Study title: STAMPOUT: Study of Antibody for Methamphetamine Outpatient Therapy
Protocol number: M200C-1801
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INFORMED CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: STAMPOUT: Study of Antibody for Methamphetamine Outpatient Therapy

PROTOCOL: M200C-1801

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Sponsor

The pharmaceutical company sponsoring this study is InterveXion Therapeutics, LLC. The study doctor and Pharmaceutical Research Associates, Inc. are being paid by InterveXion Therapeutics, LLC to conduct this study. 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. This study can be found by using the identifier 'NCT03336866'.

What is the purpose of this form?

You are being asked to take part 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 member of the study staff will read through the consent with you and discuss all the information. When you think you understand the study, you will then be asked if you agree to take part. If you agree, you will be asked to sign this consent form. Once you sign it, we will give you a signed and dated copy to keep.

You may show this consent form to family, friends, and other doctors before you sign it. You may want to discuss it with them to help you decide if you want to be part of the study. If you don't know another doctor but want a second opinion about this study, please ask. The study doctor will give you the name of another doctor that you can talk to.

What is being studied?
IXT-m200 is an investigational drug. The word "investigational" means IXT-m200 is not approved for sale by the U.S. Food and Drug Administration (FDA). The FDA has given permission to the sponsor, InterveXion Therapeutics, LLC, to use IXT-m200 in this study. IXT-m200 is an anti-methamphetamine monoclonal antibody. Monoclonal antibodies are medications that specifically stick to their target, in this case methamphetamine. This may decrease the effect. The effects of IXT-m200 will be compared to placebo, an inactive substance.

Because this is a study, IXT-m200 will only be given to you during this study and not after the study is over.

Why is this study being done?
The main purpose of this study is to look at the effects of IXT-m200 (the investigational drug) on the pharmacokinetics of methamphetamine (METH). Pharmacokinetics looks at the amount of drug in the blood; how the drug may move in the body; and what kind of effects the drug will have on the body when administered intravenously. This study will also look at the effects of IXT-m200 on methamphetamine liking effects. Additionally, the study will also explore the amount of IXT-m200 in the blood compared to placebo (no active ingredients). This study will also look at how safe and tolerable IXT-m200 is in people who have methamphetamine use disorder.

Throughout this consent form, IXT-m200 and placebo will be referred to as "study drug(s)," and methamphetamine and placebo will be referred to as "challenge drug(s)."

What do you need to know about this study?
Participants who take part in this study are otherwise healthy males and females between the ages of 21 and 50 who use methamphetamine; have METH use disorder; and are not seeking treatment.

This study is being conducted at one study center. This study center will enroll approximately 126 participants. Additionally, participants who complete the inpatient part of the study will be asked to take part in an additional 7-day inpatient period of the study.

You are being asked to participate in the study because you have admitted to using methamphetamine.

The study staff will review your current list of medicines, your medical, alcohol, tobacco and drug use history, and other information that may keep you from being in this study.

If there are any changes to your current medicines or your medical condition(s), please tell the study staff right away. If you don't tell the study staff of any changes, you may harm yourself by being in the study.

What will happen during this study?
You may be asked to be in the study for up to 4.5 months. This includes:

- Screening Period up to 30 days (questions and tests to see if you are eligible for the study). You will not be confined to the study center during the Screening period.
- An in-patient period of up to 23 days and 22 nights. For participants agreeing to take part in the Inpatient Extension Stay, the in-patient period will last up to 30 days and 29 nights.
- Up to 9 out-patient follow up visits
- Final study visit, approximately 126 days after the first dose of challenge drug.

You will be asked to come to the clinic up to 11 times. You may need to return to the study center for additional visits at the discretion of the study doctor.

DOSING AND PROCEDURES

METH Challenge:
On Day 1 of the inpatient period, you will undergo a METH Challenge. This part of the study is to find out if you can tell the difference between methamphetamine and placebo (no active ingredient). You will be randomly assigned (like flipping a coin) to receive either 30 mg methamphetamine or placebo (no active ingredients). You will receive both active and non-active doses during the METH Challenge. Each of these treatments will be separated by approximately 4 hours. The order in which you receive the challenge drugs is not known by you or the study doctor or staff. In the case of a medical emergency, however, the study doctor can find out quickly what challenge drug you were given.

Each of the two challenge drug treatments will consist of an intravenous (into a vein) infusion.

