Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH: Effects of a novel mGluR5 negative allosteric modulator on alcohol drinking, neurochemistry, and brain reactivity to alcohol cues in alcohol use disorder

Study Officials: **James Prisciandaro**
Study Principal Investigator
Medical University of South Carolina

NCT04831684

SUMMARY

You are being asked to volunteer for a Phase II clinical research study. Research studies are voluntary and include only people who choose to take part. The purpose of this study is to evaluate both the safety and effectiveness of an FDA-regulated medication presently in the initial stages of development for alcohol use disorder treatment (GET73), and to test whether GET73 alters brain chemicals and function, response to alcohol ingestion, and the desire for alcohol. You are being asked to participate specifically because the Clinical Intake and Assessment Core of the Charleston Alcohol Research Center indicated that you are eligible for it based upon results from your completed clinical interview, questionnaires, and lab work.

After agreeing to participate in this study, you will be randomly assigned to one of two medication treatment groups. You will take the assigned study medication for 8 days, complete 2 brain imaging scans and a “bar-lab” procedure, as well as a follow-up session. Questionnaires and clinical interview measures will be completed at study visits along with assessment for potential side effects from study medication.

Some of the risks may include that questions in questionnaires or clinical interviews might cause anxiety and/or emotional discomfort but trained clinicians will attempt to minimize any discomfort in the questions asked. There are potential side effects from the study medication, which are described in detail below. Research staff will ensure minimal risk during brain scanning by through several standard safety procedures. There is also a risk of loss of confidentiality, but the researchers will code your data and research information to protect privacy.

You may benefit from participating in this study by answering the interview questions and questionnaires and thinking more about your lifestyle, including alcohol and/or tobacco use. If you are interested in learning more about this study, please continue to read below.

A. PURPOSE OF THE RESEARCH

Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. You are being asked to participate in this study because you currently drink more than 20 alcohol drinks per week. This clinical research study is sponsored by the National Institute of Alcohol Abuse and Alcoholism (NIAAA)-funded Alcohol Research Center. The investigator in charge of this clinical research study at MUSC is Dr. James J. Prisciandaro. A grant from the National Institutes of Health (NIH) will sponsor this study. Portions of Dr. Prisciandaro's and his research team's salaries will be paid by this grant This clinical research study is being done at the Medical University of South Carolina and will involve approximately 125 participants.

You are being asked to fill out questionnaires, to be interviewed, to take study medication as prescribed, to undergo brain imaging scans, complete a “bar-lab” procedure where you may safely consume alcohol drinks, and provide breathalyzer and urine samples.

B. PROCEDURES

If you agree to be in this study, the following will happen:

1. You will need to have the following exams to find out if you can be in the study. These exams are part of regular care and may be done even if you do not join the study. A MD/PA will conduct a full medical history, review of medications, and a physical exam to confirm that you are physically healthy.
2. If the physical examination results show that you are eligible for the study, you will be randomly assigned to one of two groups. This means that you have a 50/50 chance (like flipping a coin) of being in either group. Neither the researchers nor you will make the choice to which group you are assigned. The two groups are Group A (Investigational drug: N-[4-(triflouromethyl) benzyl]-4-methoxybutyramide [GET73]) and Group B (placebo, an inactive substance).
3. Group A will receive GET73, the investigational drug, 2-3 times a day for a total of 8 days. Group B will receive placebo, according to the same schedule. If you are assigned to Group A, you will take a maximum total of up to 900mg per day for 8 days. All capsules will include a vitamin, riboflavin, which may cause your urine to be orange in color. If you are allergic to riboflavin, you may not be included in the study. The study medication will be provided in a blister pack with the days identified to help you in taking these medications.
4. After group assignment but before taking any study medication, and again 7 days later, you will have a Magnetic Resonance Imaging (MRI) exam after completing some surveys. Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will hear a loud machine-like noise. For the MRI exam, you will be asked to lie still in the scanner as it takes an image of your brain, followed by measurement of brain chemicals and brain function. During the first half of the MRI exam, you will be presented with a slideshow of relaxing pictures. During the second half of the MRI exam, you will be given a small sip of alcohol and then you will be asked to look at pictures, some of which pertain to alcohol, while brain function is measured. Next, we will ask you to lie still with your eyes open, while not thinking about anything in particular, so we may measure your brain activity at rest. You will need to lie still in the scanner for approximately 60 minutes. At each MRI exam, a urine sample will be collected for illicit drug screening, pregnancy testing (if female), and measurement of ethyl-glucuronide (EtG), a minor

