Cannabidiol in the Treatment of Opioid Use Disorder

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STUDY INFORMATION:
Study Title: Cannabidiol in the treatment of opioid use disorder
Study site(s): Icahn School of Medicine at Mount Sinai, Mount Sinai Hospital, Mount Sinai Beth Israel, Mount Sinai West, Mount Sinai Morningside, Mount Sinai Behavioral Health Center
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SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. You can agree to join or not. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and if all of your questions about the research study are answered. If you do join the study, the research team must share any new information with you that may change your mind about taking part.

Although Cannabidiol, which contains CBD, has been approved by the Food and Drug Administration (FDA) for a rare seizure disorder in children, CBD is processed differently in humans than in animals. Animal safety studies have not been performed with this study model and therefore the safety of this study model is unknown at this time. As a result, the purpose of this research study is to determine whether Cannabidiol (CBD) can reduce craving and relapse in individuals with opioid use disorder (OUD). The research team is trying to determine whether CBD can serve as a potential add-on treatment to reduce craving and anxiety in individuals with OUD maintained on medication assisted therapy with methadone or buprenorphine.

If you choose to take part, you will be asked to:

- Attend 16 visits over the course of 13-14 weeks
- Undergo a physical exam with vital signs, including heart rate and blood pressure
- Complete questionnaires and computer tasks relating to health, pain, drug use, and sleep
- Provide urine and blood samples and undergo an electrocardiogram
- Take oral CBD or placebo twice daily
- Participate in computer-based cue sessions that will include viewing visual stimuli of drug-related and neutral imagery that may induce craving
- Optional daily wear of the Oura Ring (which will be provided to you at no cost), that will gather daily heart rate, respiratory rate, body temperature, caloreis, steps taken and sleep information.

If you choose to take part, the main risks to you involve risk of loss of private information and mild/temporary side effects from the use of Cannabidiol, which may include feeling tired or fatigued, and experiencing headache, nausea, vomiting, diarrhea, dizziness, lightheadedness, and/or sedation.

You may benefit directly from taking part in this research. Some potential benefits include reduction of craving and anxiety and reduced relapse to illicit drug use. There will be no cost associated with

participation. You will be compensated for your participation in this study. If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

You may qualify to take part in this research study because you have a current opioid use disorder (OUD) or a history of OUD while on maintenance therapy with methadone or buprenorphine. Your participation in this research study is expected to last 13-14 weeks. There are 200 people expected to take part in this research study within the Icahn School of Medicine at Mount Sinai.

Funds for conducting this research study are provided by the National Institutes of Health (NIH) and Icahn School of Medicine at Mount Sinai. The CBD study product is provided by Brains Bioceutical Investigational Cannabidiol Product (BSPG CBD).

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

DESCRIPTION OF WHAT IS INVOLVED:

If you agree to take part in this research study, here is what may be involved:

- Research activities may take place in several buildings on the Icahn School of Medicine at Mount Sinai campus, including the lab suite at 1399 Park Ave, New York, NY and the testing suite at 1425 Madison Ave, New York, NY. In addition, you will be asked periodically during the day to input your subjective feelings on a digital diary (smartphone app) that will also provide you with a reminder to take the study drug.
- Because this research study involves the use of CBD, a note must be included in your electronic medical record that you are taking part in the research. This way, anyone involved in your medical care will know that you are a study participant, and they can work to avoid any problems or negative outcomes that could arise if they do not know.
- Individuals with OUD have an increased risk for overdose and thus death. As such, study participants will have weekly follow ups with a medical clinician (MD, physician assistant, or nurse practioner) that will also include a discussion on medication adherence and evaluation of current use of medications and other substances. Cognitive-behavior therapy and education will also be provided including harm reduction interventions and overdose prevention. Naloxone kits and training will be provided by the medical clinician. Brief intervention and referral to additional counseling will occur for any participants who need a higher level of care due to worsening of their substance use.
- We will be utilizing the Oura Ring (which is similar to a smart watch, in ring form) to collect physiological measures, such as vital signs and sleep data, we will also be integrating the eHive data collection application with the Oura Ring for streamlined data gathering. During the day, the Oura Ring measures heart rate, body temperature, activity levels, calories and steps. During sleep, the Oura Ring measures resting heart rate, heart rate variability, respiratory rate, body temperature,

