IRB Approved Template
MUST BE APPROVED
FOR SITES BEFORE USE
AS MODIFIED
Dec 09, 2021

RESEARCH SUBJECT CONSENT FORM

TITLE: OUTLAST: A PHASE 2, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, MULTIPLE-DOSE STUDY TO EVALUATE THE SAFETY AND EFFICACY OF IXT-M200 IN TREATMENT-SEEKING INDIVIDUALS WITH METHAMPHETAMINE USE DISORDER

PROTOCOL NO.: M200C-2201
IRB Protocol #20214728

SPONSOR: InterveXion Therapeutics, LLC

FUNDING: This trial is funded by the National Institute on Drug Abuse grant number DA055481

<<CF-Main Header Block - Investigator>>
INVESTIGATOR: Name
Address
City, State Zip
Country

STUDY-RELATED PHONE NUMBER(S): <<CF-Main User Defined #1>>
[24 hour number is required]

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

InterveXion Therapeutics, LLC is sponsoring this study. The study is being funded by the National Institute on Drug Abuse (NIDA), with grant number U01 DA055481, who appreciates your involvement in the study. Your study doctor will be paid for his or her work in this study.

What should I know about this research?

- Someone will explain this research to you<<CF-Main California Bill of Rights>>.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.

- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

How long will I be in this research?
We expect that your taking part in this research will last about 8 months.

Why is this research being done?
The purpose of this research is to determine whether the study drug, IXT-m200, helps to reduce methamphetamine (METH) use. We will also learn if multiple doses of IXT-m200 are safe and well-tolerated.

What happens to me if I agree to take part in this research?
If you decide to take part in this research study, the general procedures include receiving 6 monthly doses of IXT-m200 by intravenous infusion at the study site and then visiting the site for monthly checkups for 3 months. At each visit, we will take blood samples for testing and check to make sure you are still feeling well. You will be provided with behavioral therapy treatment as well. We will also ask you daily about your drug use and expect you to take saliva drug tests twice per week. The results of the drug tests will not be reported to authorities and will not have any effect on your continuing in the study. You will be treated the same whether they are positive or negative for METH.

Could being in this research hurt me?
The most important risks or discomforts that you may expect from taking part in this research include a low risk of a reaction to a dose of IXT-m200 which might appear as an allergic reaction with hives or itching, flu-like symptoms, nausea, vomiting, diarrhea, skin rashes, or low blood pressure. The study doctor will monitor you for any such potential issues.

Will being in this research benefit me?
This research may not benefit you at all. However, the most important benefit that you may experience from taking part in this research includes a reduction in the number of days or weeks that you use METH.

What other choices do I have besides taking part in this research?
Instead of being in this research, your choices may include getting standard treatment for substance use disorder as recommended by your doctor.

What else should I know about this research?
If you decide to participate in this research, you will be asked to use birth control at all times while in the study and not get pregnant or your partner pregnant. You will be asked to report

your drug use daily via a smartphone app and to take 2 saliva drug tests each week throughout the entire study.

DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

What should I know about this research?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

Why is this research being done?

The purpose of this research is to determine whether the study drug, IXT-m200, helps people with methamphetamine (METH) use disorder to reduce the number of days or weeks they use METH. We also want to learn if IXT-m200 will help improve quality of life as a benefit of reduced METH use. Finally, we will be studying whether 6 doses of IXT-m200 are safe in people with METH use disorder.

About 120 subjects will take part in this research.

We think IXT-m200 may help people stop using METH because it is a monoclonal antibody that binds METH in the blood and reduces the amount of METH that reaches the brain where it makes you feel high or stimulated. This is expected to reduce or prevent the feelings caused by taking METH that lead you to use it again. Combined with therapy, we think IXT-m200 may increase the chances that you will quit using METH.

How long will I be in this research?

We expect that your taking part in this research will last about 8 months.

What happens to me if I agree to take part in this research?

There are 10 scheduled visits to the study site. The first one is the screening visit, then there will be 9 monthly visits if you are enrolled in the study.

