# A Phase 1, Double-Blind, Randomized, Placebo-Controlled, Single-Dose Intravenous Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of IXT-m200 in Healthy Participants

**Protocol Number: M200C-2102**

**IND Sponsor: InterveXion Therapeutics, LLC**

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**INFORMED CONSENT FORM**
**AND**
**AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION**

| | |
|---|---|
| **Sponsor / Study Title:** | **InterveXion Therapeutics, LLC / "A Phase 1, Double-Blind, Randomized, Placebo-Controlled, Single-Dose Intravenous Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of IXT-m200 in Healthy Participants"** |
| **Protocol Number:** | **M200C-2102** |
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KEY INFORMATION

You are being asked to participate in this research study as a healthy participant. There is no known benefit from your participation in this study. Information learned from the study may help other people in the future. Since there is no direct medical benefit to participation, your other option is not to participate.

This consent form will review the question the study is trying to answer which is the safety and tolerability of the study drug (IXT-m200). It will review the information that will be collected from you prior to and during the course of the study as well as the study related activities.

An investigational drug is one that is not approved by the United States Food and Drug Administration (FDA). This study is trying to determine the potential safety and tolerability of the study drug after a single administration in comparison with placebo (inactive substance, purified saline water that looks like study drug). You will receive the study drug/placebo as a short intravenous (IV) infusion. In addition, you will have a series of screening and medical assessments as outlined in this consent form which will give you a greater sense of your general health. As part of the study, these assessments will be conducted at no cost to you.

Your health will be closely monitored by the study team while on study site as well as throughout the duration of the study. Please note, your participation is completely voluntary. You may withdraw from participation at any time.

**Introduction**
You are invited to take part in a research study. This research study is studying IXT-m200, which is a possible treatment for methamphetamine, or METH, use disorder. InterveXion Therapeutics, LLC is sponsoring this research study, and it is being funded by a grant from the National Institutes of Health/National Institute on Drug Abuse (NIH/NIDA). IXT-m200 is believed to work by directly binding to METH and keeping it from entering the brain, which may help people who want to stop using METH to overcome their addiction.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

**PURPOSE OF CONSENT FORM**
You are being asked to participate in a research study. It is important that you read the following explanation of the proposed procedures. This form describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes your right to withdraw from the study at any time. A qualified member of the study staff will go through the consent with you and discuss all the information. When you understand the study, you will then be asked if you agree to take part. If you agree, you will be asked to sign and date this consent form. Once you sign and date it, we will give you a signed and dated copy to keep.

**BACKGROUND AND PURPOSE**
You are being asked to participate in this research study as a healthy volunteer.

The purpose of this research study is to:

- Test the safety and tolerability of the study drug, IXT-m200.
- Investigate the pharmacokinetic (PK) properties (how the study drug moves in the body) of IXT-m200

This is a research study to test a new investigational drug. An investigational drug is one that is not approved by the United States Food and Drug Administration (FDA). This study is to determine the potential safety and tolerability of study drug after a single administration in comparison with placebo (purified saline water that looks like study drug but has no active drug in it). Throughout the study, blood will be collected for pharmacokinetic (PK) analysis to evaluate elimination of IXT-m200 after a single administration of study drug.

**What will happen during this study**
There will be approximately 9 healthy adults randomized into the study. Participants will be randomized (like the flip of a coin) to 3 grams IXT-m200 or placebo (saline water). Each will receive their dose as a 30 minute IV (intravenous) infusion, then remain at the study site overnight to complete Day 1 and Day 2 assessments (Electrocardiogram [ECG], laboratory assessments, blood draws, and vital signs). Following discharge on Day 2, participants will

return to the clinic for follow up PK and safety assessments on Day 8, then every 1-3 weeks thereafter until Day 127.

Your participation in this study will begin with a screening period to assess eligibility of participation, which could last up to 30 days prior to IXT-m200 administration. If you agree to participate in this study, you will be asked to refrain from the following during the study period:

- Ingesting or using any other investigational drug or device.
- Donating blood, plasma, platelets, eggs or sperm.