breathing disturbances, light sleep, deep sleep, REM Sleep, nighttime movement, sleep timing and sleep quality. The Oura Ring will be provided to you at no cost. Before utilizing the Oura Ring and eHive application, you will download the eHive application and carefully review the eHive platform consent to ensure your understanding of the data collection process.
  - The eHive application will collect participant information including your full name, year of birth, and contact email. No other personal information is collected.
  - If you do not own a smartphone and as a result cannot participate in the eHive program you are still able to participate in this research study.
  - You have been provided with a consent form and terms of service for the eHive platform, allowing you to gain knowledge of the eHive platform before consenting to be in this study.
- Screening Visit (Visit 1): 3-hrs to 5-hrs
  - Review of this consent document
  - Physical exam, including vitals and medical history; Electrocardiogram (stickers that record the electrical signal from the heart to check for different heart conditions are placed on the chest)
  - Urine pregnancy test (for anyone capable of becoming pregnant)
  - Routine blood draw (2-4 tubes of blood, which is about 2-4 tablespoons of blood)
  - Toxicological assessments: Alcohol and drug screening
  - MINI International Neuropsychiatric Interview, used for the detection of psychiatric conditions
  - Several questionnaires relating to health, pain, drug use and sleep
- Randomization Visit/1st Test Day (Visit 2): 3-hrs to 5-hrs
  - Vital Signs
  - Urine pregnancy test (for anyone capable of becoming pregnant)
  - Blood draw (2-4 tubes/about 2-4 tablespoons, every two weeks)
  - Toxicological assessments: Alcohol and drug screening
  - Several questionnaires relating to health, pain, drug use and sleep
  - Will be given oral CBD or placebo, prescribed twice daily
- Weekly Test Sessions 1-4, CDB 200mg/placebo twice a day (Visits 3-7): 3-hrs to 5-hrs
  - Vital signs; Electrocardiogram
  - Urine pregnancy test (for anyone capable of becoming pregnant)
  - Toxicological assessments: Alcohol and drug screening
  - Blood draw (2-4 tubes/about 2-4 tablespoons, every two weeks) and urine collection
  - Several questionnaires relating to health, pain, drug use and sleep
  - Participate in computer-based cue sessions that will include, viewing visual stimuli of drug-related and neutral imagery that may induce craving
  - Will be given oral CBD or placebo, prescribed twice daily
  - Weekly Medical check-in (By Clinician)
- Weekly Test Sessions 4-8, CBD 400mg twice a day (Visits 8-12): 3-hrs to 5-hrs
  - Vitals; Electrocardiogram
  - Urine pregnancy test (for anyone capable of becoming pregnant)
  - Toxicological assessments: Alcohol and drug screening
  - Blood draw (2-4 tubes/about 2-4 tablespoons, every two weeks) and urine collection
  - Several questionnaires relating to health, pain, drug use and sleep

- Participate in computer-based cue sessions that will include, viewing visual stimuli of drug-related and neutral imagery that may induce craving
- Will be given oral CBD, prescribed twice daily
- Weekly Medical check-in (By Clinician)

- Weekly Follow-Up Visits 1-4, Post-CBD dose (Visits 13-16): 3-hrs to 5-hrs
  - Urine pregnancy test (for anyone capable of becoming pregnant)
  - Toxicological assessments: Alcohol and drug screening
  - Blood draw (2-4 tubes/about 2-4 tablespoons, every two weeks) and urine collection
  - Several questionnaires relating to health, pain, drug use and sleep
  - Weekly Medical check-in (By Clinician)
  - Physical exam, including vitals; Electrocardiogram on last day

Randomization
This is a double-blinded, randomized, placebo control clinical trial. No one, not you, nor anyone from your medical team or from the research team will be able to choose or know what group you are assigned to or what study drug you get. It will be by chance, like flipping a coin. You will have an equal chance of being given either study drug. For this double-blinded study, neither you nor the Lead Researcher or your own doctor will know which study drug you are getting. You will receive 200mg CBD or placebo (twice daily; morning and evening) for a period of 4-weeks, followed by 400mg CBD (twice daily; morning and evening) for a period of 4-weeks. If there is an emergency, your own doctor can get this information.

