INFORMED CONSENT FORM

Official Title: Randomized, Placebo-Controlled Trial of Extended-Release Naltrexone and Monthly Extended-Release Buprenorphine for Cocaine Use Disorder (CURB-2)

NCT number: NCT05262270

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PART-1

Title of Study: NIDA CTN Protocol 0109: Randomized, Placebo-Controlled Trial of Extended-Release Naltrexone and Monthly Extended-Release Buprenorphine for Cocaine Use Disorder (CURB-2)

Consent and Authorization to be part of a Research Study
To be conducted at
Center on Substance Use and Health (CSUH)
Cove Behavioral Health
Hennepin Healthcare
Mountain Manor Treatment Center
University of California, Los Angeles Vine Street Clinic (UVSC)
University of Arkansas for Medical Sciences (UAMS)
University of Illinois Chicago (UIC)
University of Chicago
Addiction Institute of Mount Sinai
University of Texas Southwestern Medical Center (UTSW)

Key Information about this Study

The purpose of this study is to see if combined treatment with injectable Vivitrol® (XR-NTX; extended-release naltrexone) and injectable Sublocade® (XR-BUP; extended-release buprenorphine) are safe and effective for helping people cut down or stop using cocaine. The study is evaluating whether eight weeks of the medication combination can help reduce cocaine use. You will be randomly assigned to either take the active medications or a placebo. While you are taking part in this study, you will be asked to attend approximately two visits every week for up to 12 weeks and then one visit per week for four weeks. During your participation in the study, you will complete a series of self-report questionnaires, answer interview questions, engage in physical examinations, and provide blood samples for testing. If you are selected to receive the active medications, you will receive a total of three doses of XR-NTX, injected into your buttock muscle and two doses of XR-BUP, injected under the skin on your stomach during this study. If you are selected to receive placebo, you will receive three doses of placebo injected into your buttock muscle and two doses of placebo injected under the skin on your stomach.

Currently, there are no medications approved by the United States Food and Drug Administration (FDA) to treat cocaine use disorder. XR-NTX and XR-BUP are not currently approved for this diagnosis. XR-NTX is an opioid antagonist, and it is currently approved to treat alcohol use disorder and opioid use disorder. An opioid antagonist blocks the effects that you would normally experience when taking an opioid. XR-BUP is a partial opioid agonist, and it is currently approved to treat opioid use disorder. A partial opioid agonist produces similar effects to what you would normally experience when taking an opioid but to a much lesser extent. There are risks involved with XR-NTX and XR-BUP. Most side effects reported by subjects taking XR-NTX and XR-BUP were headaches, nausea, dizziness, dry mouth, depressed mood, anxiety, vomiting, constipation, increase in liver enzyme levels in the blood, fatigue pain, redness, swelling and itching at the injection site. Most frequent side effects seen in XR-NTX and XR-BUP treated subjects were, headache, nausea, constipation, vomiting, insomnia, dizziness, and fatigue.

You may not receive benefit from taking part in this study. Taking part in this study may help scientists, doctors, and people with cocaine use disorder understand more about the treatment of your disease. While taking part in this study, your health will be monitored closely at study visits.

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study. If you understand all of the information about this study and decide to participate, you will be asked to sign and date this Informed Consent Form (ICF). You will be given a copy of this to keep for your personal records.
Please take time to review this information carefully. You may talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

This is a multi-site study, meaning it will take place at several locations. Because this is a multi-site study the ICF includes two parts. This form is Part 1 and includes information that applies to all study sites, like the purpose of the study and the research procedures to be conducted.

Part 2 of the consent form will include information specific to the study site where you are being asked to enroll. This could include any research procedures specific to a study site or local contact information for the study team.

Please take your time to review this information carefully. You may talk to the assigned researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, make sure you understand what the study is about, including the risks and possible benefits to you. Once again, don't hesitate to ask the researchers any questions that you have at any time during the entire course of the study.

Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation: You do not have to participate if you do not want to. You may also leave the study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the staff or doctors at your local institution. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the local institution, your status will not be affected in any way.

General Information – "Who is conducting this research?"

Lead Investigator
The Lead Investigator (LI) is the researcher directing this study; the LI is responsible for protecting your rights, safety, and welfare as a participant in the research. The LI for this study is Madhukar Trivedi, MD, Department of Psychiatry at the University of Texas Southwestern Medical Center (UTSW). Dr. Trivedi can be contacted via email at Madhukar.Trivedi@UTSouthwestern or phone at 214.648.0188.

Research Site and Site Principal Investigator
Please refer to Part 2 of the ICF, **Local Context Information Sheet (Part 2),** for details on the research site including information about the site Principal Investigator.

Study Sponsor and Funding Agency
The study Sponsor is the person who takes responsibility for and initiates a clinical investigation. The CTN-0109 study Sponsor is Madhukar Trivedi, MD. The National Institute on Drug Abuse (NIDA), a United States federal government research institute, is funding this investigational study. NIDA is providing money so that the researchers can conduct the study.

Purpose – "Why is this study being done?"

The purpose of this study is to see if combined treatment with XR-NTX and XR-BUP is safe and effective for treating patients with cocaine use disorder.

During this study you will be taking two active medications or placebo. The active medications are XR-NTX and XR-BUP. The inactive placebo is similar to the active / original medications and is given the same way but contains no active medication properties. While you are taking part in this study, you will be asked to attend approximately two visits every week for up to 16 weeks.

All references to the word “medication” can mean extended-release naltrexone, extended-release buprenorphine, or placebo.

All references to the word “researcher” means the study doctor and research personnel at the University of Texas Southwestern Medical Center and its affiliated hospitals or clinics or the study doctor and research personnel at the research site where you are.

Investigational Use of Drug
This study involves the use of two investigational medications called XR-NTX and XR-BUP. “Investigational” means that medication combination has not yet been approved by the US Food and Drug Administration (FDA) for treating cocaine use disorder.

What are the study medications?
The study medications are XR-NTX and XR-BUP.

XR-NTX (Vivitrol®) has been approved by the FDA for treatment of alcohol use disorder and opioid use disorder. XR-NTX is manufactured or made by the company Alkermes. XR-BUP (Sublocade®) has been approved by the FDA for treatment of opioid use disorder. XR-BUP is manufactured or made by the company Indivior. The researchers believe that this combination of medications may produce an effect in your brain to block signals that contribute to negative mood changes from the withdrawal of cocaine from your body. By blocking these signals, the researchers believe the medication will reduce your cravings and need to use cocaine, reduce feelings of depression, and reduce the symptoms of cocaine withdrawal (e.g., chills, anxiety, irritability). This medication combination has not been approved for treatment of cocaine use disorder.

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

An independent ethics committee or institutional review board has approved this study.

Information about Study Participants – “Who is participating in this research?”

You are being asked to be a participant in this study because you met the initial prescreening criteria and are currently using cocaine and want to stop or cut down your cocaine use. Additional screening procedures will be completed following the signing of this consent form to confirm your eligibility to continue your participation.

This study will enroll approximately 426 study participants between the ages 18 and 65 across about 12 sites.

Information about Study Procedures – “What will be done if you decide to be in the research?”

While you are taking part in this study, you will be asked to attend approximately 22 to 26 visits with the researchers. The study is divided into four phases: Screening / Baseline Phase, Randomization / Induction Phase, Medication Phase, and Follow-Up Phase.

Screening / Baseline Phase (up to three weeks)
After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. Some of the procedures are described below as “**standard care**” and would be done even if you do not take part in this research study. You will be told which ones are for “**research only.**”

The Screening / Baseline Phase will take up to three weeks from the day you sign this informed consent form (ICF). During this phase, you will be asked to provide urine samples at each visit, we will ask you questions about your drug use, and we will test for signs of sexually transmitted diseases (STD) and pregnancy, as relevant. You will also be asked to complete several questionnaires. You will meet with a study-doctor to evaluate your overall health and discuss any medications you are currently taking. The researchers will also conduct an electrocardiogram (ECG) to measure your heart activity.

Please note that the urine and blood tests in this study are designed for research, not for medical purposes. They are not useful for finding problems or diseases. Even though the researchers are not looking at your urine or blood to find or treat a medical problem, you will be told if there is something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. The collected urine and blood test results in this study will not be used for medical purposes. The results of the urine and blood samples will not be sent to you or to your regular doctor.

You may decide that you do not want an HIV test or any other screening for infectious diseases at any time after agreeing to be in this study. If you decide you do not want to be tested for HIV or any other infectious disease, you should tell a research study team member right away. If you decide to not get tested for HIV or any other infectious disease, you can still participate in the study.

The table below provides a summary of these procedures and an estimate of the number of times you will be engaged in them.

Screening / Baseline Procedures	**Description of Procedures**	**Frequency**
Urine Sample	You will be asked to provide a urine sample to assess recent substance use at every visit. At certain visits, this sample will also assess pregnancy, certain sexually transmitted infections, and general health.	Every visit
Vital Signs	You will have your blood pressure, heart rate, and temperature taken.	Every Visit
Timeline Follow Back	You will be asked to report your recent substance use	Every visit
Self-Report Questionnaires	You will be asked to complete various questionnaires about things like your mood, your anxiety, and your pain level. It is important to complete these questions truthfully and as instructed by researchers.	Every visit
Computerized Tasks	You will be asked to complete two computerized tasks to see how you learn information and make decisions	Once
Blood Draw	You will have blood taken from a vein in your arm to check your blood count, kidney function, liver function, and amount of sugar in your blood to help determine your overall general health. Blood drawn will also be used to conduct infectious disease testing. Some of your blood will be stored for later testing, and if you agree, possibly used for genetic testing. *Note: You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.*	Once

Screening / Baseline Procedures	Description of Procedures	Frequency
HIV Test	Blood will be tested for HIV, the virus that causes AIDS; counseling will be provided before and after you get test results.	Once
Physical Examination	You will be asked to participate in a physical exam that will include measuring your height, weight, listening to your heart and lungs, obtaining your temperature, pulse, and blood pressure, as well as collecting your medical history. The physical exam will **not** include a pelvic, rectal, or breast exam.	Up to 2 times
Clinical Interview	You will be asked questions to assess for any changes in mood or physical health, and to go over your medication changes and any medication side effects.	As needed
Electrocardiogram (ECG)	You will be asked to place sticky patches on your chest that are connected to a machine that shows and records the electrical activity of your heart.	Once

The Screening/Baseline Phase may last up to three weeks. You may come in two to six times during this phase of the study. Each visit during this phase may take one to four hours. Researchers may inform you at any time during these visits whether you are eligible to continue to randomization.

Randomization / Induction (one week):
The results of the screening exams, tests, and/or procedures will be reviewed to determine if the study is right for you. If you are not a good fit for the study, researchers may discuss the reasons with you. If researchers confirm and document that you are eligible to continue, you will be randomized.

You will be placed by chance (like the flip of a coin) in one of the two study groups: active medications or placebo. A computer program will be used to assign you to a group. Neither you nor the researchers will be allowed to choose or will know which group you are assigned to. However, if needed for a medical emergency, the researchers can quickly find out which study group you are in.

- Active Medication Group (XR-NTX and XR-BUP) combination with your current medications.
    - *Injectable Extended-Release Naltrexone (XR-NTX):* You will receive your first injection (380 mg of extended-release naltrexone) after you have completed all Screening / Baseline tests and you have been randomized to a study group. A licensed medical staff of the study will inject the XR-NTX into your buttock muscle and will monitor you for any adverse (unpleasant or harmful) events. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions. Prior to each XR-NTX injection, medical staff will need to ensure you are opioid-free.
    - *Injectable Extended-Release Buprenorphine (XR-BUP):* You will receive your first injectable extended-release buprenorphine approximately three days after your first dose of XR-NTX. Researchers will inject the XR-BUP under the skin on your stomach (abdomen). You may see or feel a small bump under your skin at the injection site for several weeks. Do not rub against or massage the injection site. Researchers will monitor you for any adverse (unpleasant or harmful) events after the injection. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions.
- Placebo Group (injectable placebo) which contains no active medication in combination with your current medications.

- *Placebo for Injectable Extended-Release Naltrexone (XR-NTX):* You will receive your first injection of placebo after you have completed all Screening / Baseline tests and you have been randomized to a study group. A licensed medical staff of the study will inject the placebo into your buttock muscle and will monitor you for any adverse (unpleasant or harmful) events. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions. Prior to each placebo injection, medical staff will need to ensure you are opioid-free.