You will be asked to limit your alcohol consumption to approximately 1 drink per day (women) and 2 drinks per day (men) while in the study. Participants are required to 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.

IXT-m200 may also bind to drugs that are similar to METH. You should refrain from taking such drugs during the study period, including methamphetamine, amphetamine (including Adderall®, Dexedrine®, or Evekeo®) and MDMA (also known as ecstasy).

**Visit Schedule/Duration of Inpatient Stay:** (The total length of the study is up to 127 days)

- One outpatient screening visit.
- After Screening, you will return to check-in to the inpatient unit for 2 days/1 night (Days 1 and 2), and 10 outpatient visits will occur on Days 8, 15, 22, 29, 36, 43, 64, 85, & 106. Final Study visit is Day 127

**Screening Visit:**
Before any procedures are performed, you will be asked to sign and date this informed consent form to participate in the study. Screening procedures are intended to take one day, but may take additional days.

The following screening tests and procedures will then be performed to determine if you qualify to take part in this study:

- Review of demographics such as age, gender, race, etc.;
- Review of requirements and verifying inclusion/exclusion criteria for study participation;
- Review of your medical and psychiatric history including any medications you are taking or have taken recently;
- Height, and weight measurements and body mass index (BMI) calculation;
- A complete physical examination;
- Measurement of vital signs to check your heart rate, blood pressure, oral body temperature, SaO2 (oxygen levels), and respiratory rate. Blood pressure will be taken in Seated and semi-recumbent positions;

- Clinical laboratory tests of blood chemistry, hematology, and urinalysis. Also drug and alcohol levels;
- All testing results will be kept confidential and disclosed only as required by law. You will be notified and given information on counseling services if you have positive results. The study doctor may be required by law to report the results of these tests to the local health authority;
- A urine pregnancy test for females to determine if you are pregnant. The result of the pregnancy test must be negative for you to qualify to participate in this study;
- A Verified Clinical Trials (VCT) assessment to ensure study participation is valid;

If you qualify to take part in this study and go on to receive the study treatment, you will undergo the following study visits and procedures:

**Check in procedure: Day 1:**

Once your eligibility has been confirmed by the study doctor, you will be asked to check into the Clinic on Day 1 (Admission) until Day 2.

The following procedures will be completed on Day 1:

- A targeted physical examination;
- Participants will be asked to eat a light meal prior to arriving at the study center but not have anything but clear liquids to eat or drink for 1 hour before appointment time. Participants will be offered a light meal after dosing completion;
- Urine pregnancy tests (females only); the result must be negative to continue in the study;
- Check for adverse events (side effects);
- Confirm prior and concomitant medications;
- Inclusion/exclusion criteria;
- Admission to Inpatient Unit
- Measurement of vital signs to check your heart rate, blood pressure, oral body temperature, SaO2 (oxygen levels), and respiratory rate. Blood pressure will be taken in Seated and semi-recumbent positions;
- Blood samples are to be taken pre-dose for cytokines, PK, and Human anti-chimeric antibodies (HACA)
- Randomization and then administration of IXT-m200 or placebo

**Study Treatment:**

You will receive the study drug as a short (approximately 30 minutes) IV infusion.

You will be assigned by chance (like a flip of a coin) to receive either IXT-m200 or placebo (inactive substance). This is a double-blind study, which means neither you nor the study doctor will know to which of these study drug groups you are assigned. In case of an emergency, however, the study doctor can get this information.

The following assessments are to be performed at Day 1 following dose administration:

- Multiple triplicate 12-Lead Electrocardiogram (ECG) will be taken at 30 min post-dose.
- Measurement of sitting or semi-recumbent l signs to check your heart rate, blood pressure, body temperature, SaO2, and respiratory rate will be taken at 0.25, 0.5, 1, 2 and 4 hours (+/- 5 min) after dosing starts, and as needed afterward until normalization.
- Laboratory tests (blood and urine sampling) Samples are to be taken at screening, pre-dose and 2 hours post dose completion; also a urine drug screen.
- Additional blood samples may be taken two more times if you have an infusion reaction.
- PK samples are to be taken at 1, 4, and 8 hours after dosing.
- Check for adverse events and concomitant medications.

