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BIOMEDICAL RESEARCH ALLIANCE OF NEW YORK LLC

[INSERT NAME OF INSTITUTION]

PARTICIPANT INFORMATION AND INFORMED CONSENT – RETENTION PHASE

Title of Study:	CTN-0100: Optimizing Retention, Duration and Discontinuation Strategies for Opioid Use Disorder Pharmacotherapy (RDD)
Protocol #:	CTN-0100
Sponsor:	National Institute on Drug Abuse (NIDA)
Lead Investigator:	Roger D. Weiss, MD Professor of Psychiatry Harvard Medical School McLean Hospital 115 Mill St. Belmont, MA 02478 Phone: (617) 855 2242 Email: rweiss@mclean.harvard.edu
Site Principal Investigator:	[INSERT NAME OF SITE PI] [INSERT ADDRESS] [INSERT PHONE NUMBER] [INSERT EMAIL]

Key Study Information

You are being invited to take part in a research study. Your participation is voluntary which means you can choose whether or not you want to take part in this study. This Key Study Information is a short summary of key information you should consider when deciding whether or not to take part in this study. Further down, the consent form contains more detailed information about your participation in the study and risks that you will need to consider in making your decision.

Purpose of the Research Study

The purpose of this research study is to test strategies, including medications, to help patients with opioid use disorder stay in treatment. The two medications that the study is using are buprenorphine and naltrexone.

Other Key Information

Your participation in this study may last about 2 years and will involve up to 28 visits. We estimate that up to 1,380 volunteers who are seeking treatment for opioid use disorder and meet the eligibility requirements will participate in the study. After reviewing the medication options with your medical provider, you will be asked to choose which medication you want for treatment of opioid use disorder. You can choose either buprenorphine (administration method will be assigned to you) or injectable naltrexone. Descriptions of each medication can be found in the full consent form, which follows this summary.

You will also be assigned at random (like the flip of a coin) to one of two behavioral arms: 1) standard medical management and counseling that your treatment program typically provides, or 2) standard medical management and counseling, as well as a mobile health application, called Connections, that includes resources useful to those seeking recovery from chronic illnesses. You will also be asked to have a physical

exam and a blood draw, to provide saliva samples, to fill out questionnaires and answer questions assessing your personal information.

Foreseeable Risks and Benefits
There are risks and discomforts associated with participating in this study. A list is included in the full informed consent document. These include:

- Your opioid use disorder may get worse regardless of which of the study drugs you receive. Continued use of opioids is associated with significant risk of impairment, and risks of overdose and death.
- If you decide to stop taking your medication for opioid use disorder, your risk of overdose and death may increase.
- The medications may have side effects. Buprenorphine may have side effects similar to opioids, such as constipation or sleepiness. Naltrexone will block the effect of opioid painkillers should you need them. Injections of buprenorphine or naltrexone may cause pain and inflammation at the site of injection.

You may or may not benefit personally from being in this study. However, we hope that in the future, other people might benefit from this study due to greater knowledge gained about the treatment of opioid use disorder.

Alternatives to Participation
Participation in research is voluntary. You can choose not to participate in the study. You may also decline to answer questions that you do not want to answer. If you decide **not** to participate in this study, there are several options available to help you stop your opioid use, both here at [NAME OF SITE] and at local treatment programs. Options, independent of the study, include methadone maintenance, buprenorphine taken under the tongue (sublingual) daily, extended-release injectable buprenorphine, extended-release injectable naltrexone, residential or therapeutic communities. If you join the study and relapse, or decide to stop participating at any point, your treatment team will work with you to help you find alternative treatment.

Please continue reading this informed consent form to learn more about this study.

For questions and concerns regarding any of this information, contact [INSERT NAME OF SITE PI, PHONE NUMBER AND EMAIL ADDRESS].

INFORMED CONSENT AND AUTHORIZATION

PURPOSE AND OVERVIEW OF THE STUDY

You are being invited to take part in a research study. Your participation is voluntary which means you can choose whether or not you want to take part in this study. If you enter the study, you can stop participating at any time. The research study is explained in this consent form.

The purpose of the study is to test approaches to improve how long people stay in treatment for opioid use disorder using evidence-based medications: sublingual buprenorphine, injectable buprenorphine or injectable naltrexone. Before you decide to be a part of this study, you need to know why the research is being done, what it will involve, and the risks and potential benefits. Ask the research staff to explain anything in this form or about the study that is unclear. Please take time to read this information carefully. Feel free to discuss it with your relatives, friends, and your medical provider. If you agree to take part in the research study, you will need to sign this consent form.

You are being invited to participate in this study because you are seeking treatment for opioid use disorder. Opioid use disorder is a dangerous condition with significant risk of death from overdose, as well as worsening in one's ability to function. Evidence-based medications, including methadone, buprenorphine, and naltrexone, have been studied in large clinical trials and shown to be effective at helping people stop using opioids. However, stopping the medication for opioid use disorder may create a high risk of relapse to opioid use. Therefore, the purpose of this study is to test ways to help people with opioid use disorder stay on medication (buprenorphine or naltrexone) and stay away from opioids.

In talking with your medical provider (who may be the medical provider for this study), you will first choose whether you want to be treated with buprenorphine or with injectable naltrexone.

If You Choose Buprenorphine, you will be randomly assigned (like the flip of a coin) to receive it in one of three forms. The forms of buprenorphine are:

- Standard Dose of Sublingual Buprenorphine (16mg): This is taken daily, in the form of a film that is placed under your tongue.
  or
- High Dose of Sublingual Buprenorphine (32mg): This is taken daily, in the form of a film that is placed under your tongue.
  or
- Extended-Release Injectable Buprenorphine: This is given as an injection. You will receive up to 4 injections in the first two weeks. After that, you will receive injections around once a month.

If You Choose Extended-Release Injectable Naltrexone, you will receive monthly injections of this medicine. Further descriptions of each of the medications are included below.

Clinical Visits

You will receive standard medical management (visits with your medical provider) during the study and will be encouraged to take advantage of counseling and other psychosocial treatment available at the clinic and in your community. You will also be assigned at random (like the flip of a coin) to one of two behavioral approaches (a 50-50 chance): either the usual counseling and psychosocial treatment offered at your treatment program; or that usual treatment in addition to an app, called Connections, that delivers resources useful for those seeking recovery from chronic illnesses.

It is recommended that you stay in treatment and on medication. Medication (buprenorphine or injectable naltrexone) will be provided free of charge by the study for up to 74 weeks (about 18 months) as long as you

continue to participate in the study. At the end of the 74 weeks, your treatment team will try to help you arrange for medication to continue through insurance or other ways of payment. The study team will continue to schedule research visits with you for an additional 24 weeks (about 6 months). At regular intervals over the 98 weeks (about 2 years) after you enter the study, the research team will ask to interview you about how you are doing, and ask you to fill out questionnaires and ask you to provide urine samples. These interviews and data collection will occur whether or not you stay on medication or stay in treatment.