- *Placebo for Injectable Extended-Release Buprenorphine (XR-BUP):* You will receive your first injectable placebo approximately three days after your first dose of the XR-NTX placebo. Researchers will inject the placebo under the skin on your stomach (abdomen). You may see or feel a small bump under your skin at the injection site for several weeks. Do not rub against or massage the injection site. Researchers will monitor you for any adverse (unpleasant or harmful) events after the injection. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions.

On the day you are randomized to one of the designated groups of the study, you will be asked to provide a urine sample, which will be tested for recent substance use and pregnancy (if female). You will speak with the researchers about your mood and about any medications you are taking. If it is determined safe for you to receive your first XR-NTX or matching placebo dose, it will be administered to you. Approximately three days later, you will receive your XR-BUP or matching placebo dose. During these two visits, you will be asked to remain at the site for monitoring after you receive your injection. While you wait, you will complete some questionnaires. Each of these visits may take approximately two hours.

Medication Phase (eight weeks)
During the Medication Phase you will be expected to return to the clinic twice a week for eight weeks (a total of 16 visits). You will receive active medication or placebo injections during this time in combination with your current medications (if applicable). XR-NTX or placebo will be administered during Weeks 3 and 6 and XR-BUP or placebo will be administered during Week 4. The table below gives you an overview of the study procedures and when they will take place during the Medication Phase.

Medication Phase Procedures	Description of Procedures	Frequency
Urine Sample	You will be asked to provide a urine sample to assess recent substance use at every visit. At certain visits, this sample will also assess pregnancy, certain sexually transmitted infections, and general health.	Every Visit
Vital Signs	You will have your blood pressure, heart rate, and temperature taken.	Every Visit
Timeline Followback	You will be asked to report substance use since your last visit	Every Visit
Self-Report Questionnaires	You will be asked to complete questionnaires about things like your mood, your anxiety, and your pain level. It is important to complete these questions truthfully and as instructed by researchers.	Every Visit
Computerized Task	You will complete a computerized task to see how you learn information.	Week 8
Study Medication Administration	You will receive study medications or matching placebo on Weeks 3 & 6 for XR-NTX and on Week 4 for XR-BUP	Weeks 3, 4, and 6
Blood Draw	You will have blood taken from a vein in your arm to check your blood count, kidney function, liver function,	Weeks 4 and 8

Medication Phase Procedures	Description of Procedures	Frequency
	amount of sugar in your blood to help determine your overall general health, and to measure the amount of study medication in your blood. Blood drawn will also be used for infectious disease testing (week 8 only) and some will be stored for later testing, including genetic testing if you agree to allow it. If you agree, an additional blood sample will be collected specifically for genetic testing. *Note: You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.*	
HIV Test	Blood will be tested for HIV, the virus that causes AIDS; counseling will be provided before and after you get test results.	Week 8
Physical Examination	You will be asked to participant in a physical exam that will include measuring your height, weight, listening to your heart and lungs, obtaining your temperature, pulse, and blood pressure, as well as collecting your medical history. The physical exam will not include a pelvic, rectal, or breast exam.	Week 8
Clinical Interview	You will be asked questions to assess for any changes in mood or physical health, and to go over your medication changes and any medication side effects.	Every Visit
Electrocardiogram (ECG)	You will be asked to place sticky patches on your chest that are connected to a machine that shows and records that electrical activity of your heart.	Week 8

The amount of time each visit takes will depend on the procedures. Visits during Weeks 1, 2, 5, and 7 may take 20 to 90 minutes. Visits during Weeks 3, 4, 6, and 8 may take up to four hours

If you become incarcerated at any point during the study, you will no longer be given the study drug. The researchers may still arrange research visits and complete any needed assessments and procedures that the prison institution will allow.

Follow-Up Phase (four weeks)
During the Follow Up Phase, you will no longer receive the study medications or placebo. During the Follow Up Phase, you will attend visits once a week for four weeks (Weeks 9, 10, 11, and 12). These visits will take place at the clinic and will involve the following procedures:

Visits during Weeks 9, 10, and 11:

Follow-Up Phase Procedures	Description of Procedures for Weeks 9, 10, and 11	Frequency
Urine Sample	You will be asked to provide urine samples to assess recent substance use at every visit and pregnancy as needed.	Every Visit
Vital Signs	You will have your blood pressure, heart rate, and temperature taken.	Every Visit
Timeline Followback	You will be asked to report substance use since your last visit.	Every Visit

Follow-Up Phase Procedures	Description of Procedures for Weeks 9, 10, and 11	Frequency
Self-Report Questionnaires	You will be asked to complete questionnaires about things like your mood, your anxiety, and your pain level. It is important to complete these questions truthfully and as instructed by researchers.	Every Visit
Blood Draw	You will have blood taken from a vein in your arm to measure the amount of study medication in your blood. *Note: You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.*	Week 10
Clinical Interview	You will be asked questions to assess for any changes in mood or physical health, and to go over your medication changes and any medication side effects.	Every Visit

Week 12 Visit or Last Study Visit for Early Withdrawal:

Follow-Up Phase Procedures	Description of Procedures for Week 12 or Last Study Visit for Early Withdrawal
Urine Sample	You will be asked to provide urine samples to assess recent substance use, and pregnancy and certain sexually transmitted infections.
Vital Signs	You will have your blood pressure, heart rate, and temperature taken.
Timeline Followback	You will be asked to report substance use since your last visit.
Self-Report Questionnaires	You will be asked to complete questionnaires about things like your mood, your anxiety, and your pain level. It is important to complete these questions truthfully and as instructed by researchers.
Computerized Task	You will complete a computerized task to see how you learn information.
Blood Draw	You will have blood taken from a vein in your arm to measure the amount of study medication in your blood. *Note: You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.*
Clinical Interview	You will be asked questions to assess for any changes in mood or physical health, and to go over your medication changes and any medication side effects.

Optional Genetic Testing

The National Institute on Drug Abuse (NIDA) and the University of Texas Southwestern Medical Center (UTSW) would like to help researchers learn more about the role genes play in cocaine use disorder and other conditions. These organizations are gathering medical information and genetic material from people like you and storing it at a repository (facility where genetic material can be stored safely).

As part of the study, you will have two samples of blood drawn to be stored at the UTSW Repository for later use. Approximately two tablespoons of blood will be drawn from a vein in your arm (or other location, if necessary) with a small sterile needle. This is the standard method used to obtain blood for routine hospital tests. You have the option to decide whether the future research done with your samples involves genetic testing.

We would also like to collect an additional blood sample to be stored at the NIDA Genetics Consortium Repository and used for genetic testing. If you agree, researchers will collect an additional sample of blood at one of your scheduled blood draws. Approximately two tablespoons of blood will be drawn from a vein in your arm (or other location, if necessary) with a small sterile needle. This is the standard method used to obtain blood for routine

hospital tests. Your sample will be marked with a coded identifier and will not be personally identifiable. Neither your name nor any identifying information will be given to the researchers who receive your samples.

De-identified data, including your medical history and results of tests, can be shared by releasing it into scientific databases, including those maintained by the National Institutes of Health (NIH). Sharing this information will help advance medicine and medical research by allowing other researchers to use this information in future research projects. The data will be stored and shared in a manner that would not allow someone to identify you. Please understand that this information cannot be removed once deposited in these databases.

Will my specimens be stored for future use?
Yes, your specimens will be evaluated by research scientists studying various disorders deemed appropriate by NIDA/UTSW in the future. Some portion may be frozen or stored for the duration of the study. Stored specimens may be analyzed in the future using additional technologies without you being asked to sign another consent form. While your direct participation in this study will end as described previously, the DNA isolated from your blood samples may continue to be studied for many years. Future research on your sample may include sequencing of all or part of your DNA. This is called whole genome sequencing (WGS). WGS provides complete genetic information that is unique to you. There is no plan to inform you of future research activities that may take place at these institutions using your specimens. It can also present risks if the test results became known to others, for example you could have problems with family members or insurance companies. There is also a risk that these test results could be combined with other genetic information to identify you.

Will my samples be used to study any other diseases besides my condition?
Yes. An important part of this research is to allow for associations to be made between different diseases. Your samples may be used for broad-based research for a variety of disease states.

Will my samples be used for genetic research?
Yes. Genetic research is an important part of the investigation into the causes of these diseases. The causes of many of these diseases are believed to be the result of combinations of inherited genes and possible various exposures to the environment.

There are no plans to inform you, or your relatives, about the results of genetic studies, since at this time the information is not thought to be medically useful.

What is DNA?
DNA means *deoxyribonucleic acid*. DNA is the substance in our cells which contains information we inherited from our parents and other family members. Your genes contain DNA which predict things like physical characteristics (eye color, hair color, height, etc.) and may also be a factor in whether you develop or are at risk of developing certain illnesses or disorders.

What is genetic testing?
Genetic tests look for naturally occurring differences in a person's genes or the effects of specific genes. These differences could indicate an increased chance of getting a disease or condition. Genetic testing includes gene tests (DNA testing) and sometimes biochemical tests (protein testing) if it relates to a specific gene.

In gene tests, DNA in cells taken from a person's blood, body fluids or tissues is examined for differences. The differences can be relatively large – a piece of a chromosome, or even an entire chromosome, missing or added. Sometimes the change is very small – as little as one extra, missing or altered chemical within the DNA strand. Genes can be amplified (too many copies), over-expressed (too active), inactivated, or lost altogether. Sometimes pieces of chromosomes become switched, turned over, or discovered in an incorrect location.

How is DNA obtained?
Cells from blood or other body materials are processed in a laboratory that has special equipment that can extract DNA and identify genes.

What will happen to the samples collected for this research?
Researchers will compare information about the health of participants with the results of research tests using their DNA. Your blood samples will be used to isolate DNA for genetic analysis. Part of your blood samples may also be used to grow a long-term cell line. This immortalized cell line, called a lymphoblastoid cell line (or fibroblast cell line) will be stored in a Cell Bank and will be available for research, both now and in the future. This also allows us to perform many tests without having to ask you for additional blood samples.

How long will my samples be kept?
The repository will keep your sample until it is all gone, becomes unusable, or until the end of the study. If your samples remain stored beyond your lifetime, your samples will be used as described in this document.

May other researchers use my samples?
When you provide samples for purposes of this study, your samples become the property of the Sponsor or Funding Agency, NIDA, and may be used for future studies or provided to other investigators at other medical research facilities without any identifiers.

Who decides which research scientists may receive samples of my DNA?
NIDA will decide which researchers at this medical center and at other medical centers may receive samples of your DNA. Your samples may be used in other research only if the other research has been reviewed and approved by an Institutional Review Board (IRB).

Could my samples be used for other purposes?
No. Your samples or your DNA will only be used for research. Research tests using your samples may possibly result in inventions or procedures that have commercial value and are eligible for protection by a patent. Compensation for any future commercial developments is not available from the University of Texas Southwestern Medical Center at Dallas, its researchers or other facilities or researchers whose research may benefit from the use of your sample.

By agreeing to the use of your samples in research, you are giving your samples without expectation of acknowledgment, compensation, interest in any commercial value or patent, or interest of any other type. However, you retain your legal rights during your participation in this research.

Will the results of research tests be reported to me?
No. Researchers will use samples of your DNA only for research. The samples will not be used to plan your health care. Indicate your choice regarding participation in the optional blood genetic component of the study in Part 2 of this consent.

Optional Electroencephalogram (EEG)
Your site may not offer the option to complete an EEG. If EEG is available at your site and you choose to participate, you will complete the procedure during screening and then again during Week 8 of the study. You will have a specialized cap put on your head which will measure your brain waves. It is important for you to have clean, dry hair with no gels or other hair products because they may interfere with the electrodes' ability to measure the brain signals. You will wear this cap for approximately 30 minutes.