**Day 2:**

- Laboratory Tests- blood and urine samples will be obtained
- Wellness Check- update medical history, update medications, vital signs and physical exam
- Blood for PK

**Days 8, 15, 22, 29, 36, 43, 64, 85, 106**

- Laboratory Tests- blood and urine samples will be obtained on Days 8, 29, and 64
- Wellness Check- update medical history, update medications, vital signs and physical exam
- Blood for PK

**Day 127:**

- Wellness Check- update medical history, update medications, vital signs and physical exam
- Urine pregnancy check
- Blood for PK
- Blood for HACA

**After Study Treatment:** Because this is a research study, the study drug will be given to you only during this study and not after the study is over.

**Risks, Side Effects, and Discomforts**
IXT-m200 had been given to over 65 human study participants in two different studies when this study started. Though we don't yet know all the risks of taking IXT-m200, we do believe that it is generally safe.

There were no serious adverse events 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.

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.

**Unforeseen Risks**
Since the study drug is investigational, there may be other risks that are unknown.

**Risks of Study Procedures**

- **Electrocardiogram (ECG):** Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.
- **Blood Draw Risks:** Risks from the PK sample collection and clinical safety phlebotomy (blood drawing) procedures include infection, bleeding, bruising, blood clot formation, discomfort at the injection site, and (rarely) fainting. Phlebotomy will be conducted using careful, sterile technique to minimize these risks.
    - The total blood volume withdrawn from any single participant will not exceed 150 mL (about 10 tablespoons). If additional blood sample analysis is needed, it is possible that more than one attempt to obtain a blood sample may be necessary.

- **IV Catheter Risks:** Blood samples may be drawn from an intravenous catheter or needle in order to aid with the blood draws. A catheter is a thin tube inserted into your vein temporarily that will enable the study staff to draw blood at the various time points without inserting a needle directly into your vein multiple times. Procedure risks include bleeding, bruising, discomfort at the injection site, and rarely infection and fainting.
- If you are having suicidal thoughts call the study doctor at the telephone number on the first page of this form. If you feel in crisis, you can call 911 and/or a Nationwide Suicide Hotline that is answered 24 hours a day with a skilled, trained counselor. One example is the national Suicide Prevention Lifeline at 1-800-273-TALK (8255).
- **Nasal / Nasopharyngeal Swab:** You may experience discomfort, eyes watering, sneezing, or bleeding.

**Birth Control Restrictions**

Taking the study drug may involve risks to a pregnant woman, an embryo, fetus (unborn baby) or nursing infant. Therefore, if you are pregnant, planning to become pregnant, planning to father a child, or are breastfeeding a child, you cannot participate in this study.

Females:

In order to reduce the risk of pregnancy, participants are required to practice an adequate method of birth control, including intrauterine device (IUD); oral, dermal ("patch"), implant or injected contraceptives; tubal ligation (tubes tied); barrier methods with spermicide; or vasectomized partner throughout the study (until day 127).

If you become pregnant after you have received study drug, tell your study doctor or study staff immediately. You will still be asked to come in for follow-up visits and to continue all study assessments, however you will not receive study drug anymore. If you become pregnant, the study staff will collect information about the pregnancy, its outcome, and the health of the child after birth. Generally, follow-up will be no longer than 6 to 8 weeks after the estimated delivery date.

Males:

In order to reduce the risk of pregnancy, you must be willing to use a condom or remain abstinent while you are participating in this study.

**Benefits**

There is no known benefit from your participation in this study. Information learned from the study may help other people in the future.

**Alternatives to Participation**

This research study is for research purposes only. The only alternative is to not participate in this study.

**New Findings**
Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

**Compensation for Injury**
If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured then they will help you get the care you need.

If you are injured as a result of taking the study drug(s) or from procedures done for the purpose of this study, the sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

**Cost of Study to Participant**
There will be no charge for any of the study drug, study related procedures and study visits to you or your insurance company during your participation in the study.