DISCLOSURE OF FINANCIAL INTERESTS

This is a multi-site study supported by the National Institute on Drug Abuse (NIDA). Drs. Edward Nunes, at Columbia University Irving Medical Center/New York State Psychiatric Institute, Jennifer McNeely and John Rotrosen, at New York University Grossman School of Medicine, and Roger Weiss, at Harvard Medical School/McLean Hospital, are the national Lead Investigators of this study. [NAME OF SITE PI] is the Principal Investigator for this study at [NAME OF SITE].

MEDICATIONS

Please read the following definitions of medications that are mentioned in this consent form:

Buprenorphine: Buprenorphine is an opioid partial agonist, which means that it attaches to opioid receptors, but activates them only partially. Buprenorphine can reduce pain and cause other effects that are typical of opioids such as the "high", but usually less so than other opioids. Also, because it attaches tightly to opioid receptors, it usually blocks the effects of other opioids. If you choose to be treated with buprenorphine, you need to stay off opioids for long enough (usually around 24 hours) so that you are experiencing some opioid withdrawal symptoms before taking the first dose of buprenorphine. In this study, buprenorphine will be prescribed in one of two forms:

> Sublingual Buprenorphine (SL-BUP - Suboxone®): Sublingual (under the tongue) buprenorphine is often a combination of buprenorphine and naloxone. It is available as a pill or thin film that is placed under the tongue until it dissolves. It produces physical dependence, it can be addictive, and it can be misused. Sublingual buprenorphine can also block the effects of other opioids, and it can cause withdrawal symptoms in people who are physically dependent on other opioids. Sublingual buprenorphine is approved by the US FDA to treat opioid use disorder.
>
> In this study, sublingual buprenorphine will be provided as Suboxone® film. Suboxone® is a combination of buprenorphine and naloxone. The thin film is placed under the tongue until it dissolves. If you are randomly assigned (like the flip of a coin) to receive sublingual buprenorphine, you will be given sublingual buprenorphine film to take home and take on a daily basis.
>
> Extended-Release Injectable Buprenorphine (XR-BUP - CAM2038/BRIXADI™): Extended-release injectable buprenorphine contains buprenorphine in a liquid that is injected under the skin. This deposit slowly releases buprenorphine into the system over the next week or month. Systemic effects and side effects of injectable buprenorphine are similar to those of sublingual buprenorphine. However, injected forms of buprenorphine may also cause soreness, redness, and swelling, including small bumps under the skin, at the injection site. These local side effects are usually temporary. Injectable buprenorphine is approved by the US FDA to treat opioid use disorder. In this study, extended-release injectable buprenorphine will be provided as CAM2038/BRIXADI™.

Extended-Release Injectable Naltrexone (XR-NTX - Vivitrol®): Injectable naltrexone is an opioid antagonist, meaning that it blocks the effects of opioids. It is an extended-release (long acting) form of naltrexone that is administered as an injection into the muscles of the buttock about every 4 weeks. Injectable naltrexone is approved by the US FDA to treat opioid use disorder and also alcohol use disorder. If you choose to start the

injection of naltrexone, you first need to go through detoxification to wash opioids out of your system before naltrexone can safely be started. In this study, extended-release injectable naltrexone will be provided as Vivitrol®.

STUDY PARTICIPATION

We estimate that up to 1,380 volunteers who are seeking treatment for opioid use disorder and meet the eligibility requirements will participate in the study. You will first choose between medications, buprenorphine or injectable naltrexone, based on a discussion with your medical provider where you talk about each medication, have the opportunity to ask questions, and then make a choice. Participants will be enrolled and treated at approximately 20 outpatient treatment programs or primary care practices across the United States that are collaborating on the study. Detoxification and early abstinence may involve brief stays at inpatient and/or residential treatment settings.

In addition to the medication conditions, you will be randomized (assigned by chance, like the flip of a coin) to one of two behavioral treatment approaches: 1) standard Medical Management and counseling that your treatment program typically provides, or 2) standard Medical Management and counseling that your treatment program typically provides, as well as access to an app, called Connections. The Connections app offers digital cognitive behavioral therapy (CBT) content, CBT4CBT, in the form of videos, quizzes and interactive exercises to teach recovery skills. You will receive rewards for completing CBT modules and associated exercises. You will also receive rewards for providing urine samples that are negative for non-prescribed opioids. Rewards will be provided in the form of a cash/debit card.

Study Visits and Duration: Your participation will involve approximately 28 visits, which will take place over about 2 years. Your screening and baseline visit will take about 5 hours and can happen on more than one day. The rest of the visits will take between 30 minutes and 1.5 hours, plus time spent with your medical provider for Medical Management, counseling and other treatment. More information about study visits is in the next part of this consent form.

By taking part in this research, you are responsible for attending study visits, taking the assigned study medication, and communicating changes in your personal and health-related information to your treatment provider and the research team.

DESCRIPTION OF THE RESEARCH

Once you have reviewed this consent form with study staff and can show that you understand the procedures, risks and benefits of this study, and you have signed consent to participate, the following procedures will take place.

Screening/Baseline

You will discuss this Consent Form and the study with the study team in detail and have the opportunity to think it over and ask questions. If you want to participate, you will be asked to sign and date this informed consent form and to sign a release of medical information form so that study staff can access your medical records and clinical laboratory tests.

You will be asked to take part in a set of screening and baseline assessments that consists of a history of your substance use, medical and psychiatric history, physical examination, and a blood draw (equal to about 2 teaspoons) for liver function tests (if those are needed). You will be asked to complete questionnaires on your demographic information (such as date of birth, sex, ethnicity/race, education, employment history and marital status), current drug craving, risky behaviors, family history and origin, HIV status, family status, legal status, depression, anxiety, trauma, suicidal ideation, pain, history of intimate partner violence, quality of life, and motivations for beginning treatment.

The questionnaires used in this study ask about HIV and hepatitis C and B status. HIV and hepatitis related information may be shared with other members of the research team besides the Principal Investigator.

It is very important for the research team to be able to contact you while you are in the study (about 2 years), even if you have moved to a different treatment program or decided to discontinue treatment. It is also very important for the research that the team be able to interview you and find out how you are doing. The team will therefore ask you for information to help us locate you (such as your address, e-mail address, phone number(s), driver's license number, and social security number). We will also ask you to provide contact information for close friends or relatives whom we can contact in case we cannot reach you.