Pregnancy
If you can possibly get pregnant, a urine test for pregnancy will be done before you begin the study and the pregnancy test will be repeated at every visit.

Since you are participating in a research study that involves CBD with potential risks to a developing fetus, it is recommended, for your protection, that you not become pregnant for the duration of the study. Also, you should not participate in the study if you are producing milk to feed a child as the study drug could harm your baby. CBD in animals has been associated with harmful effects to the fetus and fetal development and as previously mentioned, you will not be allowed to participate in this study if you are pregnant or if you cannot use an appropriate contraception method.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use effective birth control. Unless you are sexually abstinent, the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings)
- An intrauterine device (IUD)
- Contraceptive injection (Depo-Provera)
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam)
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

All birth control methods (other than abstinence and sterilization) are only effective if you use them properly, start them at least one month before you begin the research study, and continue using them

throughout the research study and for 60-days after the research study ends. If you are unsure whether the method of birth control you use is approved to use while you are in this study, you should ask the Lead Researcher before you begin the study. If you are less than 1-year post-menopausal, you could still become pregnant. If you or your partner become pregnant, or may be pregnant, at any time during the study or up to 60-days after you complete the study you must tell a person from the research team immediately. The research team may stop the study drug and refer you or your partner to an obstetrician/gynecologist for follow-up. Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Semen/Sperm:

While in this study, you will be exposed to CBD. Based on studies in animals, CBD has been shown to cause male reproductive organ changes that can result in reduced male fertility. CBD can be found in semen and alter sperm. Since you are taking part in a study using CBD, it is recommended that 1) you use a condom, 2) you do not get a partner pregnant or expose them to semen, and 3) you do not donate semen. These recommendations apply both while you are taking the study drug, and for an additional 60-days after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or semen even after you stop taking the study drug. You are encouraged to tell your partner(s) and/or their doctor(s) that you are participating in this clinical trial.

Future Contact:

The researchers may wish to use your personal contact information to contact you in the future. Do you give the researchers permission to **contact you** in the future to request the collection of additional information about you, discuss how your private information, study data and/or samples might be used, or discuss possible participation in another research study?

Please initial your choice: Yes_____ No_____

If “Yes”, please indicate your preferred method of contact: (initial all that apply)

[ ] Email [ ] Phone [ ] Letter [ ] Text

USE OF YOUR DATA AND/OR SAMPLES FOR FUTURE STUDIES:

The researchers would like your permission to keep your personal information (such as, name, address, date of birth, social security number), study data and/or samples (blood, tissue, urine, saliva, or any other body matter) to use or share in future studies. You can still be part of the study if you do not allow us to use or share them. Please select Yes or No to each of the questions below. To decline all future uses/sharing please select ‘No’ each time.

(1) Will you allow the researchers to store your data and/or samples to use in future research studies?

Please initial your choice: Yes_____ No_____

If you select No, please stop here and move to the next section, '**Your Responsibilities If You Take Part in This Research**' section below."

If yes, please continue to the next question and tell us how your personal information, study data and/or samples may be used in future research studies.

(2) The researchers can store your data and/or samples in one of two ways:

a) Anonymously (no one will know who the data and/or samples came from). If you choose this option, you can't change your mind. So, if you wanted to have your data and/or samples destroyed in the future, the team could not do it as they would not know which data and/or samples were yours.
b) Linked to your identity (using a code that can show the information came from you personally). In this case you could ask for your data and/or samples to be destroyed in the future if you want that to happen.

How would you like your data and/or samples stored? Please initial **ONE** choice below:

I would like my data and/or samples stored anonymously _____

I would like my data and/or samples stored with a link to my identity through the use of a code_____

(3) Do you give the researchers permission to keep the data and/or samples, so they could use them in future studies that are **directly related** to the purpose of the current study?

Please initial your choice: Yes_____ No_____

(4) Do you give the researchers permission to keep the data and/or samples indefinitely, so they could use them for future studies that are **not related** to the purpose of the current study (for example a different area of research)?

Please initial your choice: Yes_____ No_____

(4.1) From time to time, researchers outside of medicine and related sciences would like to use data and/or samples. This might be in the fields such as anthropology, human origins, mapping human migration patterns. Do you give permission for researchers **outside the field of medicine** to use your data and/or samples?

