in accordance with either FDAAA 801 or ICJME.

YES*	NO	FDAAA 801 Requirements
☒	☐	Does your study meet the definition of an applicable clinical trial and require registration **AND** results submission in accordance with FDAAA 801? Applicable Clinical Trials include the following: • Trials of drugs and biologics: Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation • Trials of devices (see note): 1) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and 2) pediatric postmarket surveillance required by FDA The Responsible Party is defined as: • The sponsor of the clinical trial or • The principal investigator (PI) of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the PI is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of FDAAA's requirements for the submission of clinical trial information *If YES, refer to the following websites for guidance: • FDAA 801 Requirements: https://clinicaltrials.gov/ct2/manage-recs/fdaaa

		• BU IRB Policy on Clinical Trials Registration: http://www.bu.edu/orc/policies-procedures/human-subjects/ **Note: If your study meets the requirement for registration and reporting, you must submit the National Clinical Trial (NCT) Identifier # to the IRB prior to IRB approval.** NCT #:_ NCT02901041_____
YES*	**NO**	**ICMJE Requirements**
☒	☐	Does your study meet the definition of a clinical trial and require registration in accordance with ICMJE? ICMJE definition of clinical trial: Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration. *If YES, refer to the following websites for guidance: • ICMJE Clinical Trials Registration: http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/ • BU IRB Policy on Clinical Trials Registration: http://www.bu.edu/orc/policies-procedures/human-subjects/ **Note: If your study meets the requirement for registration, you must submit the National Clinical Trial (NCT) Identifier # to the IRB prior to IRB approval.** NCT #:___ NCT02901041_____

Certification / Signatures

- By submitting this protocol I attest to the fact that all research activities to be implemented related to human subjects have been completely and accurately described herein.
- I agree to conduct the describe research in an ethical manner.
- I agree to comply with all institutional policies and procedures related to human subjects research and will not begin any human subjects research activities until I have obtained full approval from the IRB.
- I agree to conduct the research as described in this protocol and not to make any changes (except to eliminate immediate harm to subjects) without first obtaining approval for the changes from the IRB.

- I agree to immediately report any unanticipated problems involving risks to subjects or others, any subject complaints, and any incidents of non-compliance with the requirements of this protocol as soon as I become aware of them.

- I agree to comply with any relevant HIPAA and FERPA regulations if applicable.

- I verify that all those responsible for the design, conduct, or reporting of the proposed program, including at minimum, all Senior/key personnel in the grant application, have completed the financial interest disclosure forms and completed training as dictated at http://www.bu.edu/orc/coi/forms/, and returned the forms to the Office for Research Compliance COI Unit. **NOTE: If anyone checked "yes" to any of the questions on either the FIND1 or NONFIND1 form, the IRB Director will contact the COI office to obtain the disclosure information.**

PI printed name _____Todd Farchione, Ph.D._____

PI Signature:_____  _____

Date: 12/12/2022

Submission
This form can be completed, signed, scanned and submitted to the IRB at irb@bu.edu. Faxed documents and handwritten materials are not accepted. Be sure to include all relevant attachments.

FACULTY Research:

The Department Chair signature is required: This application must be signed by the Department Chair for all faculty researchers. If the PI is the Department Chair then signature by the appropriate Dean is required. Department Chair signature is not required for student research. **By signing this form you are indicating that you have reviewed the application, the faculty/staff person listed as PI on this protocol is a member of your department, that he/she is qualified to serve as the PI for this study, he/she has the adequate resources, and the research utilizes acceptable practice for the discipline.**

Department Chair (print name): David Somers, Ph.D.

Department/School: Psychological and Brain Sciences

Signature:

Date: _____