Staying In-Touch
To help us keep in touch with you during the study, we will ask you for different ways to contact you so we can remind you of upcoming study visits. We will also ask you to let us know about other people who can pass you a

message to contact us. If we need to contact those people, we will not reveal any information about the study, unless you have signed a release for us to do so. We will ask you for your social security number (SSN) and similar information that may be used with public databases to locate you. We ask for this number because it can help us get in touch with you if we have trouble finding you. Your SSN will also help us with paying you for your study participation. We will only use your SSN for locating and paying you. We will always use the contact information you provide us first, before using your SSN. Keeping in touch with the researchers is required for study participation.

In addition, please be aware that if you become incarcerated while participating in this study, your decision to participate in this study will not affect your sentence, parole, or probation. Your participation cannot be used by any prison authorities, in any manner, to affect your conditions at the institution where you are held. If you do stop participating in this study, your sentence, probation, or parole will not be affected in any manner.

How long can I expect to be in this study?
This study includes up to three weeks for the Screening / Baseline Phase, one week for the Randomization / Induction phase, eight weeks for the Medication Phase, and four weeks for the Follow-Up Phase. The total duration of the study is about 16 weeks.

Could your participation end early?
There are several reasons why the researchers may need to end your participation in the study without your consent. Some possible reasons are:

- The researcher believes that it is not in your best interest to stay in the study
- You become ineligible to participate
- Your health condition changes, and you need treatment that is not allowed while you are taking part in the study
- You do not follow instructions from the researchers
- The study is stopped (may be due to reasons related to safety or funding)

Can I change my mind about participating?
Yes. You can agree to be in the study now and change your mind at any time and for any reason. You can withdraw from the study without any penalty or loss of benefits to you. Your decision will not change your regular care from your doctors.

If you decide to withdraw from this treatment early, please discuss with the research team by contacting your site Principal Investigator about your decision. Refer to the **Local Context Information Sheet (Part 2)** for contact information for the Principal Investigator at your site.

What do I have to do?
While you are in the study you **must**:

- Give correct information about your health history and health conditions
- Tell the researchers about any new medicine or drug you take during the study or any changes to your medicines or drugs
- Tell the researchers about any health problems you have during the study
- Come to all study visit appointments
- Complete all required study questionnaires
- Comply with study medication administration per the study schedule
- Not take part in any other investigational research studies
- Not take any other medications or remedies unless the researchers have approved them beforehand, including prescription and over-the-counter drugs such as vitamins and herbs

What happens if I stop the study early?

If you stop the study early, the researchers will ask that you come for a final follow-up visit to have final tests. This is to make sure that you are in good health. This information will be added to your study record.

If you have side effects after you stop the study early, the researchers may contact your other doctors who you see regularly. By signing this consent form, you agree that this information can be obtained and added to your study record unless you indicate otherwise.

If you stop the study early and withdraw your consent at any time, you agree not to limit the use of your study information collected up to the point of the end of study visit. The Sponsor will not collect any new information from you for any parts of the study from which you have withdrawn. Your collected samples will continue to be analyzed as described in this form unless you specifically ask for your samples to be destroyed. This is to protect the quality of the study.

Can I take the study medication after the study is over?
After the study is over, the research study will not continue to provide you with the study medications. The researchers will discuss your future medical care options with you.

What other treatments are there outside of this study?
Instead of taking part in this study, you may choose other alternative treatments. There are currently no FDA-approved medications to treat cocaine use disorder. The study doctor will discuss and inform you of available alternative treatment options.

What about my current medications?
You must tell the researchers about all prescription and over-the-counter medication you take. This includes vitamins and herbs and any other supplements.

Some medications are not allowed during the study. The researchers will tell you if this applies to you. No medications will be stopped solely for the purpose of making you eligible to enroll in this study. You should not stop taking any of your current medications unless your study doctor tells you to do so.

You must also tell the researchers all therapies (such as psychotherapy) you are using to help you with your cocaine use. You should also disclose any medical conditions you suffer from such as high blood pressure, diabetes, high cholesterol, heart disease, etc. Also, you should inform the researcher if anything changes with your medical history.

Risks – "What are the risks of participation in the research?"

Risks of Study Medications
All medications can cause side effects; the extent to which this occurs differs. There are risks to taking part in this investigational study. One risk is that you may have side effects while on the study medications. Side effects will usually go away soon after you stop taking study medications. In some cases, side effects can be long lasting.

There may be risks with the use of this new medication combination that are not yet known. Sometimes during a study, the Sponsor may learn new facts about the study medication combination or about cocaine use disorder. It is possible that this significant new information might make you change your mind about being in the study. If significant new information is discovered, the researchers will tell you about it right away.

Naloxone: You may receive naloxone prior to study medication injections if warranted. Naloxone is a small dose of medication that will help researchers ensure it is safe for you to initiate the study medications. Although you will be observed after administration of naloxone, you should immediately let the study medical team know if you have any of the signs of an allergic reaction so that they may obtain emergency assistance. Possible signs of an allergic reaction include hives, difficulty breathing, and / or swelling of your face, lips, tongue, or throat.

The study medications may cause some, all, or none of the side effects listed below:

Injectable Extended-Release Buprenorphine / Sublocade® (XR-BUP):
Most common / less serious side effects (approximately 5 to 10% experience these symptoms): headache, nausea, itching at the injection site, vomiting, constipation, increase in liver enzyme levels in the blood, fatigue, and pain at the injection site.

Less common/more serious side effects (less than 2% experience these symptoms): adrenal insufficiency (low function of the adrenal glands), fast / irregular heartbeat, and dizziness when standing. Long-term use of XR-BUP may cause fertility problems.

Overdose Risks: **Life-threatening respiratory depression, death, or serious harm can happen if you take benzodiazepines, sleeping pills, tranquilizers, muscle relaxants, sedatives, opioids, or if you drink alcohol in excess. It is very important to not use these substances while in the study and to tell the study staff and study clinicians all the medications and drugs that you take for any reason.**

Injections of XR-BUP or its placebo will be performed using safe and sterile techniques but may cause pain, tenderness, hardening or damage of body tissues, swelling, redness, bruising, itching, or infection at the injection site. Such injection site reactions have been the most common side effects associated with XR-BUP. The injection site will be monitored after each of the injections. You should report any injection site reactions immediately to the researchers. Any participants showing signs of injection site reactions such as a localized infection (abscess), skin infection (cellulitis), body tissue damage, or extensive swelling will be monitored by the researchers and treated accordingly. XR-BUP or its placebo will be injected into the fat layer underneath the skin. If the medication is injected by mistake into a muscle or into a lower layer of the skin, there may be a more serious injection site reaction. If this happens, you will receive the appropriate treatment and care. We will treat any pain you experience with a non-opioid analgesic whenever possible. If treatment of your pain requires opioid therapy, we will monitor you closely. XR-BUP must always be administered by a medical professional.

In rare cases, XR-BUP may cause liver injury. Signs of liver problems may include jaundice (skin or white part of your eyes turns yellow), urine turns dark, stools turn light in color, decreased appetite, stomach/abdomen pain, confusion, or nausea. For your safety, you will not be allowed to participate in the study if you have acute symptomatic hepatitis or liver failure. Researchers will also conduct tests to monitor your liver function throughout the study. Some cases of hypoglycemia have been reported in individuals taking buprenorphine. In most of these cases, individuals had predisposing risk factors, such as diabetes. There will be medical oversight throughout the study to monitor this and other risks.

Buprenorphine can be abused in this manner similar to other opioids because of the drug's properties and reactions in your body; however, the abuse potential is lower. **If you have adverse events, we can stop giving injections, but it is going to take a while to wear off. You will test positive for buprenorphine for a year or more after stopping it.**

When stopping XR-BUP, you may experience symptoms of opioid withdrawal, although this has not occurred in participants in other research studies using XR-BUP. Symptoms of opioid withdrawal include agitation, muscle aches, insomnia, nausea, and abdominal cramping.

XR-BUP may block the effects of opioid pain medications. If you need medications for pain relief while on this study, it is important that you tell your doctor that you are in a study and may be on XR-BUP. XR-BUP will not affect response to non-opioid pain medications such as aspirin or acetaminophen.

Injectable Extended-Release Naltrexone / Vivitrol® (XR-NTX):

Most common / less serious side effects (approximately 4 to 33% of people may experience these symptoms): Nausea, vomiting, diarrhea, abdominal pain, headaches, dizziness, insomnia, dry mouth, sore throat, irritated or runny nose, joint stiffness, muscle cramps, back pain, skin rash, changes in appetite, anxiety, tiredness, sleepiness, toothache, or depressed mood.

In rare cases, people who received naltrexone developed suicidal thoughts, or a type of pneumonia (lung inflammation) caused by an excess of a certain type of white blood cells in the lungs. The most serious side effect of naltrexone is liver injury, which has almost always occurred with oral doses of 1400 to 2100 mg per week. Recent study findings show that no evidence of liver injury was found in people receiving once monthly 380 mg XR-NTX injections. XR-NTX is being used every three weeks in this study rather than every four weeks as currently approved, so there may be additional unknown side effects. For your safety, you will not be allowed to participate in the study if you have acute symptomatic hepatitis or liver failure.

XR-NTX or placebo injections will be performed using safe and sterile techniques but may cause pain, tenderness, hardening or damage of body tissues, swelling, redness, bruising, itching, or infection at the injection site. Such injection site reactions have been the most common side effects associated with XR-NTX. The injection site will be monitored after each of the injections. You should report any injection site reactions immediately to the researchers. Any participants showing signs of injection site reactions such as a localized infection (abscess), skin infection (cellulitis), body tissue damage, or extensive swelling will be monitored by the researchers and treated accordingly.

XR-NTX may block the effects of opioid pain medications. If you need medications for pain relief while on this study, it is important that you tell your doctor that you are in a study and may be on XR-NTX. XR-NTX will not affect response to non-opioid pain medications such as aspirin or acetaminophen.

Overdose Risks: **Attempts to overcome opioid blockade due to XR-NTX may result in a fatal overdose. Because your tolerance is decreased, you may be more sensitive to the effects of opioids when you stop taking XR-NTX. Use of opioids after discontinuing XR-NTX may result in a fatal overdose because you may be more sensitive to lower doses of opioids.**
Let the researchers know if you have any of these serious side effects.

Withdrawal from opioids: For anyone who has opioids in their system, naloxone and naltrexone may cause opioid withdrawal symptoms such as agitation, muscle aches, insomnia, nausea, or abdominal cramping.

Allergic reaction: As with any medication, there is also the possibility of an allergic reaction. You will be monitored for about one hour following your naloxone challenge (if conducted) and study medication/placebo injections to see how you are responding.

During the study, if your problem becomes worse, your participation in the research may stop. If this happens, the researchers can discuss other care options with you.

Genetic Informational Risks
This research study includes genetic testing. Human tissue contains genes that determine many of a person's physical characteristics, such as the color of eyes and hair. In some cases, genetic testing of tissues can be used to indicate a risk for the development of certain diseases. Genetic information is unique to each individual and could potentially be used to discover possible changes in a person's future health status or life expectancy, or that of his/her children and family members.

Releasing this information to you could cause psychological distress, anxiety, or family problems. Releasing this information to others, such as including it in your medical record, may pose a possible risk of discrimination, or increase difficulty in obtaining or maintaining disability, long-term care, or life insurance.

These risks would occur if your information were released by mistake. The measures being taken to protect your privacy are discussed below and make this possibility unlikely.

Even though the results of genetic testing may not be linked to you, it is possible that people of your ethnic background may be found to be at more risk for certain diseases based on future genetic research and this information might harm you in the future as a member of the group. Also, there may be unknown risks of genetic testing in the future.

Risk of ECG
ECG patch adhesive may be cold and sticky. Shaving of hair to get the patch to stick may be required. You may develop a rash or redness where the patches were attached. This mild rash often goes away without treatment.

Risk of Urine Samples
You may experience some inconvenience or embarrassment related to providing urine samples.

Risk of Psychological Stress
Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

If you test positive for HIV, you will be informed. You may feel anxious or sad after receiving the results from a positive HIV test. Study staff will be available if you want to discuss how you are feeling.

Risk of Blood Draw
There are minor risks and discomforts associated with blood draw. Risks associated with drawing blood from your arm include minimal discomfort and/or bruising, infection, excess bleeding, or swelling of the vein and surrounding tissue. Clotting and/or fainting also are possible, although unlikely. The trained staff drawing your blood will seek to minimize these potential risks.