Randomization

Based on the information obtained during the screening visit, we will determine whether you are eligible to participate in this study. If you are eligible, you will choose between taking buprenorphine or injectable naltrexone. Patients choosing injectable naltrexone will be referred for detoxification, if needed, and started on extended-release injectable naltrexone (XR-NTX - Vivitrol®). Patients choosing buprenorphine will be randomized (by chance, like the flip of a coin, with an equal chance of getting each study drug) to treatment with either sublingual buprenorphine (SL-BUP - Suboxone®) at a standard dose (16mg/day); sublingual buprenorphine at a high dose (32mg/day); or extended-release injectable buprenorphine (XR-BUP - CAM2038/BRIXADI™). No matter what medication you are taking, you will also be randomly assigned to receive the Connections app.

Getting started on Injectable Naltrexone: If you choose injectable naltrexone, you must first detoxify from opioids to wash opioids out of your system. If you take naltrexone while opioids are still in your system, this can cause opioid withdrawal. Your clinical team will help you to accomplish the detoxification, which may involve referring you to an inpatient setting. If you have already completed detoxification and opioids are out of your system, as indicated by a urine sample tested for opioids, then you can go ahead and receive the first injection of naltrexone. If you are unable to start injectable naltrexone, you can still choose to be in the study and take buprenorphine.

If you are opioid-free, monthly injections will begin. Injectable naltrexone will be administered by intramuscular injection to the buttock. Subsequent injections will be administered approximately every 4 weeks, alternating between your left and right buttocks. At the end of the study, your treatment team will provide referrals to further appropriate treatment for opioid relapse prevention, including continued injectable naltrexone treatment, if available in the community. If you do not continue injectable naltrexone following the last injection, it is important to understand that you would no longer be tolerant to opioids. This means that even small doses of opioids could have large effects, putting you at risk for overdose and possible death if you were to use opioids. It is also possible to switch from naltrexone to other medications for treating opioid use disorder, including buprenorphine or methadone.

Sublingual Buprenorphine Induction and Treatment: If you choose buprenorphine, you first will need to abstain from opioids for long enough that you begin to experience withdrawal symptoms. Usually this means about 24 hours from last dose of opioids, but may be longer if you are coming off methadone. Once you are in withdrawal, taking the first "test dose" of buprenorphine (2mg or 4mg sublingual) should relieve the withdrawal symptoms. However, if you take the test dose of buprenorphine too soon, before experiencing enough withdrawal, then the first dose of buprenorphine could make the withdrawal worse. Once you have comfortably taken a test dose of buprenorphine, you can begin your maintenance buprenorphine.

If you have been randomly assigned to standard dose sublingual buprenorphine (16mg/day), your medical provider will try to get you to a dose of 16mg/day as quickly as possible, making adjustments for your comfort and possible side effects that you may experience.

If you are randomly assigned to high dose sublingual buprenorphine (32mg/day), your medical provider will try to get you to a dose of 32mg/day as quickly as possible, making adjustments for your comfort and possible side effects that you may experience.

Once you have started taking sublingual buprenorphine, you will be expected to take it on a daily basis. Each dose of sublingual buprenorphine is provided as a thin film that is placed under the tongue until it is completely dissolved. Sublingual buprenorphine will be dispensed at Medical Management visits with your physician or other prescriber for you to take at home. Sublingual buprenorphine will be provided to you throughout the study for 74 weeks, as long as you remain enrolled in the study. At the end of this time, if you wish to continue taking buprenorphine, the treatment team will assist you in obtaining reimbursement (for example, from your insurance) to continue it. If you do not wish to continue sublingual buprenorphine, or do not have access or the resources to continue, you may have several options. You could switch to maintenance treatment with methadone if a methadone maintenance program is available to you, or you could switch to injectable naltrexone or injectable buprenorphine if it is available (for example covered by your insurance). Or you could decide to discontinue buprenorphine, in which case you will be given a 4-week supply of sublingual buprenorphine to gradually discontinue so as to avoid experiencing withdrawal symptoms. It is important to understand that discontinuing medication, either buprenorphine or naltrexone, is potentially dangerous, because the medications provide some relative protection against overdose, and you are no longer protected once the medication is stopped.

If you are randomly assigned to either standard or high dose sublingual buprenorphine (SL-BUP), you will be expected to appear for two random medication callbacks visits. These visits will take approximately 15 minutes each, during which the study team will count the amount of sublingual buprenorphine you have and compare it to the amount dispensed.

Extended-Release Injectable Buprenorphine Induction and Treatment: If you are randomly assigned to take extended-release injectable buprenorphine, you must first get started on sublingual buprenorphine, as described above, by abstaining from opioids for long enough to begin to experience withdrawal, after which you will be given a test dose of sublingual buprenorphine. Once you have comfortably taken one or more test doses of sublingual buprenorphine, then you may receive your first injection of extended-release buprenorphine. You will receive up to 4 injections in the first two weeks to stabilize your dose. After that, injections will be administered about every 4 weeks for the duration of the study.

Study Visits During Active Study Phase: Study interventions will continue for up to 74 weeks (about 1.5 years). You will be expected to visit the clinic more often at the beginning of the study: 3 times in the first week, weekly (weeks 0-4), then every 2 weeks (weeks 4-6), and then about every 4 weeks until the completion of study-provided medication. At each visit, you will meet with research staff for study assessments. You will also meet with your physician or other prescriber (see Medical Management, just below). The physician or other prescriber will also be available between scheduled Medical Management visits for questions or problems. You will be expected to take medication as prescribed (injectable naltrexone and injectable buprenorphine monthly or sublingual buprenorphine daily). In addition, you will be encouraged to attend counseling sessions (see below).

Medical Management (MM): You are expected to attend Medical Management sessions with your physician or prescriber at the initiation of medication, in the middle of the first week and at weeks 1, 2, 3, 4, and 6, and then every 4 weeks (approximately month) until Week 74. During these MM sessions, your prescriber will discuss with you how you are progressing with your drug use and other problems. The discussion will include recommendations for abstinence from opioids and other drugs, taking your medication regularly, and sticking with other aspects of your treatment plan (counseling sessions and other treatment activities that have been recommended to you). If you were randomly assigned to Connections, then the discussion will also include how you are engaging with the app. If you are having trouble with abstinence, or with adherence to your

medication or other aspects of your treatment, you should discuss this with your physician/prescriber, who will try to help you with it. Medical Management sessions will typically last about 10-15 minutes.

Usual Counseling: Counseling (group and/or individual) may be offered in accordance with your treatment program's usual practice. All study participants are encouraged to attend offered counseling sessions. Although attendance at counseling sessions is not a requirement to remain in the study, we will ask you about the sessions you attended as well as other treatment-related activities you may have attended (such as Alcoholics Anonymous or Narcotics Anonymous meetings) as part of the study data.