metabolite of alcohol that detects recent (24-72 hours) drinking. You will be asked not to drink alcohol on the evening preceding MRIs and the “bar-lab” study visits. After your Day 7 MRI scan, you will complete a couple of computer tasks.

5. On day 4 of the study, you will receive a brief phone call from a study team member to assess any potential side effects from study medication you may be experiencing.

6. On day 8 of the study, you will complete the “bar-lab” study procedure on site. This will take approximately 11 hours and will continue until about 10 pm. You will be provided with a light lunch upon arrival. You will then be given a single alcohol drink and asked to complete questionnaires regarding your current level of intoxication, craving for alcohol, and any physical symptoms that may reduce your desire for alcohol (e.g., nausea, headache). Afterwards, you will be offered the opportunity to consume more alcohol drinks using a $16 bar credit with which you may obtain up to 8 drinks at $2 each. Any unused cash from the bar credit at the end of this period will be yours to keep. After your last drink, you will be given dinner and allowed to read, watch TV, play video games, or listen to music. You will also be given reading material about alcohol, which you must read during this period. Breath analysis will be performed on several occasions throughout the procedure and you will be required to stay on site until your breath alcohol level is below the legal limit (0.08). At the end, you will be allowed to leave in the custody of a relative or friend, who will sign an agreement that you will not drive or participate in any hazardous activity until the next morning. If no responsible person is available, you will be sent home by taxi service free of charge.

7. On day 9 of the study, you will return for a debriefing session lasting approximately 60 minutes. You will complete a few surveys and will then be seen by a counselor who will review your drinking and speak with you about potential alcohol- treatment options if you wish to pursue them, and you will complete a physical symptom questionnaire.

8. One week later, you will be contacted briefly by phone by a study team member to assess for potential side effects after discontinuation of study medication and to review your drinking since your last study visit.

9. If you are a woman of childbearing potential and /or a man capable of fathering a child before, during, and/or after participation precaution should be taken. Examples of acceptable methods of birth control for participants involved in the study includes: birth control pills, patch, IUD, condom, sponge, diaphragm with spermicide, or avoiding sexual activity that could cause you to become pregnant.

C. DURATION

Participation in the study will take about 4 visits over a period of approximately 2 weeks.

D. RISKS AND DISCOMFORTS

Medication risks: While you take part in this study, you may be at risk for side effects that may be mild, moderate or severe. Many side effects go away shortly after the treatment stops, but occasionally, side effects can be serious, long lasting, or permanent. It is not possible to tell which side effect will affect you or how mild or severe the side effect might be. We can only tell you what other people have experienced given the research to date. In the only published study, the most commonly-reported side effect among participants was headache but nausea and nasopharyngitis were also reported with one subject reporting a non-significant, decrease in heart rate of 6-8 beats per minute. Overall, across the various dosing schedules (10-900mg per day) evaluated in this published study approximately 33% of participants reported a side effect(s). On-going studies of GET73 (NCT01842503, NCT03418623) are currently using the proposed dosing schedule. Minimal complaints of mild sedation and fatigue have been reported; however, they were not directly attributable to GET73. Finally, there may be other side effects of GET73 that we do not know of yet.

You will be thoroughly assessed for all of the above potential side effects as well as potential sedative effects of GET73 including daytime sleepiness, fatigue, and dizziness. If you experience any side effects, you should report them to study personnel. You will be given a card with phone numbers to call at any time any day of the week. If you experience any of the above side effects or any others, you can call that number and speak to a study health care provider who will advise you regarding your concerns and what to do about them. The effects of GET73 on a developing fetus are not known. If you are a woman you must agree to use a reliable method of birth control while participating in this study.