Risk of Loss of Confidentiality
Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Social Media
If you gave permission to be contacted through social media, the use of social media may pose an increased risk to privacy, but staff will take every effort to minimize that risk.

Risks Related to Withdrawing from the Study
If you decide to withdraw from this treatment early, please discuss with the research team. There is no risk to you if you do not complete the final study visit procedures noted above and you can choose not to participate in them.

Reproductive Risks
Women of childbearing potential: You should not become pregnant while taking part in this study because we do not know how the study drugs/procedures could affect a fetus, if a woman becomes pregnant during the study. It is important that you talk to your study doctor about avoiding pregnancy during this study. A urine pregnancy test will be done prior to your participation in the study and may be repeated later, if needed, to make sure you are not pregnant. If you take part in this study and you are sexually active, **you and any person that you have sex with must use medically acceptable birth control (contraceptives) during the study and for four months after your last injection of study medication**. Medically acceptable birth control (contraceptives) includes:

- surgical sterilization (such as hysterectomy, bilateral oophorectomy, or “tubes tied”)
- approved hormonal contraceptives (such as birth control pills, patch, or ring; Depo-Provera, Implanon)

- barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm)
- an intrauterine device (IUD),
- monogamous relationship where male partner has had a vasectomy
- complete abstinence from sexual intercourse with a male partner

If you think you might have become pregnant while you are in this study, you must tell one of the study doctors right away so that management of the pregnancy and the possibility of stopping the study can be discussed. There is a risk that your infant might experience neonatal opioid withdrawal syndrome (NOWS). NOWS can be treated.

If you become pregnant during your participation in this research study, the researchers would like to collect follow-up information regarding your pregnancy and condition of any newborn and report this to the Sponsor.

Risks to babies who are being breastfed: Women who are breastfeeding cannot take part in this study because we do not know what effect the drugs/procedures might have on their breast milk.
Males: XR-BUP may cause infertility and inability to have an erection in males. These side effects tend to be rare, temporary, and not severe. There are no known risks for the children that male participants may father. There are no expected risks to male partners of female study participants.

Other Risks: There may possibly be other side effects that are unknown at this time. If you are concerned about other unknown side effects, please discuss this with the researchers. There may be risks that are unforeseeable.

Are there risks if you also participate in research or other investigational research studies?
Being in more than one investigational research study at the same time may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one investigational study without approval from the researchers.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking and show them your medication card from the study.

What if a research-related injury occurs?
The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section “Contact Information” for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The site principal investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – “How could you or others benefit from your taking part in this study?”

There is no direct benefit to you by participating in this study. Your participation may help future patients. During the study, your condition may stay the same, improve, or worsen.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"

Instead of taking part in this study, you may choose other alternative treatments. There are currently no FDA-approved medications to treat cocaine use disorder. The researchers will discuss and inform you of available alternative treatment options.

Payments – Will there be any payments for participation?

You will be compensated for your participation in this study. Information regarding specific forms of payment is specified on your **Local Context Information Sheet (Part 2)**. Compensation will be provided after completion of study visits noted below. Your name, address, date of birth, and social security number will be shared with a third-party solely for the purposes of compensation processing. All information will be stored in a secure database.

Visit / Assessment	Amount	# of Payments	Total
Screening and Baseline Assessments	$80	2	$160
Randomization / Induction Visits	$40	2	$80
Electroencephalogram (EEG), if applicable	$50	2	$100
Injection Administrations	$50	5	$250
Response Bias Probabilistic Reward Tasks	Avg $16	3	Avg $48
Iowa Gambling Task Incentive	Up to $5	1	Up to $5
Clinic Visits (8-week Medication Phase)	$40	16	$640
End-of-Treatment Visit Bonus (Week 8B)	$60	1	$60
Attendance Bonus (attending all expected visits in each two-week block, Weeks 1 to 4)	$30	2	$60
Attendance Bonus (attending all expected visits in each two-week block, Weeks 5 to 8)	$50	2	$100
Follow-Up & Safety Visits (Weeks 9 to 12)	$50	4	$200
Total Compensation without EEG			**$1603**
Total Compensation with EEG			**$1703**

Up to $160 will be provided for completion of the **Screening / Baseline assessments**. The amount you will be paid will be divided between the total number of Screening visits you attend and the assessments you complete at each Screening visit. A minimum of two Screening visits is required. During the **Randomization / Induction Phase (Week 0)**, you will be given $40 per visit. During the **Medication Phase (Weeks 1 to 8)**, $40 will be provided for completion of assessments and for providing a urine sample ($15 will be provided for assessments without a urine sample). You will earn $50 for each injection administration. A monetary incentive of up to $5 will be provided at the end of the Iowa Gambling Task (a specific computer task), contingent on task performance and ending the task with a net positive result. You will earn an average of $16 for completion of the Response Bias Probabilistic Reward Task based on performance each time. You may earn a visit attendance bonus of $30 (received up to two times during Weeks 1 to 4) and an attendance bonus of $50 (received up to two times during Weeks 5 to 8). An attendance bonus

is earned when you attend every visit within each two-week block of the medication phase. During the **Follow-Up Phase**, you will receive $50 for completing each visit.

The EEG component is not available at all sites. If it is available and you complete the EEG component, you will earn $100 ($50 per EEG completed). If your site does not have the EEG component or you do not participate in the EEG component, the maximum you can receive for study participation is $1603. If your site does have the EEG component and you participate in the EEG component, the maximum you can earn is $1703.
There are no funds available to pay for parking expenses, lost time away from work and other activities, lost wages, or childcare expenses. Bus passes or other transportation arrangements may be available, if needed.

An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a participant in this study.

Certificate of Confidentiality:
To help us further protect your information this research is covered under a Certificate of Confidentiality from the U.S. Department of Health and Human Services (HHS). This Certificate adds special protections for research information that identifies you and will help researchers protect your privacy.

With this Certificate of Confidentiality, the researchers cannot be forced to disclose information that may identify you in any judicial, administrative, legislative, or other proceeding, whether at the federal, state, or local level. There are situations, however, where we will voluntarily disclose information consistent with state or other laws, such as:

- to HHS for audit or program evaluation purposes;
- information regarding test results for certain communicable diseases to the Texas Department of State Health Services, including, but not limited to HIV, Hepatitis caused by a virus, Anthrax, and Smallpox;
- if you pose imminent physical harm to yourself or others;
- if you pose immediate mental or emotional injury to yourself;
- if the researchers learn that a child has been, or may be, abused or neglected; or
- if the researchers learn that an elderly or disabled person has been, or is being, abused, neglected, or exploited.

The Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about your involvement in this research study. In addition, the researchers may not use the Certificate to withhold information about your participation in this research study if you have provided written consent to anyone allowing the researchers to release such information (including your employer or an insurance company). This means that you or your family must also actively protect your privacy.

A Certificate of Confidentiality does not represent an endorsement of this research project by the Department of Health & Human Services or any other Federal government agency.

How will my information and/or blood samples be used?
With appropriate permissions, your samples and collected information may also be shared with other researchers here, around the world, and with companies. Your sample(s) and other collected information will be marked with a

coded identifier and will not be personally identifiable. Neither your name nor any identifying information will be given to the researchers who receive your samples.

By agreeing to participate in this study, your information or samples could be used for future research studies or sent to other investigators for future research studies without additional consent from you. The information that identifies you will first be removed from your information or samples. If you do not want your information or samples to be used for future research studies without your consent, you should not participate in this study.

De-identified data, including your medical history and results of tests, can be shared by releasing it into scientific databases, including those maintained by the National Institutes of Health (NIH). Sharing this information will help advance medicine and medical research by allowing other researchers to use this information in future research projects. The data will be stored and shared in a manner that would not allow someone to identify you. Please understand that this information cannot be removed once deposited in these databases.

Research policies require that private information about you be protected. This is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

Will you be contacted for future studies?
You may be contacted for future studies if the researchers think you may qualify, but you are under no obligation to participate in a new study. Participation in any additional study is entirely voluntary and refusing to volunteer for an additional study will not affect your participation in the primary study.

Contact Information – Who can you contact if you have questions, concerns, comments, or complaints?

Please see your **Local Context Information Sheet (Part 2)** for contact information for your study site. If you have questions now, feel free to ask researchers at your site. If you have additional questions, concerns, comments, or complaints later or you wish to report a problem or injury which may be related to this study please contact the individuals listed on your **Local Context Information Sheet (Part 2)**.

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees research on human subjects. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a research participant, and take any concerns, comments, or complaints you may wish to offer. You can contact the HRPP by calling the office at 214.648.3060.

Concise Summary [NIDA CTN Protocol 0109: Randomized, Placebo-Controlled Trial of Extended-Release Naltrexone and Monthly Extended-Release Buprenorphine for Cocaine Use Disorder (CURB-2)]

This is an 8-week, double-blind, randomized placebo-controlled trial of the efficacy of a combination of extended-release naltrexone (XR-NTX) and extended-release buprenorphine (XR-BUP) compared to matched placebo injections (PBO-Inj) for the treatment of cocaine use disorder (CUD).

You will have tests, exams and procedures that are for study purposes. Each clinic visit will last up to four hours.

There are risks to this study drug that are described in this document. Some risks include nausea, diarrhea, headaches, abdominal pain, increase in liver enzymes in blood, fatigue, and pain at the injection site.

If you are interested in learning more about this study, please discuss additional details with the researchers at your site.

Title of Study: NIDA CTN Protocol 0109: Randomized, Placebo-Controlled Trial of Extended-Release Naltrexone and Monthly Extended-Release Buprenorphine for Cocaine Use Disorder (CURB-2)

Consent and Authorization to be part of a Research Study
To be conducted at
Center on Substance Use and Health (CSUH)
Cove Behavioral Health
Hennepin Healthcare
Mountain Manor Treatment Center
University of California, Los Angeles Vine Street Clinic (UVSC)
University of Arkansas for Medical Sciences (UAMS)
University of Illinois Chicago (UIC)
University of Chicago
Addiction Institute of Mount Sinai
University of Texas Southwestern Medical Center (UTSW)

Key Information about this Study

The purpose of this study is to see if a combined treatment with injectable Vivitrol® (XR-NTX; extended-release naltrexone) and injectable Sublocade® (XR-BUP; extended-release buprenorphine) are safe and effective for helping people cut down or stop using cocaine. The study is evaluating whether eight weeks of the medication combination can help reduce cocaine use. You will be randomly assigned to either take the active medications or a placebo. While you are taking part in this study, you will be asked to attend approximately two visits every week for up to 12 weeks and then one visit per week for four weeks. During your participation in the study, you will complete a series of self-report questionnaires, answer interview questions, engage in physical examinations, and provide blood samples for testing. If you are selected to receive the active medications, you will receive a total of three doses of XR-NTX, injected into your buttock muscle and two doses of XR-BUP, injected under the skin on your stomach during this study. If you are selected to receive placebo, you will receive three doses of placebo injected into your buttock muscle and two doses of placebo injected under the skin on your stomach.

Currently, there are no medications approved by the United States Food and Drug Administration (FDA) treat cocaine use disorder. XR-NTX and XR-BUP are not currently approved for this diagnosis. XR-NTX is an opioid antagonist, and it is currently approved to treat alcohol use disorder and opioid use disorder. An opioid antagonist blocks the effects that you would normally experience when taking an opioid. XR-BUP is a partial opioid agonist, and it is currently approved to treat opioid use disorder. A partial opioid agonist produces similar effects to what you would normally experience when taking an opioid but to a much lesser extent. There are risks involved with XR-NTX and XR-BUP. Most side effects reported by subjects taking XR-NTX and XR-BUP were headaches, nausea, dizziness, dry mouth, depressed mood, anxiety, vomiting, constipation, increase in liver enzyme levels in the blood, fatigue and pain, redness, swelling and itching at the injection site. Most frequent side effects seen in XR-NTX and XR-BUP treated subjects were headache, nausea, constipation, vomiting, insomnia, dizziness, and fatigue.

You may not receive benefit from taking part in this study. Your taking part in this study may help scientists, doctors, and people with cocaine use disorder understand more about the treatment of your disease. By taking part in this study, your health will be monitored closely at study visits.

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study. If you understand all of the information about this study and decide to participate, you will be asked to sign and date this Informed Consent Form (ICF). You will be given a copy of this to keep for your personal records.