Screening

During your screening visit, the following procedures will happen:

- The criteria for study entry will be reviewed.
- You will be asked about your drug use history including methamphetamine and other illicit drugs, nicotine, alcohol, and marijuana
- Your demographic information (age, sex, race and ethnicity) will be recorded
- Your weight and height will be measured
- Your medical history and medications you are taking or have taken in the past year will be documented
- Your vital signs will be taken
- You will be given a general physical exam
- You will be asked questions about your mental health, including thoughts of suicide
- You will be asked to take a urine pregnancy test if female
- You will be asked to take a drug test that uses oral fluid (saliva)
- You will be asked to provide blood and urine samples for routine clinical laboratory testing (about 3-4 teaspoons of blood)
- An ECG (which measures how your heart is beating) will be performed. Sticky patches will be applied to your chest and extremities.
- You will be given a questionnaire with 4 questions asking about your quality of life called the Treatment Effectiveness Assessment

Enrollment

If you are eligible and selected to continue in the study, you will be asked to download the smartphone app for this study and sign up for a training and welcome video from a representative from DynamiCare who provides the app. You will be taught how to use the app and how to take the saliva drug tests on your own while recording yourself. You may have to complete the drug test multiple times to make sure they are done correctly before you can start the study.

You will be asked to use the smartphone app to report daily drug use through the end of the study. The DynamiCare representative will teach you to complete the drug use survey.

You will be asked to complete two saliva drug tests each week after your first dose of study drug. The smartphone app will tell you when you should complete those tests.

Throughout the study, you will be asked about any changes in your health. If you feel unwell or are seen by another doctor between visits, please tell the study doctor during a visit or by using the contact information on the front page of this form.

Dosing Days

On the first dosing day, the following procedures will be done at the study site. You will be at the site for about 5-6 hours.

- You will be given a Wellness Check which includes the following:
  - Your medical history and medications will be updated
  - You will be asked about your mental health
  - Your vital signs will be taken and you will be given a brief physical exam
  - You will be given a urine pregnancy test, if female
- You will be put into a study group by chance (like drawing straws). You have a 2 out of 3 chance of being placed in the group that receives study drug, and a 1 out of 3 chance of being in the group that gets placebo (no drug, just a fluid infusion). You cannot choose your study group.

During the research, you and the study doctor will not know which group you are in. (Your study doctor can find out in case of an emergency).

- If you are in the first approximately 60 people enrolled in the study, you will either receive 1.5 g of study drug, IXT-m200 or placebo.
- If you are in the second approximately 60 people enrolled in the study, you will either receive 3 g of IXT-m200 or placebo.

IXT-m200 is investigational, which means that it is not approved by the Food and Drug Administration (FDA).

- You will receive the dose of IXT-m200 or placebo by intravenous (IV) infusion which will take about 30 min. An IV catheter will be inserted into a vein for study drug administration.
- Blood samples will be taken two times, once before and once 4 hours after the dose of study drug to measure the amount of IXT-m200 in your blood (about 1 teaspoon each time) and once to perform routine clinical laboratory tests (about 3-4 teaspoons one time). A blood sample will also be taken to measure any immune response to the study drug (about 1 teaspoon one time). If you have an infusion reaction, your blood will be tested for cytokines which help regulate the immune system (about 1 teaspoon up to three times).
- An ECG will be performed shortly after the dosing is completed.
- While you are at the study site, you will have a therapy session with a trained therapist. They will provide cognitive behavioral therapy, a typical type of therapy provided as treatment to patients with METH use disorder.

You will return to the study site every 4 weeks for your next dose until you have received 6 total doses. Each visit will take about 5-6 hours and the same procedures will happen.

On the visit of your fourth dose, you will also be asked to complete the Treatment Effectiveness Assessment, which is a short survey about how you are doing overall. You will also be asked how you think your status has changed since the start of the study.

Between dosing days, you will have access to a recovery coach. They will be available for weekly phone or video calls and by text during working hours. The representative from DynamiCare will give you details about this.

Follow-up Visits

Once you have received all 6 doses, you will return to the study site every 4 weeks for follow-up visits. When you have completed 3 follow-up visits, you will have completed the study. Each follow-up visit should last about 1-2 hours. During the follow-up visits, the following procedures will happen:

- You will be given a Wellness Check
- Blood samples (about 1 teaspoon each time) will be taken to measure the amount of study drug in your blood and your body's immune reaction (about 1 teaspoon each time).
- At some follow-up visits, you will have a therapy session
- At some follow-up visits, blood (about 3-4 teaspoons) will be taken to perform routine clinical laboratory tests
- At some follow-up visits, you will be asked to complete the Treatment Effectiveness Assessment and asked how you think your status has changed since the start of the study.