Connections (mobile health) App: If you are assigned to receive the behavioral intervention, you will be treated with standard Medical Management and usual counseling, and also have access to an app, called Connections. You will be asked to provide your name and cell phone number or an email address in order to access the app. You will be asked to engage with the app, on your cell phone or a study provided Wi-Fi enabled device, several times per week. The Connections App includes multiple recovery and relapse prevention tools, such as an online form of cognitive behavioral therapy, which focuses on the connections between your thoughts, your behaviors, and drug use or non-use. The app also offers the opportunity to earn rewards for completing the modules, associated exercises, and for providing urine samples that are negative for non-prescribed opioids. The 8 modules are: Recognize The Triggers, Deal With Cravings, Stand Up For Yourself, Plan Don't Panic, Stop And Think, Go Against The Flow, Stay Safe, and Basics of Buprenorphine. Each module takes up to an hour to complete, can be repeated, and offers practice exercises you can review any time after completing a module. You are encouraged to discuss what you are learning from the app modules with your clinical care team. If you do not have a cell phone, the study will provide you with a device that you can use to connect to the app through Wi-Fi.

Assessments: At each visit you will be asked to respond to a number of questions and questionnaires about your drug use, craving, mood, how you are doing with the medication, your use of counseling and other treatments and services, and how you are doing overall. You will be asked to provide a urine sample to be tested for drugs. If you are taking buprenorphine, you will also be asked to provide a saliva sample three times during the study to test for specific drug levels.

Additional assessments are done less often, sometimes only once. These include updating your locator information, providing a genetics sample and a family origin questionnaire (if you have not already provided these for a related study), and questions about your risk behavior and quality of life. If you are of childbearing potential, you will be tested for pregnancy for as long as you are taking study medication.

Duration of Study Medication: You will be eligible to receive the medication assigned to you (sublingual buprenorphine-16mg, sublingual buprenorphine-32mg, extended-release injectable buprenorphine, or injectable naltrexone) through the study free of charge for up to 74 weeks from when you started. If you decide to stop or switch treatment, we want to continue to see you for study visits, so that we can find out how you are doing.

Follow-up Visits: You will be expected to attend 3 follow-up visits once the study treatment period has ended so we can learn about how you are doing, your ongoing treatment (if any), your drug use (if any) and life changes (job, family, legal, or psychiatric). Follow-up visits occur at weeks 4, 12, and 24 following the end of study-provided interventions (or weeks 78, 86, and 98 from when you started the study). It is very important that we be able to contact you to find out how you are doing, even if you have dropped out of treatment, or after the study-provided interventions portion of the study is over, so we will make every effort to contact you, including coming out to find you in the community.

If you become a prisoner (in jail or prison), we would still like to find out how you are doing. Therefore, if necessary, we will make an effort to collect follow-up data from you over the phone or in person. You will not

be able to receive your study medication if you are in jail or prison. However, once you are released from jail or prison you may return to your treatment program, and study medication may be resumed if your medical provider judges it is appropriate, and if you remain eligible. It is important to be taking one of the evidence-based medications for opioid use disorder before you leave jail/prison or resume medication immediately on returning to the community. This is because if you leave jail/prison on no medication you will have lost your tolerance for opioids, and the period after leaving prison is a high-risk time for opioid overdose and death. Details of the nature of the research will not be shared with staff at the jail or prison, and visits, whether in person or by phone, will only take place if your confidentiality can be maintained.

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 jail or 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.

GENETICS

Your genes are in the cells in your body. Genes make you different from anyone else. Some genes are responsible for inherited traits like hair and eye color. Some genes affect the chances that a person will get a certain disease or how their body responds to drugs. A saliva sample will be collected for DNA, so we can see whether your genetics relate to how you do in treatment and in this research study.

NIDA will store the genetic material in a central place in New Jersey, the NIDA Genetics Consortium Repository. Your DNA sample will be stored there permanently. Your sample will be de-identified, which means that your name or other identifying information will not be connected to it, only a code number. Researchers at this site and the study's Data and Statistical Center (DSC) and Clinical Coordinating Center (CCC) will have the code numbers that connect your genetic information to your identifying information. The DSC and CCC are run by Emmes. The genetics researchers will not have access to the link between your identifying information and your code number. At no time will your name or address or any other identifying information be released for research purposes. Your DNA may be used not only for this study, but for other research studies in the future.

Future Genetics Studies: Samples will be stored for an unlimited amount of time; genetic material (DNA, saliva components and cells) will remain frozen at the central repository and will be tested in future genetics studies (but only after removal of information that could identify you as the source of the material, as described below under "Confidentiality of Genetic Information"). From the frozen cells, researchers may create a living tissue sample called a "cell line." This cell line provides an unlimited supply of genetic material for future studies, therefore you will not have to provide any additional saliva samples. 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. The researchers will keep your sample until it is all gone, becomes unusable, or until the researchers or sponsor decide to discard the sample. If your sample remains stored beyond your lifetime, your sample will be used as described in this document.

Results of Genetics Studies: Knowledge of how genes and other factors affect health and disease is gathered by studying groups of people. This study and other genetics studies are not meant to test your individual medical status but are for research only. Therefore, neither you nor your medical provider will be given the results of the research on your genetic material. However, the researchers will share what they learn with other health professionals and scientists through research publications. If you have questions about whether any genetic tests would be useful to you, please ask your medical provider or health professional.

COSTS
You will not be charged for study medication, Medical Management sessions, laboratory tests, or assessments completed as a part of the study. The added behavioral intervention (Connections), if you are assigned to it, is provided free of charge by the study.

However, you or your third-party payer (insurance company, Medicaid, etc.) will be responsible for costs related to any standard substance use treatment or other services received that are not part of the research study, including detoxification and the on-going counseling and other psychosocial relapse prevention treatment that we encourage during the study (you are not required to attend these, and the study will not otherwise provide or reimburse for these services).

REIMBURSEMENT
You will receive reimbursement to offset costs of time and travel, and to provide incentives for attending study visits.

Milestone	**Amount**
Screening	$50 in [INSERT FORM OF PAYMENT]
Randomization	$50 in [INSERT FORM OF PAYMENT]
Baseline	$50 in [INSERT FORM OF PAYMENT]
Research visits at weeks 14, 38, and 62	$50 per visit in [INSERT FORM OF PAYMENT]
Research visits at weeks 26, 50, and 74	$100 per visit in [INSERT FORM OF PAYMENT
Follow-up visits at weeks 78 and 86	$30 per visit in [INSERT FORM OF PAYMENT]
Follow-up visit at week 98	$100 in [INSERT FORM OF PAYMENT]

Tax law may require the payer (e.g., research institution or third party) to report the amount of payment you receive from that payer to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally, this reporting would take place if you receive $600 or more from the payer in a calendar year. You would be responsible for paying the taxes on the payment you received from the study.

Your biospecimens, with or without identifiers, may be used for commercial profit and you will not share in this profit.