Please take time to review this information carefully. You may talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about

your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

This is a multi-site study, meaning it will take place at several locations. Because this is a multi-site study the ICF includes two parts. This form is Part 1 and includes information that applies to all study sites, like the purpose of the study and the research procedures to be conducted.

Part 2 of the consent form will include information specific to the study site where you are being asked to enroll. This could include any research procedures specific to a study site or local contact information for the study team.

There is separate consent form that describes an optional collection of a blood sample for genetic testing and the option to allow genetic testing to be performed on other blood samples. Additionally, a copy of the California Experimental Subject's Bill of Rights is included in Part 2.

Please take your time to review this information carefully. You may talk to the assigned researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, make sure, you understand what the study is about, including the risks and possible benefits to you. Once again, don't hesitate to ask the researchers any questions that you have at any time during the entire course of the study.

Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation: You do not have to participate if you do not want to. You may also leave the study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the staff or doctors at your local institution. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the local institution, your status will not be affected in any way.

General Information – "Who is conducting this research?"

Lead Investigator

The Lead Investigator (LI) is the researcher directing this study; the LI is responsible for protecting your rights, safety, and welfare as a participant in the research. The LI for this study is Madhukar Trivedi, MD, Department of Psychiatry at the University of Texas Southwestern Medical Center (UTSW). Dr. Trivedi can be contacted via email at Madhukar.Trivedi@UTSouthwestern or phone at 214.648.0188.

Research Site and Site Principal Investigator

Please refer to Part 2 of the ICF, **Local Context Information Sheet (Part 2),** for details on the research site including information about the site Principal Investigator.

Study Sponsor and Funding Agency

The study Sponsor is the person who takes responsibility for and initiates a clinical investigation. The CTN-0109 study Sponsor is Madhukar Trivedi, MD. The National Institute on Drug Abuse (NIDA), a United States federal government research institute, is funding this investigational study. NIDA is providing money so that the researchers can conduct the study.

Purpose – "Why is this study being done?"

The purpose of this study is to see if combined treatment with XR-NTX and XR-BUP is safe and effective for treating patients with cocaine use disorder.

During this study you will be taking two active medications or placebo. The active medications are XR-NTX and XR-BUP. The inactive placebo is similar to the active / original medications and is given the same way but contains no active medication properties. While you are taking part in this study, you will be asked to attend approximately two visits every week for up to 16 weeks.

All reference to the word "medication" can mean extended-release naltrexone and extended-release buprenorphine or placebo.

All reference to the word "researcher" means the study doctor and research personnel at the University of Texas Southwestern Medical Center and its affiliated hospitals or clinics or the study doctor and research personnel at the research site where you are.

Investigational Use of Drug
This study involves the use of two investigational medications called XR-NTX and XR-BUP. "Investigational" means that medication combination has not yet been approved by the U.S. Food & Drug Administration (FDA) for treating cocaine use disorder.

What are the study medications?
The study medications are XR-NTX and XR-BUP.

XR-NTX (Vivitrol®) has been approved by the FDA for treatment of alcohol use disorder and opioid use disorder. XR-NTX is manufactured or made by the company Alkermes. XR-BUP (Sublocade®) has been approved by the FDA for treatment of opioid use disorder. XR-BUP is manufactured or made by the company Indivior. The researchers believe that this combination of medications may produce an effect in your brain to block signals that contribute to negative mood changes from the withdrawal of cocaine from your body. By blocking these signals, the researchers believe the medication will reduce your cravings and need to use cocaine, reduce feelings of depression, and reduce the symptoms of cocaine withdrawal (e.g., chills, anxiety, irritability). This medication combination has not been approved for treatment of cocaine use disorder.

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

An independent ethics committee or institutional review board has approved this study.

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you met the initial prescreening criteria and are currently using cocaine and want to stop or cut down your cocaine use. Additional screening procedures will be completed following the signing of this consent form to confirm your eligibility to continue your participation.

This study will enroll approximately 426 study participants between the ages 18 and 65 across about 12 sites.

Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, you will be asked to attend approximately 22 to 26 visits with the researchers. The study is divided into four phases: Screening / Baseline Phase, Randomization / Induction Phase, Medication Phase, and Follow-Up Phase.

Screening / Baseline Phase (up to three weeks)
After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. Some of the procedures are described below as "**standard care**" and would be done even if you do not take part in this research study. You will be told which ones are for "**research only.**"

The Screening / Baseline Phase will take up to three weeks from the day you sign this ICF. During this phase, you will be asked to provide urine samples at each visit, we will ask you questions about your drug use, and we will test for signs of sexually transmitted diseases (STD) and pregnancy, as relevant. You will also be asked to complete several questionnaires. You will meet with a study-doctor to evaluate your overall health and discuss any medications you are currently taking. The researchers will also conduct an electrocardiogram (ECG) to measure your heart activity.

Please note that the urine and blood tests in this study are designed for research, not for medical purposes. They are not useful for finding problems or diseases. Even though the researchers are not looking at your urine or blood to find or treat a medical problem, you will be told if there is something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. The collected urine and blood test results in this study will not be used for medical purposes. The results of the urine and blood samples will not be sent to you or to your regular doctor.

You may decide that you do not want an HIV test or any other screening for infectious diseases at any time after agreeing to be in this study. If you decide you do not want to be tested for HIV or any other infectious disease, you should tell a research study team member right away. If you decide to not get tested for HIV or any other infectious disease, you can still participate in the study.

The table below provides a summary of these procedures and an estimate of the number of times you will be engaged in them.

Screening / Baseline Procedures	**Description of Procedures**	**Frequency**
Urine Sample	You will be asked to provide a urine sample to assess recent substance use at every visit. At certain visits, this sample will also assess pregnancy, certain sexually transmitted infections, and general health.	Every visit
Vital Signs	You will have your blood pressure, heart rate, and temperature taken.	Every Visit
Timeline Follow Back	You will be asked to report your recent substance use	Every visit
Self-Report Questionnaires	You will be asked to complete various questionnaires about things like your mood, your anxiety, and your pain level. It is important to complete these questions truthfully and as instructed by researchers.	Every visit
Computerized Tasks	You will be asked to complete two computerized tasks to see how you learn information and make decisions	Once
Blood Draw	You will have blood taken from a vein in your arm to check your blood count, kidney function, liver function, and amount of sugar in your blood to help determine your overall general health. Blood drawn will also be used to conduct infectious disease testing. Some of your blood will be stored for later testing, and if you agree, possibly used for genetic testing.	Once

Screening / Baseline Procedures	Description of Procedures	Frequency
	Note: You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.	
HIV Test	You will be tested for human immunodeficiency virus (HIV), the virus that causes AIDS; counseling will be provided before and after you get test results.	Once
Physical Examination	You will be asked to participate in a physical exam that will include measuring your height, weight, listening to your heart and lungs, obtaining your temperature, pulse, and blood pressure, as well as collecting your medical history. The physical exam will **not** include a pelvic, rectal, or breast exam.	Up to 2 times
Clinical Interview	You will be asked questions to assess for any changes in mood or physical health, and to go over your medication changes and any medication side effects.	As needed
Electrocardiogram (ECG)	You will be asked to place sticky patches on your chest that are connected to a machine that shows and records the electrical activity of your heart.	Once

The Screening / Baseline Phase may last up to three weeks. You may come in two to six times during this phase of the study. Each visit during this phase may take one to four hours. Researchers may inform you at any time during these visits whether you are eligible to continue to randomization.

Randomization / Induction (one week):
The results of the screening exams, tests, and/or procedures will be reviewed to determine if the study is right for you. If you are not a good fit for the study, researchers may discuss the reasons with you. If researchers confirm and document that you are eligible to continue, you will be randomized.

You will be placed by chance (like the flip of a coin) in one of the two study groups: active medications or placebo. A computer program will be used to assign you to a group. Neither you nor the researchers will be allowed to choose or will know which group you are assigned to. However, if needed for a medical emergency, the researchers can quickly find out which study group you are in.

- Active Medication Group (XR-NTX and XR-BUP) combination with your current medications.
    - *Injectable Extended-Release Naltrexone (XR-NTX):* You will receive your first injection (380 mg of extended-release naltrexone) after you have completed all Screening / Baseline tests and you have been randomized to a study group. A licensed medical staff of the study will inject the XR-NTX into your buttock muscle and will monitor you for any adverse (unpleasant or harmful) events. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions. Prior to each XR-NTX injection, medical staff will need to ensure you are opioid-free.
    - *Injectable Extended-Release Buprenorphine (XR-BUP):* You will receive your first injectable extended-release buprenorphine approximately three days after your first dose of XR-NTX. Researchers will inject the XR-BUP under the skin on your stomach (abdomen). You may see or feel a small bump under your skin at the injection site for several weeks. Do not rub against or massage the injection site. Researchers will monitor you for any adverse (unpleasant or harmful) events after the injection. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions.

- Placebo Group (injectable placebo) which contains no active medication in combination with your current medications.

    - *Placebo for Injectable Extended-Release Naltrexone (XR-NTX):* You will receive your first injection of placebo after you have completed all Screening / Baseline tests and you have been randomized to a study group. A licensed medical staff of the study will inject the placebo into your buttock muscle and will monitor you for any adverse (unpleasant or harmful) events. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions. Prior to each placebo injection, medical staff will need to ensure you are opioid-free.

    - *Placebo for Injectable Extended-Release Buprenorphine (XR-BUP):* You will receive your first injectable placebo approximately three days after your first dose of the XR-NTX placebo. Researchers will inject the placebo under the skin on your stomach (abdomen). You may see or feel a small bump under your skin at the injection site for several weeks. Do not rub against or massage the injection site. Researchers will monitor you for any adverse (unpleasant or harmful) events after the injection. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions.

On the day you are randomized into one of the designated groups of the study, you will be asked to provide a urine sample, which will be tested for recent substance use and pregnancy (if female). You will speak with the researchers about your mood and about any medications you are taking. If it is determined safe for you to receive your first XR-NTX or matching placebo dose, it will be administered to you. Approximately three days later, you will receive your XR-BUP or matching placebo dose. During these two visits, you will be asked to remain at the site for monitoring after you receive your injection. While you wait, you will complete some questionnaires. Each of these visits may take approximately two hours.

Medication Phase (eight weeks)
During the Medication Phase you will be expected to return to the clinic twice a week for eight weeks (a total of 16 visits). You will receive active medication or placebo injections during this time in combination with your current medications (if applicable). XR-NTX or placebo will be administered during Weeks 3 and 6 and XR-BUP or placebo will be administered during Week 4. The table below gives you an overview of the study procedures and when they will take place during the Medication Phase.

Medication Phase Procedures	Description of Procedures	Frequency
Urine Sample	You will be asked to provide a urine sample to assess recent substance use at every visit. At certain visits, this sample will also assess pregnancy, certain sexually transmitted infections, and general health.	Every Visit
Vital Signs	You will have your blood pressure, heart rate, and temperature taken.	Every Visit
Timeline Followback	You will be asked to report substance use since your last visit	Every Visit
Self-Report Questionnaires	You will be asked to complete questionnaires about things like your mood, your anxiety, and your pain level. It is important to complete these questions truthfully and as instructed by researchers.	Every Visit
Computerized Task	You will complete a computerized task to see how you learn information.	Week 8

Medication Phase Procedures	Description of Procedures	Frequency
Study Medication Administration	You will receive study medications or matching placebo on Weeks 3 & 6 for XR-NTX and on Week 4 for XR-BUP	Weeks 3, 4, and 6
Blood Draw	You will have blood taken from a vein in your arm to check your blood count, kidney function, liver function, amount of sugar in your blood to help determine your overall general health, and to measure the amount of study medication in your blood. Blood drawn will also be used for infectious disease testing (week 8 only) and some will be stored for later testing, including genetic testing if you agree to allow it. If you agree, an additional blood sample will be collected specifically for genetic testing. *Note: You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.*	Weeks 4 and 8
HIV Test	You will be tested for human immunodeficiency virus (HIV), the virus that causes AIDS; counseling will be provided before and after you get test results.	Week 8
Physical Examination	You will be asked to participant in a physical exam that will include measuring your height, weight, listening to your heart and lungs, obtaining your temperature, pulse, and blood pressure, as well as collecting your medical history. The physical exam will not include a pelvic, rectal, or breast exam.	Week 8
Clinical Interview	You will be asked questions to assess for any changes in mood or physical health, and to go over your medication changes and any medication side effects.	Every Visit
Electrocardiogram (ECG)	You will be asked to place sticky patches on your chest that are connected to a machine that shows and records that electrical activity of your heart.	Week 8

The amount of time each visit takes will depend on the procedures. Visits during Weeks 1, 2, 5, and 7 may take 20 to 90 minutes. Visits during Weeks 3, 4, 6, and 8 may take up to four hours.