PK Subset

If you are asked, and agree, to participate in the 'PK subset', you will do everything listed above plus the following:

- On the first and last dosing days, you will have one additional blood sample taken (about one teaspoon each time) at 1 hour after the dose of study drug.
- You will return to the study site for additional blood samples (about one teaspoon each time) the day after the first dose, then weekly for three weeks.
- You will also return to the study site for additional blood samples (about one teaspoon each time) the day after the last dose, then weekly for three weeks.

There are 8 total extra visits which should not last more than one hour for participating in the PK subset. The information collected during these visits will help the sponsor learn more precisely about the amount of study drug in your blood over time.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

- Comply with the instructions from the study staff
- Report daily drug use via the smartphone app
- Complete the saliva drug screens each week when requested by the app
- Practice an adequate method of birth control, including intrauterine device (IUD); oral, dermal ("patch"), implant or injected contraceptives; tubal ligation; barrier methods with spermicide; or vasectomized partner throughout the study and until 90 days after receiving the last dose of study drug.

- Limit alcohol consumption to approximately 1 drink per day for women and 2 drinks per day for men while in the study
- Not participate in any other clinical study or take other investigational drugs or use investigational devices
- Not to donate blood, plasma, platelets, eggs or sperm while in the study

The study drug may change the way drugs similar to METH are eliminated from the body, so participants should avoid taking drugs such as amphetamine (including Adderall®, Dexedrine®, or Evekeo®) or MDMA (also known as ecstasy) for the duration of study participation.

Could being in this research hurt me?

IXT-m200 had already been given to over 75 human study participants in four different studies when this study started. We don't yet know all the risks of taking IXT-m200.

There were no serious adverse reactions in the previous studies. One participant had an infusion reaction halfway through the IXT-m200 infusion. The participant had a brief period of bronchospasm and wheezing. Bronchospasm is a sudden constriction of the muscles in the walls of the bronchioles (airway). The infusion was stopped and the participant was treated. The participant fully recovered from the incident.

IXT-m200 is a monoclonal antibody. Risks of taking a monoclonal antibody may include allergic reactions such as hives or itching, flu-like symptoms including chills, fatigue, fever, and muscle aches and pains, nausea, vomiting, diarrhea, skin rashes, or low blood pressure.

As with taking any drug, there is a risk of allergic reaction. Allergic reactions can be serious and/or life threatening and sometimes lead to death. Some symptoms of allergic reactions are rash, difficulty breathing, and wheezing, sudden drop in blood pressure, swelling around the mouth, throat or eyes, a fast heart rate, and sweating. Seek treatment and alert the study doctor and study staff immediately if you have any of these symptoms.

Risks associated with drawing blood from your veins may include lightheadedness, pain, bruising, and bleeding at the site of needle puncture, inflammation of the vein, and sometimes infection.

During the placement of an IV catheter into a vein, you may experience pain and/or bruising at the site where the IV is placed and blood is taken. In the event the IV fails to work properly, a direct needle stick into a vein may be needed to obtain blood for one or more time-points. You may experience dizziness, lightheadedness, and/or fainting. Localized bruising, clotting, and infections may occur. Scarring damage to a vein is also possible.

The loss of confidentiality is a potential risk of being in this study because the study inclusion criteria require recreational use of METH. We will protect information about you and your

taking part in this research study to the best of our ability. However, absolute confidentiality cannot be guaranteed.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes Federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that Federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States Federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the Federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by Federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

If you have any side effects or concerns, you should tell the study doctor or study staff immediately. If you don't tell the study doctor and/or study staff the truth about any side effects or concerns, you may harm yourself by being in this study. If it is an emergency or if you cannot contact the study staff or study doctor, you should call 911 immediately.

In addition to these risks, taking part in this research may harm you in unknown ways.

Taking part in this research may hurt a pregnancy or fetus in unknown ways. These may be minor or so severe as to cause death.