If you become a prisoner (including being in jail or prison, being on probation or parole, or being under house arrest or electronic monitoring), you may still be eligible to receive reimbursement for your continued participation if your institution approves the amount and method of reimbursement.

NEW INFORMATION
If any new information is learned about this study that might affect your willingness to stay in this study, you will be told about it promptly.

POTENTIAL RISKS AND DISCOMFORTS
The following are risks and discomforts that you may experience during your participation in this research study. There are risks of drug misuse, stress, emotional distress, inconvenience and possible loss of privacy and confidentiality associated with participating in a research study.

Drug Overdose and Death from Overdose: The medications you will be offered in this study, either buprenorphine or naltrexone, may reduce the risk of overdose while you are taking them. However, once you stop taking these medications, your risk of overdose and death goes up**. Drug overdose is a serious and common risk among people who are dependent on heroin, fentanyl, or other opioids. Overdose is often fatal.** This is because heroin and other opioids reduce the body's natural drive to breathe, and you can stop

breathing and die. Alcohol and other drugs, including sedating drugs like benzodiazepines (such as Xanax) or stimulants like cocaine or methamphetamine, can also increase the risk of overdose, especially if you combine them with heroin or other opioid drugs. When you have been taking drugs regularly, your body becomes less sensitive to them. This is called tolerance. When you stop taking drugs, or cut down, you lose tolerance, your body becomes more sensitive to the drugs again, and the risk of a dangerous overdose goes up. **Therefore, it is important for you to understand that if you are drug-free, for example after you detoxify, your system is more sensitive to heroin and other opioid drugs. This means that the amount of heroin, fentanyl, or other opioids that you used to take (at times when you were using drugs regularly in the past) could cause you to overdose, stop breathing, and die. It is also important to understand that if you get heroin, fentanyl, or other opioids that are not prescribed, you do not know what dose they contain, and the amount may be high enough to cause you to overdose and die. This is particularly true now that fentanyl and other drugs similar to fentanyl are commonly present in what is sold as heroin or other drugs. Fentanyl and other drugs similar to fentanyl can be deadly even in tiny doses.** The medications you will be offered in this study, either injection naltrexone or buprenorphine, may reduce the risk of overdose while you are taking them. However, once you stop taking these medications, your risk of overdose and death goes up.

Attempts to overcome the opioid blockade that occurs while being in treatment with injectable naltrexone, or with buprenorphine, 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 injectable naltrexone. Use of opioids after discontinuing injectable naltrexone may result in a fatal overdose because you may be more sensitive to lower doses of opioids. Use of opioids after stopping buprenorphine can also be dangerous for the same reasons.

A number of deaths have been reported in people who use sublingual buprenorphine in combination with benzodiazepines, such as Valium or sleeping pills. Using sedating drugs (such as benzodiazepines, alcohol, gabapentin, etc.) in combination with buprenorphine can be hazardous and may result in overdose and death. Please be sure to advise the study medical clinician of all medications you are taking.

Because of the above risks, you should ensure you have naloxone readily available for emergency treatment of opioid overdose while receiving or discontinuing buprenorphine or naltrexone treatment. While you will be given access to naloxone by the study team, you should also discuss the need to have naloxone on hand in an emergency with your family members or close friends.

Risk of Relapse: Relapse to regular drug use is common among people with a history of opioid use disorder, or who have just recently detoxified or stopped their medication for opioid use disorder. Relapse is associated with a number of bad outcomes, including overdose and death (see above), needle use and associated risks (infections, hepatitis, HIV), impaired judgment and functioning, legal problems, and being arrested and put in jail. It is important for you to tell us how you are doing, including your drug use. If you are using drugs, the study team and your treatment program will try to help you. In that circumstance, you may be able to continue the study medications and counseling (buprenorphine, naltrexone). However, if you are not doing well on the study drug, your physician/prescriber and clinical team may decide you need to change treatment—for example changing medication to methadone maintenance, or going to residential treatment.

Procedures That May Cause Discomfort or Inconvenience

Interview/Questionnaires: During the interviews, some of the questions asked may be on topics that are sensitive and may cause you embarrassment. You can refuse to answer any question that you do not wish to answer.

Blood Draws/Injection Procedures: There may be some discomfort like a needle-prick from the blood drawing procedure and medication injection, and in some cases, mild bruising may occur. Blood draw and injection procedures will be performed using safe and sterile techniques. Risks from specific injectable medications are listed below. Although all testing and reporting is considered confidential and covered by federal and state standards for security, there is always a risk that others may learn of your participation. Lab results (except for the genetic tests) will be reported to the medical staff of this study so that they may contact you regarding your results. [THIS SECTION WILL NEED TO BE CONSISTENT WITH STATE AND LOCAL REGULATIONS. IN ADDITION, SPECIFICS RE: LOCAL TREATMENT RESOURCES MAY BE PROVIDED.]

Expected Risks of the Study

Medication Risks: All medications have side effects. The known side effects of the study medications are detailed below. There is also the possibility of an allergic reaction and there may be additional risks that are not known at this time or that are unforeseeable. For anyone who has opioids in their system, naloxone, injectable naltrexone, and buprenorphine may cause opioid withdrawal symptoms.

Risks Associated with Getting Started on Extended-Release Injectable Naltrexone, Sublingual Buprenorphine, or Extended-Release Injectable Buprenorphine: Starting one of these medications requires withdrawing from opioids you are currently taking, either completely (naltrexone) or partially (buprenorphine). Therefore, you are likely to experience some withdrawal symptoms. These may include anxiety, insomnia, irritability, fatigue, nausea, vomiting, diarrhea, muscle aches, and other flu-like symptoms. It is important to drink fluids, so you do not become dehydrated. It is important to let the medical providers who are taking care of you know how you are feeling, since the study drug can be adjusted to try to make you more comfortable.

Extended-Release Injectable Naltrexone (XR-NTX - Vivitrol®): The most common side effect of injectable naltrexone includes some degree of opioid withdrawal. Even after detoxification, where opioids have been washed out of the system, some people will experience symptoms consistent with mild opioid withdrawal for several weeks, mainly fatigue, difficulty sleeping, and low appetite. These usually clear up after several weeks, and they should not recur at subsequent visits. Other side effects of injectable naltrexone may include constipation, nausea, drowsiness, psychiatric problems (such as depressed mood or anxiety), vomiting, dizziness, headaches, itching, stomach pain, dry mouth, fatigue, difficulty sleeping, flushing of the skin, and sweating. In rare cases, people who received injectable 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 potential side effect of naltrexone is liver injury, which has occurred with large daily oral naltrexone doses of 200 to 300 mg per day, which is much higher than the effective daily dose of injectable naltrexone. Recent study findings show that no evidence of liver injury was found in people receiving once-monthly naltrexone injections like the one we will use in this study. For your safety, you will not be allowed to participate in the study if you have acute symptoms of hepatitis or liver failure.