Please initial your choice: Yes_____ No_____

a. If the future research in a different area can be done without having to know that the data and/or samples came from you personally, that will be done.

b. If the future research in a different area requires that it is known specifically who the data and/or samples came from, then one of the following will be done:

I. If you allowed the researchers to contact you in the future, they may be able to contact you to explain why your data and/or samples is needed and what will be done with it. Your permission will be asked to use your data and/or samples in that research project.

II. If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical (for example, because you have moved), your data and/or samples may still be used. The Institutional Review Board (IRB) will be asked for permission to use the data and/or samples linked to your identity. The IRB can give permission for researchers to use and share identifiable health information without contacting you, but only if it determines that sharing the data and/or samples will not be more than minimal risk to you or your privacy. The IRB is a hospital or medical school, whose job it is to protect people who participate in research.

(5) Do you give permission to have your data and/or samples given **to other researchers,** including those at Mount Sinai, other medical or scientific institutions and for-profit companies, for use in research within the limits you have chosen above?

Please initial your choice: Yes_____ No_____

(6) Do you give permission to have portions of your data and/or samples deposited in large public databases (repositories) for use in research with the limits you may have chosen above? Please read the paragraphs below which explains repositories, then initial your choice:

Please initial your choice: Yes_____ No_____

To do more powerful research, it is helpful for researchers to share data and/or samples from the people they study. They do this by putting data and/or samples into a repository. A repository is where something is stored safely for a specified period of time. Data and/or samples from one study may be stored in a repository along with data and/or samples from other studies. Sample repositories are commonly called biobanks, while data repositories are commonly called databases. Researchers can then use the data and/or samples from multiple studies to learn even more about health and disease. If you agree to take part in this study, some of your genetic and health information might be placed into one or more scientific databases, but they will not share your direct identifiers (for example, name, address, date of birth). These databases are maintained by either Icahn School of Medicine at Mount Sinai, another institution, the federal government, or private companies. Any researcher who wants to do a study using data and/or samples from the repository must apply for permission. There are different ways of reviewing such requests. Researchers with an approved study may be able to see and use your data, along with that from many other people. Researchers may use your samples for genetic sequencing and other experimental testing. Researchers will always have a duty to protect your privacy and to keep your information confidential, but there are always risks associated with data and/or sample collection and sharing. They are described in more detail in the Risks section.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study, you will be responsible for the following:

- *Refrain from arriving at the study site with signs of alcohol intoxication or drug intoxication*
- *Refrain from arriving at the study site with opioid withdrawal symptoms*
- *Refrain from participating in another pharmacotherapeutic trial for the duration of this study*
- *Refrain from taking dietary supplements, grapefruit juice,* any medication, or combination of medications and supplements known to alter the metabolism of, or interact with CBD (buproprion, rifampin, barbiturates, phenothiazines, cimetidine, etc.)
- Refrain from breastfeeding, becoming pregnant or not using an appropriate method of contraception such as hormonal contraception (oral hormonal contraceptives, Depo-Provera, Nuva-Ring), intrauterine device (IUD), sterilization, or double barrier method (combination of any two barrier methods used simultaneously, i.e. condom, spermicide, diaphragm)
- Refrain from taking any CBD that is not provided to you by the study for the duration of this study

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

There will not be any costs to you if you agree to take part in this study. If you agree to take part in this study, you could be paid up to $2,000 for your time and effort. Full study visit payments will require negative urine drug tests for illicit drugs or illegally obtained prescription medications, and will be deferred if you are intoxicated or fail a urine or breathalyzer test. If you do not complete all of the study procedures for the 16 visits or you withdraw from the study for any reason, you will only receive payment for the visits and procedures you completed. The breakdown of reimbursement for completing all 16 visits and procedures is as follows:

- Visit 1 (Screening Visit): $60 ($30 if does not compete all screening procedures)
- Visit 2 (Randomization Visit/1st Test Day): $100
- Visits 3-7 (physiology/toxicology): EKG visit: $60 + $110/visit x 4 visits = $500
- Optional completion of daily digital diary for first 4 weeks of the study intervention: $200
- Visits 8-12 (physiology/toxicology): EKG visit: $60 + $110/visit x 4 visits = $500
- Visits 13-16 (follow-up post-intervention; physiology/toxicology): $100/visit x 4 visits = $400
- Optional completion of daily digital diary for the last portion of the study: $240

You will be issued a physical plastic debit card that your funds are loaded onto and can be used at your discretion. When a visit is completed, funds will be approved and loaded onto your physical card. You will be given the equivalent value of a round-trip MetroCard, which will be added to the card after each study visit. The funds will be available within 1 business day and can be used at your discretion.