Follow-Up Phase (four weeks)
During the Follow-Up Phase, you will no longer receive the study medications or placebo. During the Follow-Up Phase, you will attend visits once a week for four weeks (Weeks 9, 10, 11, 12). These visits will take place at the clinic and will involve the following procedures:

Visits during Weeks 9, 10, and 11:

Follow-Up Phase Procedures	Description of Procedures for Weeks 9, 10, and 11	Frequency
Urine Sample	You will be asked to provide urine samples to assess recent substance use at every visit and pregnancy as needed.	Every Visit
Vital Signs	You will have your blood pressure, heart rate, and temperature taken.	Every Visit

Follow-Up Phase Procedures	Description of Procedures for Weeks 9, 10, and 11	Frequency
Timeline Followback	You will be asked to report substance use since your last visit.	Every Visit
Self-Report Questionnaires	You will be asked to complete questionnaires about things like your mood, your anxiety, and your pain level. It is important to complete these questions truthfully and as instructed by researchers.	Every Visit
Blood Draw	You will have blood taken from a vein in your arm to measure the amount of study medication in your blood. *Note: You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.*	Week 10
Clinical Interview	You will be asked questions to assess for any changes in mood or physical health, and to go over your medication changes and any medication side effects.	Every Visit

Week 12 Visit or Last Study Visit for Early Withdrawal:

Follow-Up Phase Procedures	Description of Procedures for Week 12 or Last Study Visit for Early Withdrawal
Urine Sample	You will be asked to provide urine samples to assess recent substance use, and pregnancy and certain sexually transmitted infections.
Vital Signs	You will have your blood pressure, heart rate, and temperature taken.
Timeline Followback	You will be asked to report substance use since your last visit.
Self-Report Questionnaires	You will be asked to complete questionnaires about things like your mood, your anxiety, and your pain level. It is important to complete these questions truthfully and as instructed by researchers.
Computerized Task	You will complete a computerized task to see how you learn information.
Blood Draw	You will have blood taken from a vein in your arm to measure the amount of study medication in your blood. *Note: You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.*
Clinical Interview	You will be asked questions to assess for any changes in mood or physical health, and to go over your medication changes and any medication side effects.

Optional Genetic Testing

This study may include an optional collection of a blood sample for genetic testing and the option to allow genetic testing to be performed on other blood samples. You may choose not to have the blood sample for genetic testing collected or to allow your other blood samples to be used in future genetic research and still be in this study. You will be given a separate consent form to review related to these optional genetic samples.

Optional Electroencephalogram (EEG)

Your site may not offer the option to complete an EEG. If EEG is available at your site and you choose to participate, you will complete the procedure during screening and then again during Week 8 of the study. You will have a specialized cap put on your head which will measure your brain waves. It is important for you to have clean, dry hair with no gels or other hair products because they may interfere with the electrodes' ability to measure the brain signals. You will wear this cap for approximately 30 minutes.

Staying In-Touch
To help us keep in touch with you during the study, we will ask you for different ways to contact you so we can remind you of upcoming study visits. We will also ask you to let us know about other people who can pass you a message to contact us. If we need to contact those people, we will not reveal any information about the study, unless you have signed a release for us to do so. We will ask you for your social security number (SSN) and similar information that may be used with public databases to locate you. We ask for this number because it can help us get in touch with you if we have trouble finding you. Your SSN will also help us with paying you for your study participation. We will only use your SSN for locating and paying you. We will always use the contact information you provide us first, before using your SSN. Keeping in touch with the researchers is required for study participation.

In addition, please be aware that if you become incarcerated while participating in this study, your decision to participate in this study will not affect your sentence, parole, or probation. Your participation cannot be used by any prison authorities, in any manner, to affect your conditions at the institution where you are held. If you do stop participating in this study, your sentence, probation, or parole will not be affected in any manner.

How long can I expect to be in this study?
This study includes up to three weeks for the Screening / Baseline Phase, one week for the Randomization / Induction Phase, eight weeks for the Medication Phase, and four weeks for the Follow-Up Phase. The total duration of the study is about 16 weeks.

Could your participation end early?
There are several reasons why the researchers may need to end your participation in the study without your consent. Some possible reasons are:

- The researcher believes that it is not in your best interest to stay in the study
- You become ineligible to participate
- Your health condition changes, and you need treatment that is not allowed while you are taking part in the study
- You do not follow instructions from the researchers
- The study is stopped (may be due to reasons related to safety or funding)

Can I change my mind about participating?
Yes. You can agree to be in the study now and change your mind at any time and for any reason. You can withdraw from the study without any penalty or loss of benefits to you. Your decision will not change your regular care from your doctors.

If you decide to withdraw from this treatment early, please discuss with the research team by contacting your site Principal Investigator about your decision. Refer to the **Local Context Information Sheet (Part 2)** for contact information for the Principal Investigator at your site.

What do I have to do?
While you are in the study you **must**:

- Give correct information about your health history and health conditions
- Tell the researchers about any new medicine or drug you take during the study or any changes to your medicines or drugs
- Tell the researchers about any health problems you have during the study
- Come to all study visit appointments
- Complete all required study questionnaires
- Comply with study medication administration per the study schedule
- Not take part in any other investigational research studies
- Not take any other medications or remedies unless the researchers have approved them beforehand, including prescription and over-the-counter drugs such as vitamins and herbs

What happens if I stop the study early?
If you stop the study early, the researchers will ask that you come for a final follow-up visit to have final tests. This is to make sure that you are in good health. This information will be added to your study record.

If you have side effects after you stop the study early, the researchers may contact your other doctors who you see regularly. By signing this consent form, you agree that this information can be obtained and added to your study record unless you indicate otherwise.

If you stop the study early and withdraw your consent at any time, you agree not to limit the use of your study information collected up to the point of the end of study visit. The Sponsor will not collect any new information from you for any parts of the study from which you have withdrawn. Your collected samples will continue to be analyzed as described in this form unless you specifically ask for your samples to be destroyed. This is to protect the quality of the study.

Can I take the study medication after the study is over?
After the study is over, the research study will not continue to provide you with the study medications. The researchers will discuss your future medical care options with you.

What other treatments are there outside of this study?
Instead of taking part in this study, you may choose other alternative treatments. There are currently no FDA-approved medications to treat cocaine use disorder. The study doctor will discuss and inform you of available alternative treatment options.

What about my current medications?
You must tell the researchers about all prescription and over-the-counter medication you take. This includes vitamins and herbs and any other supplements.

Some medications are not allowed during the study. The researchers will tell you if this applies to you. No medications will be stopped solely for the purpose of making you eligible to enroll in this study. You should not stop taking any of your current medications unless your study doctor tells you to do so.

You must also tell the researchers all therapies (such as psychotherapy) you are using to help you with your cocaine use. You should also disclose any medical conditions you suffer from such as high blood pressure, diabetes, high cholesterol, heart disease, etc. Also, you should inform the researcher if anything changes with your medical history.

Risks – "What are the risks of participation in the research?"

Risks of Study Medications

All medications can cause side effects; the extent to which this occurs differs. There are risks to taking part in this investigational study. One risk is that you may have side effects while on the study medications. Side effects will usually go away soon after you stop taking study medications. In some cases, side effects can be long lasting.

There may be risks with the use of this new medication combination that are not yet known. Sometimes during a study, the Sponsor may learn new facts about the study medication combination or about cocaine use disorder. It is possible that this significant new information might make you change your mind about being in the study. If significant new information is discovered, the researchers will tell you about it right away.

Naloxone: You may receive naloxone prior to study medication injections if warranted. Naloxone is a small dose of medication that will help researchers ensure it is safe for you to initiate the study medications. Although you will be

observed after administration of naloxone, you should immediately let the study medical team know if you have any of the signs of an allergic reaction so that they may obtain emergency assistance. Possible signs of an allergic reaction include hives, difficulty breathing, and / or swelling of your face, lips, tongue, or throat.

The study medications may cause some, all, or none of the side effects listed below:

Injectable Extended-Release Buprenorphine / Sublocade® (XR-BUP):
Most common / less serious side effects (approximately 5 to 10% experience these symptoms): headache, nausea, itching at the injection site, vomiting, constipation, increase in liver enzyme levels in the blood, fatigue, and pain at the injection site.

Less common/more serious side effects (less than 2% experience these symptoms): adrenal insufficiency (low function of the adrenal glands), fast / irregular heartbeat, and dizziness when standing. Long-term use of XR-BUP may cause fertility problems.

Overdose Risks: **Life-threatening respiratory depression, death or serious harm can happen if you take benzodiazepines, sleeping pills, tranquilizers, muscle relaxants, sedatives, opioids, or if you drink alcohol in excess. It is very important to not use these substances while in the study and to tell the study staff and study clinicians all the medications and drugs that you take for any reason.**

Injections of XR-BUP or its placebo will be performed using safe and sterile techniques but may cause pain, tenderness, hardening or damage of body tissues, swelling, redness, bruising, itching, or infection at the injection site. Such injection site reactions have been the most common side effects associated with XR-BUP. The injection site will be monitored after each of the injections. You should report any injection site reactions immediately to the researchers. Any participants showing signs of injection site reactions such as a localized infection (abscess), skin infection (cellulitis), body tissue damage, or extensive swelling will be monitored by the researchers and treated accordingly. XR-BUP or its placebo will be injected into the fat layer underneath the skin. If the medication is injected by mistake into a muscle or into a lower layer of the skin, there may be a more serious injection site reaction. If this happens, you will receive the appropriate treatment and care. We will treat any pain you experience with a non-opioid analgesic whenever possible. If treatment of your pain requires opioid therapy, we will monitor you closely. XR-BUP must always be administered by a medical professional.

In rare cases, XR-BUP may cause liver injury. Signs of liver problems may include jaundice (skin or white part of your eyes turns yellow), urine turns dark, stools turn light in color, decreased appetite, stomach/abdomen pain, confusion, or nausea. For your safety, you will not be allowed to participate in the study if you have acute symptomatic hepatitis or liver failure. Researchers will also conduct tests to monitor your liver function throughout the study. Some cases of hypoglycemia have been reported in individuals taking buprenorphine. In most of these cases, individuals had predisposing risk factors, such as diabetes. There will be medical oversight throughout the study to monitor this and other risks.

Buprenorphine can be abused in this manner similar to other opioids because of the drug's properties and reactions in your body, however, the abuse potential is lower. **If you have adverse events, we can stop giving injections, but it is going to take a while to wear off. You will test positive for buprenorphine for a year or more after stopping it.**

When stopping XR-BUP, you may experience symptoms of opioid withdrawal, although this has not occurred in participants in other research studies using XR-BUP. Symptoms of opioid withdrawal include agitation, muscle aches, insomnia, nausea, and abdominal cramping.

XR-BUP may block the effects of opioid pain medications. If you need medications for pain relief while on this study, it is important that you tell your doctor that you are in a study and may be on XR-BUP. XR-BUP will not affect response to non-opioid pain medications such as aspirin or acetaminophen.

Injectable Extended-Release Naltrexone/Vivitrol® (XR-NTX):
Most common / less serious side effects (approximately 4 to 33% of people may experience these symptoms): Nausea, vomiting, diarrhea, abdominal pain, headaches, dizziness, insomnia, dry mouth, sore throat, irritated or runny nose, joint stiffness, muscle cramps, back pain, skin rash, changes in appetite, anxiety, tiredness, sleepiness, toothache, or depressed mood.