Injectable naltrexone may cause pain, tenderness, hardening or damage of body tissues, swelling, redness, bruising, itching, or infection at the injection site. The injection site will be monitored after each of the injections. You should report any injection site reactions immediately to the study team. 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 study medical staff and treated accordingly.

Injectable naltrexone may block the effects of opioid pain medications. If you need medications for pain relief while in this study it is important that you tell your medical provider you are on injectable naltrexone. Injectable naltrexone will not block the effects of non-opioid pain medications such as aspirin or acetaminophen (Tylenol®) or ibuprofen (Advil®, MOTRIN®).

When starting injectable naltrexone, you may be asked to take a naloxone challenge. Naloxone is an opioid blocker like naltrexone, but it wears off more quickly. It is used to test that your system is ready to start naltrexone. Naloxone could cause acute symptoms of opioid withdrawal (anxiety, irritability, muscle and body aches, nausea, sweating and diarrhea). It is important that you tell the study staff about any current or recent opioid use at the time of the naloxone challenge, in addition to providing a urine sample, to minimize the chances of a positive naloxone challenge.

Sublingual Buprenorphine (SL-BUP - Suboxone®): Side effects commonly observed with the administration of sublingual buprenorphine-naloxone film include sore(s) in mouth or on tongue, partial loss of sensation of touch, headache, nausea, vomiting, constipation, signs and symptoms of withdrawal, insomnia, pain, swelling of the limbs, excessive sweating, and mouth lesions. Hypoglycemia (low blood sugar) has been observed; in most cases, the person has a predisposing risk factor (e.g., diabetes). Buprenorphine itself causes physical dependence and can result in withdrawal symptoms when sublingual buprenorphine is stopped. Sublingual buprenorphine can also cause drowsiness and breathing that is slow and shallow.

It is important never to inject ("shoot-up") sublingual buprenorphine. Injecting sublingual buprenorphine may cause serious withdrawal symptoms such as pain, cramps, vomiting, diarrhea, anxiety, sleep problems, and cravings. Also, films contain components other than the medications which could cause serious damage if they get into your bloodstream.

Sublingual buprenorphine may also impair mental or physical abilities involved in such activities as driving or operating machinery. You are advised not to engage in such activities for at least 6 hours after taking the first dose of sublingual buprenorphine. The researchers will be happy to discuss alternative methods of transportation with you such as getting a ride from a family member or friend, or taking a taxi or bus.

Extended-Release Injectable Buprenorphine (XR-BUP - CAM2038/BRIXADI™): Extended-release injectable buprenorphine delivers into your system levels of buprenorphine that are similar to those obtained from sublingual buprenorphine. Therefore, the side effects, risks, and dangers of extended-release injectable buprenorphine are similar to those of sublingual buprenorphine (see above).

Also, injection of extended-release buprenorphine may cause localized soreness, redness and swelling, to include small bumps under the skin, at the injection site. This usually clears up after a few days, but you should be sure to let your physician/prescriber or other team members know if the injection site is red, swollen, or painful and not improving.

Other Prescription Drugs: Several prescription drugs may cause problems when taken with the study drugs. The medical provider will carefully review all of the drugs you are taking before giving you the study drugs. If any other health care provider prescribes any new drug(s) for you while you are in this study, please tell the medical provider before you take the new drug. You could also have that provider talk to your medical provider before prescribing the new drug. There may be risks that are unforeseeable.

Pregnancy: The risks of these medications in pregnancy are not well known, so pregnant people will not be allowed to enter the study. People of childbearing potential will have pregnancy tests done during screening and then monthly while on the study medications. People who are able to bear children must agree to use an acceptable birth control method for the duration of the study. If you become pregnant during the study, you may need to discontinue the study medication, and start on different medication. This will depend on which medication you are taking and the judgement of your physician/prescriber and clinical team. Sublingual buprenorphine and methadone maintenance treatment have been shown to be safe and effective for treating pregnant patients with opioid use disorder, and are recommended. Injectable naltrexone and monthly injectable buprenorphine are not yet considered safe during pregnancy. If you are receiving one of those and become pregnant then your physician/prescriber may refer you to other treatment options. The research staff

will wish to follow the outcome of any pregnancy and condition of any newborn and report this to the study sponsor.

Risks of Genetics Studies

The Sponsor has taken steps to safeguard your genetic testing information, so the risk of loss of confidentiality is small. However, if confidentiality is broken, results of genetic testing may become available to insurance carriers or employers. The knowledge of this information has the potential to lead to discrimination in employment or insurance. Someone with a known genetic condition indicating a susceptibility to develop a disease or condition might be denied a job or a promotion, or denied health or life insurance, because they are regarded as a health risks and therefore an economic risk. Carriers for a genetic disorder might be discriminated against and viewed as having the potential to have a child with a genetic condition.

There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers (except those with fewer than 15 employees) to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

There may be risks to you (or to your embryo or fetus, if you become pregnant) that are currently unforeseeable.

POTENTIAL BENEFITS

There is no guarantee that you will benefit or your condition will improve as a result of your participation in this study. It may stay the same or get worse. However, the information learned from this study may help other people with this condition in the future.

ALTERNATIVES TO PARTICIPATING IN THE STUDY

If you do not want to be in this study, your eligibility for treatment at [NAME OF UNIVERSITY AND/OR SITE] will not be affected. You can still get treatment to which you have access and are otherwise entitled. If you decide not to participate in this study, there are several options available to help you stop your opioid use; these include methadone maintenance treatment, treatment with naltrexone or buprenorphine, or residential or therapeutic communities, independent of the study. Study and treatment program staff will provide referrals to local treatment programs at your request. If you do enroll in the study and relapse to opioid use or decide to drop out of the study at any point, study staff will work with you to help you find alternative treatment.

CONFIDENTIALITY

Private, identifiable information about you may be used or shared. This section of the consent/ authorization form describes how your information may be used and shared, and the ways in which [NAME OF UNIVERSITY AND/OR SITE] will safeguard your privacy and confidentiality.

If you agree to be in this study, [NAME OF SITE PI] and the study team will ask you to complete questionnaires, and interviews, and will collect blood, saliva and urine samples which may be used to conduct drug toxicology tests. The results of these tests will be kept in your research folder, which will be kept in a locked file in a secure location with access granted only to study personnel. The study's Data and Statistical Center (DSC) and Clinical Coordinating Center (CCC), both part of Emmes will have access to this information. These data will also be kept secure.

Other persons and organizations, including co-investigators, [NAME OF UNIVERSITY AND/OR SITE], federal and state regulatory agencies including the US Food and Drug Administration (US FDA), NIDA, and the Institutional Review Board(s) (IRB(s)) overseeing the research may receive your information during the course of this study. Except when required by law, study information shared with persons and organizations outside of [NAME OF UNIVERSITY AND/OR SITE] will not identify you by name, social security number, address,

telephone number, or any other direct personal identifier. The monitor(s), auditor(s), the IRB(s), and regulatory authorities will be granted direct access to your original medical records for verification of 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.