Will it cost me money to take part in this research?

No, all of the services provided as part of this research will be provided at no cost to you.

Will being in this research benefit me?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits to you include a reduction in the number of days or weeks that you use METH and a possible reduction in blood pressure increases resulting from METH use. You may also

receive a benefit from the therapy provided to all participants, no matter what group you are placed in.

What other choices do I have besides taking part in this research?

Instead of being in this research, your choices may include:

- Receiving treatment as usual per the recommendations of your doctor. This may include behavioral therapy or medications.

What happens to the information collected for this research?

Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor
- People who work with the research sponsor, including Syneos Health<<CF-Main SMO Company 1>><<CF-Main Affiliated IN Language 1>> and DynamiCare Health
- Government agencies, such as the Food and Drug Administration and the Department of Health and Human Services
- WCG IRB, the Institutional Review Board (IRB) that reviewed this research
- Data and safety monitoring committees
- The National Institute on Drug Abuse who funded this study
- Other regulatory agencies

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

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

Data or specimens collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

Who can answer my questions about this research?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by WCG IRB. An IRB is a group of people who perform independent review of research studies. You may talk to them at 855-818-2289 or researchquestions@wcgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

What if I am injured because of taking part in this research?

If you are injured or get sick because of being in this research, call the study doctor immediately. The study doctor will provide emergency medical treatment. Your insurance may be billed for this treatment. The sponsor will pay any charges that are not covered by insurance policy or the government, provided the injury was not due to your underlying illness or condition and was not caused by you or some other third party. No other payment is routinely available from the study doctor or sponsor.

Can I be removed from this research without my approval?

The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- It is in your best interest
- You have a side effect that requires stopping the research
- You need a treatment not allowed in this research
- You become pregnant or have another condition that is not allowed
- The research is canceled by the FDA or the sponsor
- You are unable to take the research medication
- You are unable to keep your scheduled appointments or do not comply with instructions from the study staff
- The Sponsor or investigator request you are removed

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

What happens if I agree to be in this research, but I change my mind later?

If you decide not to take any further doses of the study drug, please tell the research team. You will be asked to continue participating in the other study procedures and assessments.

If you decide to leave this research and not participate any further, contact the research team so that the investigator can conduct early termination procedures:

- You will be given a Wellness Check

- Two blood samples (about 1 teaspoon) will be taken to measure the amount of study drug in your blood and your body's immune reaction (about 1 teaspoon).
- Blood (about 3-4 teaspoons) will be taken to perform routine clinical laboratory tests
- You will be asked to complete the Treatment Effectiveness Assessment and asked how your status has changed since beginning the study.

Will I be paid for taking part in this research?

<<CF-Main Payment for Part. Paragraph>>For taking part in this research, you may be paid up to a total of $[Amount]. Your compensation will be based on the total number of study requirements you complete and will not depend on your drug test results.

Requirement	Payment per each	Additional payments for PK subset
Screening visit	$20	
Daily drug use questionnaire	$0.50	
Weekly bonus for all questionnaires completed	$1.50	
Saliva test	$5.00	
Study site visit	$40	$10
PK subset visit		$40
Possible total compensation	$935	$1275

Your specimens (even if identifiers are removed) will be transferred to a commercial organization for testing and may be used for commercial profit. You will not share in this commercial profit.
<<CF-Main Financial Disclosure>>

Statement of Consent:

Your signature documents your consent to take part in this research.

Signature of adult subject capable of consent	Date
Signature of person obtaining consent	Date

<<CF-Main California HIPAA>>

Statement of Consent for the PK subset:

Your signature documents your consent to take part in this research as part of the PK subset.

Signature of adult subject capable of consent	Date
Signature of person obtaining consent	Date

****For Sites in California****

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

Who may use and give out information about you?
The study doctor and the study staff. [They may also share the research information with [enter SMO company name], an agent for the study doctor. delete if the site does not have an SMO]

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- The institution where the research is being done,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Institutional Review Board (IRB)

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This permission will be good until December 31, 2070.

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 study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

Authorization:
I have been given the information about the use and disclosure of my health information for this research study. My questions have been answered.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

AUTHORIZATION SIGNATURE:

_____ _____

Signature of Subject **Date**