In rare cases, people who received naltrexone developed suicidal thoughts, or a type of pneumonia (lung inflammation) caused by an excess of a certain type of white blood cells in the lungs. The most serious side effect of naltrexone is liver injury, which has almost always occurred with oral doses of 1400 to 2100 mg per week. Recent study findings show that no evidence of liver injury was found in people receiving once monthly 380 mg XR-NTX injections. XR-NTX is being used every three weeks in this study rather than every four weeks as currently approved, so there may be additional unknown side effects. For your safety, you will not be allowed to participate in the study if you have acute symptomatic hepatitis or liver failure.

XR-NTX or placebo injections will be performed using safe and sterile techniques but may cause pain, tenderness, hardening or damage of body tissues, swelling, redness, bruising, itching, or infection at the injection site. Such injection site reactions have been the most common side effects associated with XR-NTX. The injection site will be monitored after each of the injections. You should report any injection site reactions immediately to the researchers. Any participants showing signs of injection site reactions such as a localized infection (abscess), skin infection (cellulitis), body tissue damage, or extensive swelling will be monitored by the researchers and treated accordingly.

XR-NTX may block the effects of opioid pain medications. If you need medications for pain relief while on this study, it is important that you tell your doctor that you are in a study and may be on XR-NTX. XR-NTX will not affect response to non-opioid pain medications such as aspirin or acetaminophen.

Overdose Risks: **Attempts to overcome opioid blockade due to XR-NTX may result in a fatal overdose. Because your tolerance is decreased, you may be more sensitive to the effects of opioids when you stop taking XR-NTX. Use of opioids after discontinuing XR-NTX may result in a fatal overdose because you may be more sensitive to lower doses of opioids.**

Let the researchers know if you have any of these serious side effects.

Withdrawal from opioids: For anyone who has opioids in their system, naloxone and naltrexone may cause opioid withdrawal symptoms such as agitation, muscle aches, insomnia, nausea, or abdominal cramping.

Allergic reaction: As with any medication, there is also the possibility of an allergic reaction. You will be monitored for about one hour following your naloxone challenge (if conducted) and study medication/placebo injections to see how you are responding.

During the study, if your problem becomes worse, your participation in the research may stop. If this happens, the researchers can discuss other care options with you.

Risk of ECG
ECG patch adhesive may be cold and sticky. Shaving of hair to get the patch to stick may be required. You may develop a rash or redness where the patches were attached. This mild rash often goes away without treatment.

Risk of Urine Samples
You may experience some inconvenience or embarrassment related to providing urine samples.

Risk of Psychological Stress
Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

If you test positive for HIV, you will be informed. You may feel anxious or sad after receiving the results from a positive HIV test. Study staff will be available if you want to discuss how you are feeling.

Risk of Blood Draw
There are minor risks and discomforts associated with blood draw. Risks associated with drawing blood from your arm include minimal discomfort and/or bruising, infection, excess bleeding, or swelling of the vein and surrounding tissue. Clotting and/or fainting also are possible, although unlikely. The trained staff drawing your blood will seek to minimize these potential risks.

Risk of Loss of Confidentiality
Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Social Media
If you gave permission to be contacted through social media, the use of social media may pose an increased risk to privacy, but staff will take every effort to minimize that risk.

Risks related to Withdrawing from the Study
If you decide to withdraw from this treatment early, please discuss with the research team. There is no risk to you if you do not complete the final study visit procedures noted above and you can choose not to participate in them.

Reproductive Risks

Women of childbearing potential: You should not become pregnant while taking part in this study because we do not know how the study drugs/procedures could affect a fetus, if a woman becomes pregnant during the study. It is important that you talk to your study doctor about avoiding pregnancy during this study. A urine pregnancy test will be done prior to your participation in the study and may be repeated later, if needed, to make sure you are not pregnant. If you take part in this study and you are sexually active**, you and any person that you have sex with must use medically acceptable birth control (contraceptives) during the study and for four months after your last injection of study medication**. Medically acceptable birth control (contraceptives) includes:

- surgical sterilization (such as hysterectomy, bilateral oophorectomy, or “tubes tied”)
- approved hormonal contraceptives (such as birth control pills, patch, or ring; Depo-Provera, Implanon)
- barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm)
- an intrauterine device (IUD)
- monogamous relationship where male partner has had a vasectomy
- abstinence from sexual intercourse with a male partner

If you think you might have become pregnant while you are in this study, you must tell one of the study doctors right away so that management of the pregnancy and the possibility of stopping the study can be discussed. There is a risk that your infant might experience Neonatal opioid withdrawal syndrome (NOWS). NOWS can be treated.

If you become pregnant during your participation in this research study, the researchers would like to collect follow-up information regarding your pregnancy and condition of any newborn and report this to the Sponsor.

Risks to babies who are being breastfed: Women who are breastfeeding cannot take part in this study because we do not know what effect the drugs/procedures might have on their breast milk.

Males: XR-BUP may cause infertility and inability to have an erection in males. These side effects tend to be rare, temporary, and not severe. There are no known risks for the children that male participants may father. There are no expected risks to male partners of female study participants.

Other Risks: There may possibly be other side effects that are unknown at this time. If you are concerned about other unknown side effects, please discuss this with the researchers. There may be risks that are unforeseeable.

Are there risks if you also participate in research or other investigational research studies?
Being in more than one investigational research study at the same time may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one investigational study without approval from the researchers.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking and show them your medication card from the study.

What if a research-related injury occurs?
If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The site principal investigator can provide you with more information.

Benefits – "How could you or others benefit from your taking part in this study?"

There is no direct benefit to you by participating in this study. Your participation may help future patients. During the study, your condition may stay the same, improve, or worsen.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"

Instead of taking part in this study, you may choose other alternative treatments. There are currently no FDA-approved medications to treat cocaine use disorder. The researchers will discuss and inform you of available alternative treatment options.

Payments – Will there be any payments for participation?

You will be compensated for your participation in this study. Information regarding specific forms of payment is specified on your **Local Context Information Sheet (Part 2)**. Compensation will be provided after completion of study visits noted below.

Visit / Assessment	Amount	# of Payments	Total
Screening and Baseline Assessments	$80	2	$160
Randomization / Induction Visits	$40	2	$80
Electroencephalogram (EEG), if applicable	$50	2	$100
Injection Administrations	$50	5	$250
Response Bias Probabilistic Reward Tasks	Avg $16	3	Avg $48
Iowa Gambling Task Incentive	Up to $5	1	Up to $5
Clinic Visits (8-week Medication Phase)	$40	16	$640
End-of-Treatment Visit Bonus (Week 8B)	$60	1	$60
Attendance Bonus (attending all expected visits in each two-week block, Weeks 1 to 4)	$30	2	$60
Attendance Bonus (attending all expected visits in each two-week block, Weeks 5 to 8)	$50	2	$100
Follow-up & Safety Visits (Weeks 9 to 12)	$50	4	$200
Total Compensation without EEG			**$1603**
Total Compensation with EEG			**$1703**

Up to $160 will be provided for completion of the **Screening / Baseline assessments**. The amount you will be paid will be divided between the total number of Screening visits you attend and the assessments you complete at each Screening visit. A minimum of two Screening visits is required. During the **Randomization / Induction Phase (Week 0)**, you will be given $40 per visit. During the **Medication Phase (Weeks 1 to 8)**, $40 will be provided for completion of assessments and for providing a urine sample ($15 will be provided for assessments without a urine sample). You will earn $50 for each injection administration. A monetary incentive of up to $5 will be provided at the end of the Iowa Gambling Task (a specific computer task), contingent on task performance and ending the task with a net positive result. You will earn an average of $16 for completion of the Response Bias Probabilistic Reward Task based on performance each time. You may earn a visit attendance bonus of $30 (received up to two times during Weeks 1 to 4) and an attendance bonus of $50 (received up to two times during Weeks 5 to 8). An attendance bonus is earned when you attend every visit within each two-week block of the medication phase. During the **Follow-Up Phase**, you will receive $50 for completing each visit.

The EEG component is not available at all sites. If it is available and you complete the EEG component, you will earn $100 ($50 per EEG completed). If your site does not have the EEG component or you do not participate in the EEG component, the maximum you can receive for study participation is $1603. If your site does have the EEG component and you participate in the EEG component, the maximum you can earn is $1703.

There are no funds available to pay for parking expenses, lost time away from work and other activities, lost wages, or childcare expenses. Bus passes or other transportation arrangements may be available, if needed.

An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board

and other groups that have the responsibility of monitoring research may want to see study records which identify you as a participant in this study.

Certificate of Confidentiality:
To help us further protect your information this research is covered under a Certificate of Confidentiality from the U.S. Department of Health and Human Services (HHS). This Certificate adds special protections for research information that identifies you and will help researchers protect your privacy.

With this Certificate of Confidentiality, the researchers cannot be forced to disclose information that may identify you in any judicial, administrative, legislative, or other proceeding, whether at the federal, state, or local level. There are situations, however, where we will voluntarily disclose information consistent with state or other laws, such as:

- to HHS for audit or program evaluation purposes;
- information regarding test results for certain communicable diseases to the Texas Department of State Health Services, including, but not limited to HIV, Hepatitis caused by a virus, Anthrax, and Smallpox;
- if you pose imminent physical harm to yourself or others;
- if you pose immediate mental or emotional injury to yourself;
- if the researchers learn that a child has been, or may be, abused or neglected; or
- if the researchers learn that an elderly or disabled person has been, or is being, abused, neglected or exploited.

The Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about your involvement in this research study. In addition, the researchers may not use the Certificate to withhold information about your participation in this research study if you have provided written consent to anyone allowing the researchers to release such information (including your employer or an insurance company). This means that you or your family must also actively protect your privacy.

A Certificate of Confidentiality does not represent an endorsement of this research project by the Department of Health & Human Services or any other Federal government agency.

How will my information and/or blood samples be used?
With appropriate permissions, your samples and collected information may also be shared with other researchers here, around the world, and with companies. Your sample(s) and other collected information will be marked with a coded identifier and will not be personally identifiable. Neither your name nor any identifying information will be given to the researchers who receive your samples.

By agreeing to participate in this study, your information or samples could be used for future research studies or sent to other investigators for future research studies without additional consent from you. The information that identifies you will first be removed from your information or samples. If you do not want your information or samples to be used for future research studies without your consent, you should not participate in this study.

De-identified data, including your medical history and results of tests, can be shared by releasing it into scientific databases, including those maintained by the National Institutes of Health (NIH). Sharing this information will help advance medicine and medical research by allowing other researchers to use this information in future research projects. The data will be stored and shared in a manner that would not allow someone to identify you. Please understand that this information cannot be removed once deposited in these databases.

Research policies require that private information about you be protected. This is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical

care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

Will you be contacted for future studies?
You may be contacted for future studies if the researchers think you may qualify, but you are under no obligation to participate in a new study. Participation in any additional study is entirely voluntary and refusing to volunteer for an additional study will not affect your participation in the primary study.

Contact Information – Who can you contact if you have questions, concerns, comments, or complaints?

Please see your **Local Context Information Sheet (Part 2)** for contact information for your study site. If you have questions now, feel free to ask researchers at your site. If you have additional questions, concerns, comments, or complaints later or you wish to report a problem or injury which may be related to this study please contact the individuals listed on your **Local Context Information Sheet (Part 2)**.

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees research on human subjects. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a research participant, and take any concerns, comments, or complaints you may wish to offer. You can contact the HRPP by calling the office at 214.648.3060.

Concise Summary [NIDA CTN Protocol 0109: Randomized, Placebo-Controlled Trial of Extended-Release Naltrexone and Monthly Extended-Release Buprenorphine for Cocaine Use Disorder (CURB-2)]

This is an 8-week, double-blind, randomized placebo-controlled trial of the efficacy of a combination of extended-release naltrexone (XR-NTX) and extended-release buprenorphine (XR-BUP) compared to matched placebo injections (PBO-Inj) for the treatment of cocaine use disorder (CUD).

You will have tests, exams and procedures that are for study purposes. Each clinic visit will last up to four hours.

There are risks to this study drug that are described in this document. Some risks include nausea, diarrhea, headaches, abdominal pain, increase in liver enzymes in blood, fatigue, and pain at the injection site.

If you are interested in learning more about this study, please discuss additional details with the researchers at your site.

