Principal Investigator: Dr. Thomas Mellman, MD.
Study Number: 2015-1333
Title: Suvorexant and Trauma–related Insomnia (A placebo controlled trial with polysomnography)

Informed Consent for Clinical Research
Georgetown-Howard Universities Center for Clinical and Translational Science (GHUCCTS)

INSTITUTION: **HOWARD UNIVERSITY**

INTRODUCTION

You are invited to consider participating in this study. The study is called Suvorexant and Trauma-related Insomnia (A placebo controlled trial with polysomnography).
Please take your time to make your decision. Consider discussing it with your family and friends. It is important that you read and understand several general principles that apply to all who take part in our studies:

(a) Taking part in the study is entirely voluntary;

(b) Personal benefit to you may or may not result from taking part in the study, but knowledge may be gained from your participation that will benefit others;

(c) You may decline to participate or you may withdraw from the study at any time without loss of any benefits to which you are entitled and without jeopardizing your access to care, treatment and health services unrelated to the research.

The purpose and nature of the study, possible benefits, risks, and discomforts, other options, your rights as a participant, and other information about the study are discussed below. Any new information discovered, at any time during the research, which might affect your decision to participate or remain in the study will be provided to you. You are urged to ask any questions you have about this study with the staff members who explain it to you. You are urged to take whatever time you need to discuss the study with your physician, hospital personnel and your family and friends. The decision to participate or not is yours. If you decide to participate, please sign and date where indicated at the end of this form. The investigator (person in charge of this research study) is Dr. Thomas Mellman.

The research is being sponsored by Merck & Co. Merck & Co. is called the sponsor and up to $523,000 is being paid to Howard University to conduct this study with Thomas Mellman as the primary investigator. Merck is also the maker of the drug being evaluated in this study. Dr. Mellman occasionally serves as a paid consultant to Merck.

WHY IS THE STUDY BEING DONE?

You are being asked to participate in this study because Dr. Mellman and his staff aim to investigate the effectiveness of suvorexant for trauma-related insomnia. Sleep problems are common among those with exposure to trauma and can contribute to other mental and physical problems. Medications and other treatments

aimed at reducing PTSD have not been very effective for helping insomnia. Suvorexant was recently approved by the Federal Drug Administration for the treatment of insomnia but it has not been evaluated for treating insomnia related to trauma. It works in a way that is different from other available medications for insomnia.

You may not participate in this study if any of the following apply to you:

1. Severe psychiatric disorders (not including insomnia, PTSD and specific phobias) such as bipolar and psychotic disorders, and moderately severe alcohol or drug use disorders within the past year.
2. Certain sleep disorders other than insomnia including sleep recording findings indicating sleep apnea.
3. Consistent (daily) use of medication other than medications taken for blood pressure or nonnarcotic medications for pain and/or inflammation, or medical conditions that compromise sleep;
4. History of moderate to severe traumatic brain injury or mild traumatic brain injury with ongoing post-concussive symptoms;
5. Having or having had a plan or the intention to commit suicide in the past 6 months or a concerning history of prior suicidal behavior;
6. Caffeine use exceeding 5 cups of coffee per day;
7. Regular bedtimes after 3AM, rise times after 10AM, or napping > 1hour/day;
8. Pregnancy or breastfeeding, or expecting to conceive while in the study;
9. Positive urine test for drugs.

The purpose of this study is to find out what effects (good and bad) suvorexant has on you and your trauma-related insomnia.

This research is being done because standard treatments have not worked well for insomnia with posttraumatic stress disorder and medication indicated for treating insomnia has not focused specifically on people whose sleep problems are related to trauma.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Participants in the study are referred to as subjects.

About 105 subjects will take part in this study and all will be recruited at this site.

WHAT IS INVOLVED IN THE STUDY?

Interviews and questionnaires: involve answering questions asked by a member of the research team or filling out forms. These will include questions about traumatic experiences, your sleep patterns, symptoms related to stress and depression, and your personal and medical history. These questionnaires and interviews will vary in their time to complete, depending on which are required for that particular visit (typically one hour and no longer than two hours).

Sleep recording (polysomnography): The recordings require you to sleep over night in Howard University's Clinical Research Unit on three different nights (two before and one during medication treatment). Monitors will be attached to your scalp and face by tape or removable adhesive, and your chest on the first night. You will be asked to go to bed at your normal bed time and then wake up naturally in the morning.

Suvorexant and Placebo Treatment: You will take your medication 30 minutes before bed every night of the six-week investigation. You will have the opportunity to express your comments and concerns about the medication each week (with the opportunity to change your dosage during the first 2 weeks if indicated). You will be asked to discontinue medication after 6 weeks, and then complete a follow-up 1 week after stopping. A study clinician will discuss options for further treatment with you at this time.

You will be randomly assigned (like flipping a coin) into one of 2 study groups: to take either suvorexant (the active medication) or placebo (like a sugar pill) 30 minutes before going to bed. There is a 50% chance of receiving either of these treatments. The initial dose will be 10mg, after an evaluation an increase to 20 mg may be recommended. Neither you nor the researchers will choose or know what group you will be in. You will have an equal chance of being placed in either group. You will be given a study medication and it will either contain Suvorexant or placebo (pills with no medicine).