In order to assign a physical card to you and load funds onto the card, your name, address, and date of birth is required. Registration is restricted to those 18 years and older; if a participant is a minor, card can be assigned to a consenting parent or legal guardian with the collection and entry of their personal information.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally, this happens if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

It is possible that products may someday be developed with the help of your data and/or samples, and there are no plans to share any profits from such products with you.

POSSIBLE BENEFITS:

This study is not designed to benefit you personally. However, there is a chance this study may benefit you, but this is not guaranteed. Others may benefit from what researchers learn from the study. While in the study, possible benefits to you may include reduction of craving and anxiety and reduced relapse to illicit drug use. Researches may learn whether Cannabidiol (CBD) can reduce craving and relapse in individuals with opioid use disorder (OUD). This study may benefit researchers in learning whether CBD can serve as a potential add-on treatment to reduce craving and anxiety in individuals with OUD maintained on opioid agonist therapy.

POSSIBLE RISKS AND DISCOMFORTS:

Physical risks of Cannabidiol: You may or may not experience discomfort while taking oral CBD. However, mild or temporary side effects have been reported in past studies of Cannabidiol. Physical risks may include fatigue, abdominal pain, GI upset, headache, nausea, vomiting, sedation, dizziness, mild elevation in blood pressure, diarrhea, flatulence, dry eye, breakthrough menstrual bleeding, mild anemia, mild elevation of liver function tests, elevated white blood cell count, rash, decreased appetite, weakness, insomnia, sleep disorder or poor quality sleep. Given the risk of sleep disorder, sedation, dizziness or fatigue, you should exercise caution around driving and operating dangerous or heavy machinery.

Additionally, in other studies involving patients with liver disease and/or patients with severe, refractory epilepsies, elevated liver enzymes levels in the blood were observed with the use of Cannabidiol. These participants also took other anti-seizure drugs for their condition that may have contributed to the elevated liver enzymes. Cannabidiol is not listed as a carcinogen (a substance that causes cancer) by the International Agency for Research on Cancer, some laboratory tests have, however, demonstrated that Cannabidiol may alter DNA (the genetic material inside cells) in animals.

Blood draw risks: Risks associated with blood draws may include bleeding, bruising, and pain at the injection site. After the blood draw you may experience dizziness or may faint.

Cue-induced craving in-lab session risks: It is possible that you could experience prolonged elevation of desire for the drug following the craving sessions, but the research team will provide a safe environment to minimize the probability of adverse events following a craving episode. To minimize any potential increase in craving beyond the laboratory session, previously established relaxation

procedures known to decrease drug craving will be used. In addition, psychological debriefing will be done with you after all sessions to ensure that you are clinically stable when you leave the study site. You will be monitored in person during designated study sessions, and by phone between sessions. Throughout the study, both objective (vitals, urine testing) and subjective (craving, stress, anxiety, feeling of imminent relapse) measures will be carefully assessed by the study medical clinicians. If relapse is imminent, or if any mental or physical symptom occurs that would require medical attention, you will be offered to consult with a Mount Sinai physician or other mental health provider, either as an outpatient, an inpatient or in the ER depending on the severity of the symptoms. A physician will be available at any time during the study for consultation or examination. You will also be provided with contact information of a research team member, and with a list of resources and clear steps to follow in case of physical or psychological deterioration.

Psychological risks (for example, embarrassment, fear, or guilt): This study also involves interviews and self-report questionnaires. These procedures do not deviate from standard practice and pose no major risk. One risk of the study is that some individuals may find certain questions in the research instruments uncomfortable or difficult to answer. Research staff are trained to clarify the questions and inform participants that they have the option of not answering specific questions, or even not participating in the study at all. Furthermore, should any participant experience severe emotional distress during a study visit, they will be referred by the trained research staff to a prearranged mental health provider.