When your study information is disclosed outside of [NAME OF UNIVERSITY AND/OR SITE] as part of the research, the information that can identify you as listed above will be removed and your records will be assigned a unique code number. [NAME OF UNIVERSITY AND/OR SITE] will not disclose the code key, except as required by law.

Confidentiality of Your Medical Records

Your medical records will be kept in accordance with state and federal laws concerning the privacy and confidentiality of medical information. If your participation in this research is for treatment or diagnostic purposes, the facility in which you are treated may ask you to sign a separate informed consent document for specific procedures or treatment, and that informed consent form may be included in the medical record of that facility. The confidentiality of your medical record is also protected by federal privacy regulations, as described below.

Confidentiality of Your Study Information

Your study records include information that identifies you and that is kept in research files. We will try to keep this information confidential, but we cannot guarantee it. If data from this study are to be published or presented, you will not be identified in any way.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or bio-specimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence (for example, if there is a court subpoena) unless you have consented for this use. Information, documents, or bio-specimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research participants. The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law to prevent serious harm of yourself or others, including child and/or elder abuse. [THIS SENTENCE MAY NEED TO BE TAILORED TO MEET LOCAL REGULATIONS]. Further, in instances when there is concern that urgent clinical assessment may be needed to protect your personal safety or welfare and the study medical provider is not readily available, researchers may need to disclose medical and health-related research data to non-study care providers in order to support that urgent care. Any information disclosed in support of this urgent care may be added into your medical record. This information would still be covered by the protections applied to Protected Health Information in a patient care setting.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health, which is funding this project. You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

By agreeing to be in this research and signing below, you are giving your consent to share research information with others at [NAME OF SITE].

Retention of Your Study Information

The study results will be kept in your research record for at least 3 years or until after the study is completed, whichever is longer. At that time, either the research information not already in your medical record will be destroyed or information identifying you will be removed from such study results at [NAME OF UNIVERSITY AND/OR SITE]. Any de-identified information may be used for future research studies or sent to another investigator for future research studies without getting additional informed consent from you. Any research information in your medical record will be kept indefinitely. [THIS SECTION TO BE TAILORED TO LOCAL REGULATIONS]

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

Additionally, de-identified data from this study will be available to researchers on another website, http://datashare.nida.nih.gov/ after the study is complete and the data analyzed. The primary outcome(s) publication will also be included, along with the underlying primary data, in the data share repository, and 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.

AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH INFORMATION

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The Principal Investigator must get your authorization (permission) to use or give out any health information that might identify you. If you choose to be in this study, the Principal Investigator will get personal information about you. This may include information that might identify you. HIV related information may be shared with other members of the research team besides the principal investigator.

The Principal Investigator may also get information about your health, including:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research about laboratory test results
- Results from diagnostic and medical procedures including but not limited to X-rays, physical examinations and medical history
- Billing records

Information about your health may be used and given to others by the Principal Investigator and staff. They might see the research information during and after the study. Your information may be given to the sponsor of this research. “Sponsor” includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor. Information about you and your health which might identify you may be given to:

- [NAME OF UNIVERSITY AND/OR SITE], Principal Investigator [NAME OF SITE PI] and members of the research team
- Every health care provider who provides services to you in connection with this study

- Any individuals and organizations that analyze your health information in connection with this study in accordance with the study's protocol
- The following research sponsors and the people and companies they use to oversee, administer, or conduct the research: The National Institutes of Health, Columbia University Irving Medical Center/New York State Psychiatric Institute, the Research Foundation for Mental Hygiene, New York University Grossman School of Medicine, McLean Hospital, Harvard Medical School, and Weill Cornell Medicine
- Indivior, the company providing the study drug (sublingual buprenorphine, Suboxone®)
- Braeburn, the company providing the study drug (extended-release injectable buprenorphine, CAM2038/BRIXADI™)
- CHESS Health, the company providing the Connections (mobile health) app
- Champlain Toxicology Laboratory, the central laboratory for the study
- NIDA Genetics Consortium Repository
- [LABORATORY(IES) PARTICIPATING SITE IS USING]
- The U.S. Food and Drug Administration (US FDA)
- Department of Health and Human Services agencies
- Governmental agencies in other countries
- Biomedical Research Alliance of New York (BRANY)
- The members and staff of [INSERT NAME OF SITE]'s affiliated Institutional Review Board
- The members and staff of [INSERT NAME OF SITE]'s affiliated Privacy Board The Patient Advocate or Research Ombudsman (if applicable)
- Members of the [NAME OF UNIVERSITY AND/OR SITE] Clinical Trials Office/Office of Research and Sponsored Programs (if applicable)
- Clinical Coordinating Center / Contract Research Organization: Emmes
- Data and Statistics Coordinating Center / Contract Research Organization: Emmes
- Accrediting agencies
- Data safety monitoring boards
- Health insurers and payers

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the U.S. federal privacy laws. However, these groups are committed to keeping your personal health information confidential. If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose. The information may be given to the FDA. It may also be given to governmental agencies in other countries. This is done so the sponsor can receive marketing approval for new products resulting from this research. The information may also be used to meet the reporting requirements of governmental agencies.

This authorization does not have an expiration date. If you do not withdraw this authorization in writing, it will remain in effect indefinitely.

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. You do not have to sign this consent form. If you choose not to sign this consent form, you will not be able to be in this research study. Your decision not to sign this consent form will not have any effect on your medical care and you will not lose any benefits or legal rights to which you are entitled. You have the right to review and copy your health information. However, if you decide to be in this

study and sign this permission form, you may not be allowed to look at or copy your information until after the research is completed.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the Principal Investigator using the contact information on the front of this informed consent form. If you withdraw your permission, you will not be able to continue being in this study, but you will not have any penalty or loss of access to treatment or other benefits to which you are entitled. When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

DELETE IF SITE IS NOT IN NY:
Notice Concerning HIV-Related Information: HIV-related information that either is collected as part of the research or that may already exist in your medical record might be accessed for the research by the research staff and the study sponsor, but will not be shared with others without your authorization, unless federal or state law requires the disclosure. You have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights or New York City Commission on Human Rights. These agencies are responsible for protecting your rights.

DELETE IF SITE IS IN NY:
Notice Concerning HIV-Related Information: HIV-related information that either is collected as part of the research or that may already exist in your medical record might be accessed for the study by the research staff and the study sponsor, but will not be shared with others without your authorization, unless federal or state law requires the disclosure. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the agencies responsible for protecting your rights.