Standard procedures being done because you are in this study.

- All participants from both study groups will be asked to fill out questionnaires and answer questions about sleep, symptoms related to stress, mental health, personal and medical history in the Howard University Clinical Research Unit. Assessment procedures include the following:

1. **Demographic and Health Questionnaire-** includes questions about your gender, race/ethnicity, income, health and education. (Estimated completion time: 3 minutes)

2. **Physical Examination –** includes measurement of vital signs and height and weight, and a brief physical exam conducted by a physician or a nurse practitioner.

3. **Urine toxicology screening** – measuring whether there is alcohol or drugs in your urine.

4. **Urine pregnancy test** (women only) – examining whether you are pregnant through your urine sample. Because the study involves medication, you will be required to avoid pregnancy while you are participating in the study.

5. **Duke Structured Interview Schedule for DSM-5 Sleep Disorders (DSISD) –** Interview assessing types of sleep disorders (30 minutes**)**

6. **Structured Clinical Interview for DSM-5 (SCID-5)** – Interview about mental health symptoms and disorders. (45 minutes)

7. **Life Event Checklist (LEC)** – A survey of exposure to specific traumatic events (5 **minutes)**

8. **The Clinician Administered PTSD Scale (CAPS)** – interview about the presence and severity of symptoms related to traumatic stress (30 minutes, screening, and week 1, 3, 6**)**

9. **The Columbia-Suicide Severity Rating Scale (C-SSRS)** – A questionnaire that evaluates whether a person is having suicidal thoughts and behaviors (10 minutes, each visit (screening, baseline, week 1, 2, 3, 6, follow up)

10. **Insomnia Severity Index (ISI)** – A self-report measure that assesses the severity of insomnia symptoms. (2 minutes)

11. **Sleep Diaries** - A diary that is filled out in the morning to report how you slept during the night. (2 minutes every morning over week 1 and 2, 3,6, and follow up)

12. **Polysomnography (PSG)** – You will be monitored overnight in the Howard University Clinical Research Unit with several small electrode sensors that are placed on the scalp, chin, and over the heart which measure brain and heart activity during sleep. Other monitors measure breathing and will be included on the first night but not the second or third recording. If eligible you will be asked to participate in three overnight sleep recordings.

Please advise the researchers of any medications you are taking. In addition, if you are taking any over-the-counter drugs or herbal supplements which you have obtained from the drug store, grocery store, etc., you should advise the researchers.

HOW LONG WILL I BE IN THE STUDY?

You will take the study medication for 6 weeks unless you or a study clinician choose for you to withdraw. The study clinician may decide to take you off this study if it is in your medical best interest, your condition worsens, or new information about the drug becomes available. You will be asked to discontinue medication after 6 weeks, and then complete a follow-up 1 week after stopping. A study clinician will discuss options for further treatment with you at this time.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first.

WHAT ARE THE RISKS OF THE STUDY?

Risks and side effects related to the (procedures, drugs, or devices) we are studying include:

In prior studies, the most common side effect reported was feeling tired or drowsy during the day. This risk was more common with suvorexant than placebo (7 percent versus 3 percent). Because of this you should be cautious about driving when you first take the medication.

Less likely side effects (less than one percent in prior studies) that could occur include:

- temporary inability to move or talk (sleep paralysis) for up to several minutes while you are going to sleep or waking up
- temporary weakness in your legs that can happen during the day or at night.
- "sleep-walking" or doing other activities when you are asleep like eating, talking, having sex, or driving a car.

Avoidance of Pregnancy: The medicines and procedures used in this study may be unsafe for an unborn baby, an infant, sperm, and eggs. If you, as a subject of study, are a woman of child bearing potential, you must agree to avoid pregnancy during your participation in this study. If you do become pregnant during the study, you should immediately notify Dr. Mellman at 202-806-7818/202-865-6100 (after hours). In addition, if you are already pregnant or are breast feeding, you cannot participate in this study.

There may also be side effects, other than those listed that we cannot predict. Many side effects go away shortly after the (drug /intervention) is stopped, but in some cases side effects can be serious, long lasting or permanent. For more information about risks and side effects contact the investigator at 202-806-7818

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. Probable benefits may include falling asleep faster and staying asleep longer.

We cannot promise that you will experience medical benefits from participating in this study. We hope the information learned from this study will benefit others in the future.

WHAT OTHER OPTIONS ARE THERE?

Whether you participate in this study or not, you will receive care to manage your symptoms and keep you comfortable. Instead of being in this study, you have these options:

- Prazosin, studies suggest that this is can reduce nightmares in posttraumatic stress disorder.
- Cognitive behavioral therapy has been effective for treating insomnia.
- A number of medications such as Ambien are used for insomnia but are not established for trauma-related insomnia.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to protect your medical records and other personal information to the extent allowed by law. However, we cannot guarantee absolute confidentiality. Medical records of research study participants are stored and kept according to legal requirements. You will not be identified in any reports or publications resulting from this study. In addition to the researchers and research institution(s) conducting this study, organizations that may request to inspect and/or copy your research and medical records for quality assurance, data analysis and other research related and operational or administrative purposes, include groups such as:

Merck & Co., Food and Drug Administration, GHUCCTS Institutional Review Board (IRB), and Howard University.