Risk of loss of private information: There is always a risk of loss of private, confidential information; this risk always exists, but there are procedures in place to minimize the risk. A breach of confidentiality regarding your substance use and substance use problems could conceivably result in negative legal or social consequences for you. As such, measures to maintain strict confidentiality will be taken.

Social and economic risks: Social and economic risks exist whenever there is the possibility that participating in research or the revelation of data collected in the course of the research, if disclosed to individuals or entities outside of the research, could negatively impact others' perceptions of the participant. Social risks can range from jeopardizing the individual's reputation and social standing, to placing the individual at-risk of political or social reprisals. However, we will take all required measures to minimize the risk of a breach of confidentiality. Economical risks may include having to miss work or school for study visits or having to initially pay out-of-pocket to travel to the study visits. Participants are provided with a round-trip MetroCard for local travel after each study visit, as well as a ClinCard for payment of completed study visits.

Breastfeeding or pregnancy risks: If you are breastfeeding, are pregnant or become pregnant, this research may hurt your baby or your pregnancy in ways that are unknown. The unknown risks could be minor or major, such as death for the pregnancy. You should not become pregnant or get someone pregnant while you take part in this study. Please read the acceptable methods of birth control found under the Description of What Is Involved section of this document.

Legal and economic risks (violation of parole, loss of employment or employment opportunity): If you are on parole or if random drug tests are routinely administered at your place of employment, you

should know that since Cannabidiol is derived from one of the natural components of the Cannabis plant that contains tetrahydrocannabinol (THC), there is a very small chance a drug screening test for THC may show up as positive. The risk, however, is extremely minimal. A blood test may be able to rule out THC in your system as blood tests are more sensitive than urine tests. If your parole or your employment might be at risk because of a false positive THC, please inform a member of the research team. You will be provided with a letter that attests to the fact that you are in a clinical trial that may have caused a false positive result.

Group risks: Although your name will not be given to researchers, basic information such as your race, ethnic group, and sex may be shared. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or discrimination.

Privacy risks: Because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Since the database contains genetic information, a break in security may also pose a potential risk to blood relatives as well as yourself. For example, it could be used to make it harder for you (or a relative) to get or keep a job or insurance. If your private information was misused, it is possible you would experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.

Risk with use of Oura Ring: If you are being provided with an Oura Ring, you should understand that you are agreeing to data sharing and privacy agreements with Oura Health Oy and Ouraring Inc. However, Oura Ring will not know who you are since you will be assigned a specific Mount Sinai ID number and Study ID number. You will not sign an individual agreement with Oura Ring since the ring will be owned by Mount Sinai and Mount Sinai will not share any of your personal identification information with Oura Health. If you already have your own Oura Ring, it cannot be used for your participation in this study, as that ring (and the privacy agreement you already signed with the company) will be completely separate from the ring you will be given for participation in this study.

OTHER OPTIONS TO CONSIDER:

You may decide not to take part in this research study. If you decide not to take part, this will not affect the clinical care you receive at Mount Sinai. The choice is totally up to you.

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If you are injured or made sick from taking part in this research study, you will get medical care. Generally, it will be billed to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, copayments, and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this study at any time. No matter what you choose, your care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the study, please contact the Lead Researcher or the research staff.

If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the Lead Researcher can collect information from your routine medical care. If you agree, this data will be handled the same as research data.

You may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you stop being in the research study, the research team may not remove information they have already placed in the study database, and may continue to use that data as part of this study. The research team may ask you whether they can continue to collect information from your medical record.

If you decide you don't want your data and/or samples to be used for research anymore, you can contact the researcher and ask to have your data and/or samples withdrawn or labeled so that they will not be used in additional projects or shared. If your data and/or samples have already been shared with researchers, those researchers will be asked to stop using them. However, if any data and/or samples have already been shared without your identity or a linking code, it won't be possible to retrieve them. Data and/or samples that have already been used will not be affected by your decision. If your data and/or samples have already been deposited in an external repository, the study team will request that your data and/or samples be removed.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent. Additional reasons for removal from the study may include:

- Inability to cooperate with the requirements of the study
- You are found to be pregnant by a urine pregnancy test

Participation may be terminated by the investigator or the Institutional Review Board without the participant's consent at any time if the study ends, if the participant is not compliant with the research protocol or if continuing the research poses a serious risk to the participant.