COMPENSATION/TREATMENT IN THE EVENT OF INJURY
For medical emergencies, call 911. All forms of medical (or mental health) diagnosis and treatment – whether routine or experimental – involve some risk of injury. In addition, there may be risks associated with this study that we do not know about. In spite of all precautions, you might develop medical complications from being in this study.
If you sustain any injury during the course of the research or experience any side effect to a study drug or procedure, please contact the Principal Investigator [NAME OF SITE PI] at the following telephone number [SITE PI PHONE NUMBER]. If such complications arise, the treatment team will assist you in obtaining appropriate medical treatment but this study does not provide financial assistance for medical or other injury-related costs. No other compensation will be offered by the Sponsor, [INSERT NAME OF INSTITUTION] OR the Biomedical Research Alliance of New York. You do not give up any rights to seek payment for personal injury by signing this form.

VOLUNTARY PARTICIPATION AND AUTHORIZATION
Your decision as to whether or not to take part in this study is completely voluntary (of your free will). If you decide not to take part in this study, it will not affect the care you receive and will not result in any loss of benefits to which you are otherwise entitled. You will be told of any significant new findings developed during the course of the research that may influence your willingness to continue to participate in the research. Your decision as to whether to give your Authorization for the use and disclosure of your protected health information for this study is also completely voluntary. If you decline to give your Authorization or if you withdraw your Authorization, you may not participate in the study.

WITHDRAWAL FROM THE STUDY
If you decide to take part in the study, you may withdraw from participation at any time without penalty or loss of benefits to which you would otherwise be entitled. If you do decide to withdraw your consent, we ask that you contact [NAME OF SITE PI] in writing and let them know that you are withdrawing from the study. Their mailing address is [ADDRESS OF SITE PI].

The Principal Investigator or another member of the study team will discuss with you any considerations involved in discontinuing your participation in the study. You will be told how to withdraw from the study and may be asked to return for a final check-up.

The study medical provider may also decide to withdraw you from the study for certain reasons, even if you would like to continue. Some possible reasons for withdrawing a participant from the study include:

- Worsening health or other conditions that might make it harmful for you to continue,
- Failure to keep appointments, follow directions or take study medications as instructed,
- A serious adverse reaction to drug therapy,
- The need for treatment not allowed by the study, or
- Termination or cancellation of the study by the sponsor, NIDA.

If you withdraw or are withdrawn or discontinued from the study, the study staff will work with you to help you find alternative treatment in the community as described above.

Withdrawal of Samples for Genetics Studies: If you wish to withdraw your samples from the NIDA Genetics Consortium Repository, you must contact [NAME AND ADDRESS OF SITE PI/EMAIL ADDRESS OF SITE PI] in writing and let them know you want to withdraw your samples. They will tell the repository to destroy all of your genetic material and the coded link between your medical information and the genetic material. Because your identity will be kept secret by using a code number, the repository can destroy your genetic material without ever knowing your name or other personal information. The repository can use this code number to tell researchers not to include your data in their research without telling them your name or other personal information about you. However, the resulting data from the research will not be discarded. De-identified copies of DNA and/or growing cells made from your samples will not be destroyed because your code number will not be on them to identify them as yours. Samples sent to other scientists cannot be identified and destroyed because your code number was removed before the samples were shipped to other medical centers.

PERMISSION TO CONTACT YOU ABOUT FUTURE RESEARCH
As part of agreeing to participate in this study, you authorize the site principal investigator and their co-investigators to contact you about future research on substance use disorder within the [DEPARTMENT, DEVISION, OR CENTER] provided that this future research is approved by an IRB of record and that the principal investigator and co-investigator are affiliated with the research protocol. Someone from [NAME OF SITE PI]'s research staff might contact you in the future and they will tell you about a research study. At that time, you can decide whether or not you are interested in participating in a particular study, and there is no obligation to participate. You will then have the opportunity to contact the researcher to schedule an appointment to be fully informed about the research project.

CONTACT PERSON(S)
If you have any questions or to request information relating to this research or your participation in it, if you want to voice a complaint or concern about this research, or if you have a research-related injury, you may contact the Principal Investigator [NAME OF SITE PI] at [SITE PI PHONE NUMBER].

If you have any questions about your rights as a research participant or complaints regarding this research study, or you are unable to reach the research staff, you may contact a person independent of the research

team at the Biomedical Research Alliance of New York Institutional Review Board (BRANY) at 516-318-6877. Questions, concerns or complaints about research can also be registered with the Biomedical Research Alliance of New York Institutional Review Board at https://www.brany.com/report-concerns/.

CONSENT TO PARTICIPATE

AGREEMENT TO PARTICIPATE AND AUTHORIZATION FOR THE USE OR DISCLOSURE OF PROTECTED HEALTH INFORMATION

Part of the consent process includes your Authorization to use Protected Health Information (PHI) for the purposes of this study, as described above. If you do not want to authorize the use of this PHI, you should not agree to be in this study.

- I have read this consent form, *or*
- It was read to me by: _____
- Any questions I had have been answered by: _____

Participating in another research project at this time does not exclude you from participating in this study, but you should let us know if you are and discuss it with the study clinician.

I voluntarily agree to participate in this research program at [INSERT SITE NAME].

I understand that I am entitled to and will be offered a copy of this signed Consent/Authorization.

By signing this Consent/Authorization, I give my Authorization for the uses and disclosures of my protected health information as described above.

Print Name of Person Consenting to Study	Signature of Person Consenting to Study	Date
Print Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date

COMPREHENSION QUIZ
CTN-0100: Optimizing Retention, Duration and Discontinuation Strategies for Opioid Use Disorder Pharmacotherapy (RDD)

1. My participation in this study is entirely voluntary.	□ True	□ False
2. Naltrexone and buprenorphine are both approved by the United States Food and Drug Administration to treat opioid use disorder.	□ True	□ False
3. The investigators will make every effort legally possible to protect my privacy and confidentiality.	□ True	□ False
4. The study will provide medication for up to 74 weeks (about 1.5 years).	□ True	□ False
5. I will be allowed to choose which form of buprenorphine I take.	□ True	□ False
6. I will be assigned at random to either receive, or not receive, an added behavioral intervention consisting of the Connections app.	□ True	□ False
7. Research follow-up visits will occur at weeks 4, 12 and 24 following the end of the study-provided treatment period.	□ True	□ False
8. If I relapse, there is a risk of overdose and death from taking opioids.	□ True	□ False
9. The study is guaranteed to help me stop using opioids.	□ True	□ False
10. My sample for genetic testing will be labeled with my name and date of birth.	□ True	□ False
11. The study medical provider may end the medication provided by the study to protect my health and safety, even if I would like to continue.	□ True	□ False

Signature of Participant _____ Date _____

Signature of Person Authorized to Obtain Consent _____ Date (must be same as participant's) _____