Please note that administrative personnel involved in processing your payment for participation will be aware of your identity.

CLINICALTRIALS.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.

DATA SECURITY

If information about your participation in this study is stored in a computer, we will take the following precautions to protect it from unauthorized disclosure, tampering, or damage:
The principal investigator will be responsible for data management and maintaining confidentiality. Subject confidentiality will be protected to the full extent required by law and applicable local, State and Federal regulations and guidelines, including HIPAA. All patients will be assigned study numbers to replace specific identifying information. All data will be compiled in electronic form. Throughout the process of creating the database the integrity and security of the data will be monitored by the principal investigator and will occur on a weekly basis. All electronic data will be stored on secure, password-protected computers and drives and only authorized personnel will have access to the data. The principal investigator will oversee and monitor all aspects of the study.

WHAT ARE THE COSTS?

Study subjects will not have to pay for the study drug/treatment. There is no additional cost to you or your insurance company in relation to this study.

You or your insurance company will be charged for continuing medical care and/or hospitalization that are not a part of the study. You may find a National Cancer Institute guide: "Clinical Trials and Insurance Coverage – a Resource Guide" helpful. You may ask your doctor for a copy, or it is available on the world wide web at http://cancer.gov/clinicaltrials/insurance.

POLICY/PROCEDURES FOR RESEARCH RELATED INJURY

The Policy and Procedure of Merck & Co. are as follows:
The sponsor will not pay for care necessitated by a research related injury

The Policy and Procedure of Howard University is as follows:
If you are injured as a result of the research procedures, emergency medical care will be provided; however, financial compensation will not be available. Howard University Hospital may provide short-term and long-term medical care for any injury resulting from your participation in research here. However, if you are for some reason denied medical care, you have the right to pursue legal representation to help you gain medical care for your injury.

PAYMENT FOR PARTICIPATION

There is no cost to participants in this research study. You will receive payments to offset the time, inconvenience and transportation needs of study participation: $50 for the first visit, $25 for the other visits and $125 for each overnight sleep recording.

You should not expect anyone to pay you for pain, worry, lost income, or non-medical care costs that occur from taking part in this research study.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part in or leave the study at any time. If you choose to not take part in or to leave the study, your regular care will not be affected nor will your relations with your physicians, other personnel and the hospital or university. In addition, you will not lose any of the benefits to which you are entitled.

We will tell you about new information that may affect your health, welfare, or participation in this study.

By signing this form, you do not lose any of your legal rights.

NEW FINDINGS

Throughout the study, we will tell you if there is new information we receive about treatments that may be appropriate for you, about the experimental treatments under investigation in this study, and any information that may affect your interest in remaining in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, any problems, unexpected physical or psychological discomforts, or if you think that something unusual or unexpected is happening, call Dr. Thomas Mellman at (202) 806-7818 or after hours through the page operator at (202) 865-6100. Be sure to inform your physician of your participation in this study.

For questions about your rights as a research participant, contact the GHUCCTS Institutional Review Board at:

Address: Georgetown University Medical Center
Telephone: (202) 687-1506
3900 Reservoir Road, N.W.
SW104 Med-Dent
Washington, D.C. 20057

Withdrawal by investigator, physician, or sponsor

The investigators, physicians or sponsors may stop the study or take you out of the study at any time should they judge that it is in your best interest to do so, if you experience a study-related injury, if you need additional or different medication, or if you do not comply with the study plan. They may remove you from the study for various other administrative and medical reasons. They can do this without your consent.

MAKING YOUR CHOICE

Please read the sentence below and think about your choice. Please circle "Yes" or "No" then add your initials and date after you answer. No matter what you decide to do, it will not affect your care. If you have any questions, pleas talk to your study doctor or nurse, or call the Institutional Review Board at 202-687-1506

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RESEARCHER'S STATEMENT

I have fully explained this study to the subject. As a representative of this study, I have explained the purpose, the procedures, the benefits and risks that are involved in this research study. Any questions that have been raised have been answered to the individual's satisfaction.

_____	_____	_____
Signature of person obtaining the consent	Print Name of Person	Date

I, the undersigned, have been informed about this study's purpose, procedures, possible benefits and risks, and I have received a copy of this consent. I have been given the opportunity to ask questions before I sign, and I have been told that I can ask other questions at any time. I voluntarily agree to participate in this study. I am free to withdraw from the study at any time without need to justify my decision. This withdrawal will not in any way affect my future treatment or medical management and I will not lose any benefits to which I am otherwise entitled. I agree to cooperate with Dr. Thomas Mellman and the research staff and to inform them immediately if I experience any unexpected or unusual symptoms.

_____	_____	_____
Signature of Subject	Print Name of Subject	Date