CONTACT INFORMATION:

If you have any questions, concerns or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher at phone number 212.824.9314.

If there is an emergency, please call 911 or go to the emergency room. Let the emergency room staff know you are in a research study so they can contact the Lead Researcher if needed.

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are encouraged to talk to the Lead Researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?
PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

What PHI is collected and used in this research study, and might also be shared with others?

As part of this study, the research team at the hospital(s) involved in the research will collect your name, address, telephone number, birthdate, admission date, discharge date, e-mail address, social security number and medical records number.

During the study, the researchers will gather information by:

- Reviewing and/or taking your medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate, and temperature.
- Taking blood and urine specimens
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- The New York State Prescription Drug Monitoring Program will be accessed by the investigators to make sure that you are not taking prescription drugs that might interact with the study drug and cause harm to you.
- Accessing your electronic medical record in Epic

Why is your PHI being used?
Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who you are or that you took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example:

- The Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants and may need to see your information.
- If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your PHI?
As part of the study, the Lead Researcher, research team and others in the Mount Sinai workforce may disclose your PHI, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The United States Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP) (the government organization that is responsible for protecting human research participants).
- Outside laboratories that will be performing laboratory analysis

- The commercial sponsor and/or their representative (who will use the results for submissions to the Food and Drug Administration (the government organization that approves drugs or devices for medical use): Brains Bioceutical Investigational Cannabidiol Product (BSPG CBD).
- The sponsoring government agency and/or their representatives who need to confirm the accuracy of the results submitted to the government or the use of government funds: NIH.
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration.

In almost all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. The Certificate of Confidentiality obtained from the Department of Health and Human Services will not be used to prevent disclosure to local authorities of child abuse and neglect, or harm to self or others. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, *OHRP, as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document, you are authorizing this access.* The results of this research may be published. However, your name and other identifying information will be kept confidential.

For how long will Mount Sinai be able to use or disclose your PHI?
Your authorization for use of your PHI for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will not be able to access your medical records. This is done to prevent the knowledge of study results from affecting the reliability of the study. Your information will be available should an emergency arise that would require your treating physician to know this information to best treat you. You will have access to your medical record and any study information that is part of that record when the study is over or earlier, if possible. The research team is not required to release research information to you that is not part of your medical record.

Do you need to give the researchers permission to obtain, use or share your PHI?
NO! If you decide not to let the research team obtain, use or share your PHI, you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment, or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff. The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your PHI.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing your medical records or asking questions about your medical history or conditions, it is possible that they may learn information related to your HIV status. If that is the case, the following information concerns you. If researchers are not reviewing your medical records or asking questions about your medical history or conditions, then you may ignore the following section.

Notice Concerning HIV-Related Information
If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Certificate of Confidentiality
To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services. This is intended to ensure that your identity as a participant in this research study will not have to be disclosed as a result from a subpoena, for the purpose of identifying you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings other than to the FDA or OHRP as identified above.

The research staff will not share any of your personal information, study data and/or samples with anyone who is not a member of the research team, including any family members or friends, other than those identified above. However, you should know that if it is learned that you or someone else is threatened with serious harm, such as a child or an elderly person being abused, the research team may notify the appropriate authorities if necessary to protect you or others. A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. This means that you and your family must also actively protect your own privacy. If an insurer or employer learns about your research participation, and you agree that they can have your research information, then the researchers may not use the Certificate of Confidentiality to keep this information from them.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

ADULT PARTICIPANT:
Your signature below documents your permission to take part in this research study and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

_____	_____	_____	_____
Signature of Participant	Printed Name of Participant	Date	Time

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

_____	_____	_____	_____
Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:
When a witness is required to observe the consent process, it should be documented below (for example, when a participant is illiterate, visually impaired, or this document accompanies a short form consent).

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the participant.

_____	_____	_____	_____
Signature of Witness	Printed Name of Witness	Date	Time