Randomization: The treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

Placebo: If you are in the group that receives placebo, your condition will go without potentially active treatment for approximately 1 week.

Unknown risks: The experimental treatment may have unknown side effects. The researchers will let you know if they learn anything during the course of the study that might make you change your mind about participating in the study.

MRI risks: There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will be excluded from participation in this research study. We will

also keep the examining room locked so that no one carrying metal objects can enter while you are in the scanner. Please inform the study staff if you have a history of claustrophobia (extreme anxiety in close spaces). This may also be a contraindication to participation in the study.

Alcohol Ingestion: While this study does not require you to change your alcohol drinking habits (except as noted above), you must be informed that the combined effects of GET73 and alcohol are not completely known. Therefore, you should be careful about driving and using machinery if you do drink.

In the "bar-lab" portion of the study, it is possible that alcohol may upset your stomach and cause effects of intoxication and increased craving for alcohol. You will be monitored during the procedure and not permitted to leave until your breathalyzer reading is below the legal limit. You will also not be allowed to personally drive away from the research site. If any significant adverse event should occur during the session, or if the risk of sending you home after the procedure is deemed to be too high, then you will be required to stay in the hospital overnight. However, this has not been necessary in well over 400 subjects who have participated in similar studies.

Psychological risk: Some of the questions the researchers ask you may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you can skip it and go to the next question.

E. MEDICAL RECORDS and/or CERTIFICATE OF CONFIDENTIALITY

Information about your study participation will not be in your medical record. This means that neither your research participation nor any of your research results will be included in any MUSC medical record.

F. COSTS

There will be no cost to you as a result of participation in this clinical research study. This research protocol is not an alcohol treatment study and there is no expectation that anything that you receive during your participation can be considered treatment. You will not be able to participate in this research protocol if you want treatment for your alcohol problems prior to, or during, participation. If, on the day you are given alcohol at the study site, for some reason related to the study participation you are unable to go home safely, you may stay in the hospital at no cost to you. If the study medication is associated with any adverse events requiring medical care, these costs will be borne by you or your insurance carrier.

G. PAYMENT TO PARTICIPANTS

You will receive $25 at your intake visit and $391.00 cash less $2 for each drink (up to 8) ordered during the “bar-lab” procedure at the end of your participation in the research protocol as described above. This money will be given to you after you finish the debriefing session. Payments that you receive from MUSC for participating in a research study are considered taxable income per IRS regulations. Payment types may include, but are not limited to: checks, cash, gift certificates/cards, personal property, and other items of value. If the total amount of payment you receive from MUSC reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

H. ALTERNATIVES

Though this is a Phase II clinical research study evaluating both the safety and the effectiveness of GET73, there is direct focus on treating alcohol problems. You may choose not to participate in this study. If you should choose to seek treatment either before or after your participation in this clinical research study there are a number of options. Most types of treatment for alcohol problems involve some form of counseling. Alcoholics Anonymous provides free self-help groups and counselors such as social workers, addiction counselors or psychologists provide a fee for service-based treatment. Sometimes individuals need to be detoxified from alcohol and this may involve taking medications in the hospital or as an outpatient. There are medications that also assist people in reducing or stopping their drinking such as naltrexone, acamprosate and antabuse. If you would like more information about any of these options please ask the research study personnel who may also make a referral will be made if you so desire.

I. DATA SHARING

Information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

J. DISCLOSURE OF RESULTS

In case if any abnormalities determined during the course of this study will be pointed out to you and, if necessary, aid will be assisted in making a clinical appointment for a more complete evaluation.

K. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

L. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

M. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

N. CLINICAL TRIALS.GOV

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

O. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities not related to this study. Please initial by your choice below:

____Yes, I agree to be contacted

____No, I do not agree to be contacted

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. James J. Prisciandaro at 843-792-1433. I may contact the Medical University of SC Patient and Family Care Liaison (843) 792-5555 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

_____	_____
Signature of Person Obtaining Consent Date	Name of Participant

_____
Signature of Participant Date