INFORMED CONSENT FORM

Official Title: Randomized, Placebo-Controlled Trial of Extended-Release Naltrexone and Monthly Extended-Release Buprenorphine for Cocaine Use Disorder (CURB-2)

NCT number: NCT05262270

Document date: 05-20-24

PART-2

Title of Study: NIDA CTN Protocol 0109: Randomized, Placebo-Controlled Trial of Extended-Release Naltrexone and Monthly Extended-Release Buprenorphine for Cocaine Use Disorder (CURB-2)

Consent and Authorization to be part of a Research Study
to be conducted at
University of Texas Southwestern Medical Center

Who is conducting the study?
Sidharth Wakhlu, MD, Department of Psychiatry, University of Texas Southwestern Medical Center, is the Principal Investigator (PI) responsible for conducting this study. The PI can be contacted by email (sidarth.wakhlu@utsouthwestern.edu) or phone (214.645.6905).

This information sheet will describe any information that you are required to know and is specific to the University of Texas Southwestern Medical Center (UTSW). You will be given Part 1 of the informed consent document that will describe the purpose of the study and what will be done. You may talk to the researchers about this study if you have any questions.

Your doctor is a research investigator in this study. He is interested in both your medical care, welfare, and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

Compensation

You will be compensated for your participation in this study. This compensation is for your time and to help with costs involved with your participation Additionally, assistance with transportation may be provided at the discretion of the study team.

You will be issued a UT Southwestern Greenphire ClinCard, which can be used as a credit or debit card. Compensation will be credited to the card at the **completion / end** of each study visit. Your name, address, date of birth, and social security number will be shared with a third-party solely for the purposes of compensation processing. Your social security number is needed to process your payments. Study payments are considered taxable income and are reportable to the IRS. Should you decide not to provide your social security number, or your social security number does not match the name on file with the IRS, your study participation payment will be decreased in accordance with the current IRS tax rate. All information will be stored in a secure fashion.

Your Greenphire ClinCard will be credited at the end of each study visit. Amount will be based on **completed** assessments. For the schedule of compensation for each **completed** assessment, please refer to Part 1 of the consent form.

Please note that if you are on record as owing money to the State of Texas, such as for back child support or a delinquent student loan, the payment may be applied to that debt.

An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year unless it's a reimbursement.

Costs – Will taking part in this study cost anything?

Study participants will be provided with study medication and study related procedures at no cost to them or their insurance.

The sponsor will provide the study drug/device at no cost to you during this study.

What if a research-related injury occurs?

The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section "Contact Information" for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

Neither the University of Texas Southwestern Medical Center or affiliates a program to pay you if you are hurt or have other bad results from being in the study. If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Additional information about your local site

Research policies require that private information about you be protected, and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

What is Protected Health Information (PHI)?

Protected Health Information (PHI) is information about a person's health that includes information that would make it possible to figure out who it belongs to. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to researchers to see and use your health information for this study. In carrying out this study, the health information we will see and use about you will include: your medical history, blood work, information we get from your medical record, information contained in your underlying medical records related to your medical history and prior treatments, information that is created or collected during your participation in the study including medical and treatment history, information you give us during your participation in the study such as during interviews or from questionnaires, results of blood tests; demographic information like your age, marital status, the type of work you do, and the years of education you have completed.

We will get this information by asking you or by looking at your medical records as relevant.

How will your PHI be shared?

Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- The Sponsor (Dr. Trivedi) and the Funding Agency (National Institute on Drug Abuse, NIDA). The Sponsor includes any people, entities, groups, or companies working for or with the Sponsor or owned by the Sponsor. The Sponsor will receive written reports about your participation in the research. The

Sponsor may look at your health information to assure the quality of the information used in the research.
- The Research offices at the University of Texas Southwestern Medical Center.
- The members of the local study team.
- Indivior and Alkermes, the companies that make the study medications.
- The following collaborators at other institutions that are involved with the study: University of California, Los Angeles, and UT Health San Antonio.
- DSMB/DSMC, the committee that checks the study data on an ongoing basis, to determine if the study should be stopped for any reason.
- The Institutional Review Board (IRB), Human Research Protection Program Office and the Compliance Office of the University of Texas Southwestern Medical Center, and other groups that oversee how research studies are carried out.
- The Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug or device research.
- Representatives of domestic and foreign governmental and regulatory agencies may be granted direct access to your health information for oversight, compliance activities, and determination of approval for new medicines, devices, or procedures.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use, and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location, or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

The Genetic Information Nondiscrimination Act (GINA) is a federal law that will protect you in the following ways:
- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when deciding to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

What happens to information collected about me?
The following information explains how your medical and health records and the research data collected about you for the study may be used and disclosed.

Regulatory authorities, such as the Food and Drug Administration, as well as members of the ethics committee/institutional review board (IRB), employees at the study site, representatives of the Sponsor (Dr. Trivedi), and representatives of the funding agency (NIDA) may review your medical records to verify study procedures and/or data without violating your confidentiality, to the extent permitted by the applicable laws and regulations. By signing this consent form, you are authorizing such access.

Researchers will keep your personal medical records and a list that links each participant's name to his or her

code number for at least 15 years.

After your encoded Protected Health Information is disclosed to the Sponsor and Funding Agency, the results of the study may be reanalyzed later and may be combined with the results of other studies. The Funding Agency and people who work with the Funding Agency may use the results of this study for other research purposes, including:

- Reviewing the safety or effectiveness of the study medication and other products or therapies
- Evaluating other products or therapies for patients
- Developing a better understanding of disease
- Improving the design of future clinical trials

You are participating in a multi-site research study and your information may also be shared with researchers at associated sites for purposes of data analysis. Your records will be kept by the Sponsor and Funding Agency for as long as necessary. During that time, they will be kept confidential to the extent permitted by law.

De-identified data (which cannot be used to identify you) from this study will be available to researchers on another website, https://datashare.nida.nih.gov/ after the study is complete and the data analyzed. The primary outcome(s) publication for the full study will also be included along with study underlying primary data in the data share repository, and it will also be deposited in PubMed Central http://www.pubmedcentral.nih.gov/. These websites will not include information that can identify you. You can view these websites at any time.

The results of the study may be published in a medical book or journal or presented at meetings for educational purposes. If the results of the study are published, you will not be personally identified, and your identity will not be disclosed.

By signing this form, you are permitting direct access to and use of your medical records and information by the individuals and entities identified above for the purposes described. These entities may post information on your medical records regarding the medications you are taking.

By signing this document, you also give permission to the researchers to disclose the study results to the Sponsor, the Funding Agency, and representatives of the Sponsor or Funding Agency. The study results will not contain information that directly identifies you. The Sponsor will prevent those that do not need to access the results from viewing the results. Neither the Sponsor nor the Funding Agency will attempt to identify the study participant.

Can I get a copy of my medical records?
You have a right to see and make copies of your medical records. However, to ensure the reliability of the study, you agree that you will not be able to see or copy your records related to the study until the Sponsor and Funding Agency have completed all work related to the study. At that time, you may ask to see the study files related to your participation in the study, and you may ask the researchers to correct any study-related information about you that is wrong.

What if I change my mind and do not want my information used or disclosed?
The permission to use or disclose your protected health information for this study does not have an expiration date. If you no longer want to share your protected health information, you may cancel your permission at any time by writing to the researchers at your research site.

Sidarth Wakhlu, MD
University of Texas Southwestern Medical Center
Center for Depression Research and Clinical Care
1440 Empire Central Drive,
Level 3 Mood Disorders,
Dallas, Texas, 75247

If you cancel your permission after you have started in the study, the researchers will stop collecting your health information. Although they will stop collecting new information about you, they will need to use the information they have already collected to evaluate the study results. If you start the study and then cancel your permission, you will not be able to continue to participate in the study or receive any medications as part of the study. This is because the researchers would not be able to collect the information needed to evaluate the study medications.

How long will your PHI be used?
Your records will be kept by the Sponsor and Funding Agency for as long as necessary. During that time, they will be kept confidential to the extent permitted by law. You may cancel this authorization at any time according to the appropriate section on the previous page. By signing this form, you agree to let us use and disclose your health information for purposes of the study until the end of the study. This permission to use your personal health information expires when the research ends, and all required study monitoring is over.

How will your PHI be protected?
To protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. These code numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of UT Southwestern Medical Center for review or testing.

Research policies require that private information about you be protected, and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. As required by law, if you test positive for an HIV Infection, Hepatitis B, Hepatitis C, Chlamydia, and/or Gonorrhea, our staff must report this result to the Texas Department of State Health Services.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties, but you will not be allowed to participate in the study.

After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to Sidharth Wakhlu, MD. If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the researchers if you have a need to review your PHI collected for this study.

Because of the type of research, you can only access your PHI when the study is done. At that time, you have the right to see and copy the medical information we collect about you during the study, for as long as that information is kept by the researchers and other groups involved.

Contact Information – Who can you contact if you have questions, concerns, comments, or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments, or complaints later or you wish to report a problem which may be related to this study please contact:

Primary contact:
Sidarth Wakhlu, MD at Sidarth.Wakhlu@UTSouthwestern.edu or 214.645.6905

Secondary contact:
If primary is not available, contact
McKenna Dougherty at McKenna.Dougherty@UTSouthwestern.edu or 469.602.2362
Isabella Huddleston at Isabella.Huddleston@UTSouthwestern.edu or 817.262.9157

Additionally, you may also contact the Department of Psychiatry after-hours or during holidays at 214.648.5555.

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees investigational treatment on patients. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a treatment patient, and take any concerns, comments, or complaints you may wish to offer. You can contact the HRPP by calling the office at 214.648.3060.

This form is yours to keep.

Comprehension Quiz Questionnaire

CTN-0109: CURB-2
COMPREHENSION QUESTIONS

- My participation in this study is completely voluntary. ☐ True ☐ False
- Information about me will NOT be given to others under any circumstances. ☐ True ☐ False
- I will be asked to attend clinic visits 2 times per week during the 8-week medication phase. ☐ True ☐ False
- There are no risks or discomforts if I participate in this research study. ☐ True ☐ False
- If I do not participate in this study, there are other possible treatment options for me. ☐ True ☐ False
- The study doctor may end my participation in this research study to protect my health and safety, even if I would like to continue. ☐ True ☐ False
- I will receive compensation for my study participation. ☐ True ☐ False
- The EEG study procedure will be available across all study sites. ☐ True ☐ False

Research Consent & Authorization Signature Section

Permission for Specific Study Procedures

You will be given a copy of this consent form to keep.

Do you agree to let us collect a blood sample for NIDA genetic testing? *(Please initial either yes or no.)*

Yes Initials_____

No Initials_____

Do you agree to allow your blood samples stored at the UTSW Repository to be used for future genetic research? *(Please initial either yes or no.)*

Yes Initials_____

No Initials_____

If EEG is offered, do you agree to take part in it? *(Please initial either yes or no or indicate if not applicable.)*

Yes Initials_____

No Initials_____

or

Not Applicable Initials_____

Do you agree to let us contact your other doctors about your participation in this study? *(Please initial either yes or no or indicate if not applicable.)*

Yes Initials_____

No Initials_____

or

Not Applicable Initials_____

Do you agree to be contacted for future studies if the researchers think you may qualify? *(Please initial either yes or no.)*

Yes Initials_____

No Initials_____

Statement of Consent

If you agree to participate in this research and agree to the use of your protected health information in this research, sign this section. You will be given a copy Part 1 and Part 2 of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE FOLLOWING STATEMENTS ARE TRUE:

- You have read (or been read) the information provided above which is printed in English. This is a language that you read and understand.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.
- You have freely decided to participate in this research, or you are voluntarily giving your consent for another person to participate in this study because you believe this person would want to take part if able to make the decision and you believe it is in this person's best interest.
- You understand that a copy of the Part 1 and Part 2 signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.
- You authorize the collection, use and sharing of your protected health information (another person's protected health information) as described in this form.

Adult Signature Section

Printed Name of Participant	Signature of Participant	Date	Time AM PM
Printed Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date	Time AM PM

Blind or Illiterate Signature Section *At the time of consent, also complete this section if consent is obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English (e.g., blind, physically unable to write, etc.)*

Declaration of witness:

By signing below, I confirm I was present for the entire consent process. The method used for communication (e.g., verbal, written, etc.) with the subject was: _____.

The specific means (e.g., verbal, written, etc.) by which the subject communicated agreement to participate was: _____.

Printed Name of Witness	Signature of Witness	Date	Time AM PM