**Compensation for Study Participation**
You will be paid up to a total of up to $2175 if you complete this study. You will be paid for the visits you complete according to the following schedule:

- Visit Screening - $150
- Travel - Up to $80 roundtrip
- Visits:
  **Day 1** $350 (inpatient stay), **Day 2** $150, **Day 8** $150, **Day 15** $150, **Day 22** $150, **Day 29** $150, **Day 36** $150, **Day 43** $150, **Day 64** $150, **Day 85** $150, **Day 106** $150,
- End of Study Visit: **Day 127** $150

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid for all completed study visits at the end of each visit.

If you have any questions regarding your compensation for participation, please contact the study staff.

We will reimburse you up to a total of $80 roundtrip for the cost of traveling to your study visits. If there is a need for you to come in for additional Screening visits or Follow-up visits you will be reimbursed for each visit up to $80 round trip.

**Please note/Payment Schedule:**

Study compensation will be paid according to a specified schedule for administrative purposes. Payment will be divided into 3 parts. First, you will be paid $80 for round trip travel on the day of your screening visit.

On Day 2 of the study (day of discharge), you will receive $80 roundtrip for travel and if you complete all procedures that are required from Day 1 through Discharge Day, you will receive $350 for Day 1 and $150 for Day 2. All subsequent visits will be paid as followed: **Day 8** $150, **Day 15** $150, **Day 22** $150, **Day 29** $150, **Day 36** $150, **Day 43** $150, **Day 64** $150, **Day 85** $150, **Day 106** $150, end of study visit: **Day 127** $150. All payments will be paid via Clincard (a debit card that will be provided to you on which your stipends will be deposited).

**Voluntary Participation/Withdrawal**

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

Your study doctor may end your participation in this study at any time, with or without your consent for any of the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

If you leave the study for any reason, the study doctor may ask you to have some end-of-study tests for your safety.

**Confidentiality**

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The Investigator, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This

means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

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.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. 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.

**Future Research Studies**

Your private information or biospecimens collected during this study will not be used or distributed for future research studies, even if identifiers are removed.

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.

**Questions or Concerns about the Study**

You can ask questions about this consent form or the study (before you decide to start the study, at any time during the study, or after completion of the study). Questions may include:

- Who to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a study participant;

- Eligibility to participate in the research;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;
- Other questions, concerns, or complaints.

**Whom to Contact About This Study**

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care or hospitalization is required, alert the physician that you are participating in this research study.

An Institutional Review Board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00057374.

**Health Care Provider Notification Option**

I consent to having my family doctor or primary health care provider notified by the study site of my participation in this study and/or any significant findings related to my health (please check yes or no).

❒**YES** (If yes, please complete the information below)

❒**NO**

| | |
|---|---|
| Name and address of family doctor or primary health care provider: | Name: |
| | Address: |
| | |
| Telephone and Fax Number: | Tel: |
| | Fax: |

**CONSENT**

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

_____

Participant's Printed Name

_____ _____

Participant's Signature Date

_____

Printed Name of the Person Conducting the Consent Discussion

_____ _____

Signature of the Person Conducting the Consent Discussion Date

**AUTHORIZATION TO USE AND DISCLOSE**
**PROTECTED HEALTH INFORMATION**

If you decide to be in this study, the study doctor and research team will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the research team may share health data about you with authorized users. Authorized users may include:

- Representatives of InterveXion Therapeutics, LLC.
- Representatives of Clinilabs
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US Federal and state agencies.
- The National Institute on Drug Abuse who funded this study.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- A data safety monitoring board which oversees this research

Your health data will be used to conduct and oversee the research, including for instance:

- To see if IXT-m200 is safe.
- To compare IXT-m200 to placebo.

Once your health data has been shared with authorized users, it may no longer be protected by Federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

**STATEMENT OF AUTHORIZATION**

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of the Person Obtaining the Authorization

_____ _____
Signature of the Person Obtaining the Authorization Date