The first dose will be given in the morning, approximately 1 hour after you have eaten a light meal or snack. The second dose will be given approximately 4 hours after the first dose. You will be given a light meal or snack approximately 3 hours after the morning dose and 1 hour before the afternoon dose.

If you are eligible to continue on to the Treatment Phase of the study (see description below), you will undergo additional METH Challenges as described above on Days 5, 12 and 19 of the in-patient period. If you are asked and agree to take part in the extended in-patient stay, you will undergo an additional METH Challenge on Day 26 of the extended in-patient period.

Treatment Phase:
During the Treatment phase of the study, up to four groups of participants will be randomly (like flipping a coin) assigned to receive IXT-m200 or placebo as an intravenous (into a vein) infusion given over 2 hours. You will be assigned to one of the groups below:

Group 1:
If you are assigned to Group 1, you will be randomly assigned to receive one of the treatments listed below:
- IXT-m200-6 mg per kg of body weight
- placebo

About 12 participants will be assigned to receive IXT-m200 and 6 participants will be assigned to receive placebo.

Group 2:
If you are assigned to Group 2, you will be randomly assigned to receive one of the treatments listed below:
- IXT-m200-6 mg per kg of body weight
- IXT-m200-20 mg per kg of body weight
- placebo

About 6 participants will be assigned to receive IXT-m200-6 mg/kg, 6 participants will be assigned to receive IXT-m200-20 mg/kg and 6 participants will be assigned to receive placebo.

Group 3:
If you are assigned to Group 3, you will be randomly assigned to receive one of the treatments listed below:
- IXT-m200-6 mg per kg of body weight
- IXT-m200-20 mg per kg of body weight
- placebo

About 12 participants will be assigned to receive IXT-m200-6 mg/kg, 12 participants will be assigned to receive IXT-m200-20 mg/kg and 12 participants will be assigned to receive placebo.

Group 4:
If you are assigned to Group 4, you will be randomly assigned to receive one of the treatments listed below:
- IXT-m200-20 mg per kg of body weight
- placebo

About 36 participants will be assigned to receive IXT-m200 and 18 participants will be assigned to receive placebo.

You will take part in only one of the four groups listed above and receive only one of the study drug treatments listed above. You will not be able to choose which group you are assigned to. The treatment you are assigned is not known by you or the study doctor or staff. In the case of a medical emergency, however, the study doctor can find out quickly what study drug you were given.

You will receive your assigned study drug treatment on Day 4 of the inpatient period. You will be given a light meal or snack approximately 1 to 2 hours prior to dosing. You will be required to lie down or remain in a semi-sitting position while you receive the study drug and remain in such position for 2 hours following dosing. Water will be restricted from 1 hour prior to dosing until 2 hours after dosing. You will receive a standardized lunch approximately 4 hours after dosing starts.

STUDY PROCEDURES

Screening Visit

Before entering the study, you will be asked to read, sign, and date this consent form. If you choose to continue, the screening evaluation process will include the following procedures:

- Your demographic information (age, sex, race and ethnicity) will be recorded.
- Your weight and height will be measured. Body Mass Index (BMI) will be calculated using your height and weight.
- Your medical and surgical history will be recorded, including history of alcohol and smoking status, and evaluation of drug and alcohol dependence.
- A psychiatric evaluation and an assessment of methamphetamine and other drug use.
- You will be asked questions about your history of suicide and suicidal thoughts.
- Any prescription or non-prescription medications you have taken within the past 12 months will be documented.
- Your vital signs will be taken after you have been lying down for 5 minutes, including pulse, respiration (breathing) rate, blood pressure, oral temperature, and pulse oximetry (a clip will be placed lightly on your finger to measure your blood oxygen levels).
- An ECG (measures how your heart is beating) will be performed after you have been lying down for 5 minutes. Sticky patches will be applied to your chest and extremities; if your chest hair is heavy, it may be necessary to clip some hair so that the patches will stick to your skin. Female subjects may need to remove bras for the ECG.

- Routine clinical laboratory tests such as blood hematology, serum chemistry and urinalysis will be conducted. For women, a blood sample will be collected for a pregnancy test. Approximately two teaspoons of blood will be collected.
- Blood tests for Hepatitis A, Hepatitis B, Hepatitis C, and HIV (the virus that causes AIDS) will be given. Approximately 1 teaspoon of blood will be collected. If your test results show that you have Hepatitis or HIV, the study doctor will notify the local state health agency to report your condition. The results of your test(s) will be made known to local health agencies as required by law. If needed, the study doctor or study staff member will either recommend treatment to you or refer you to your primary care provider. If you test positive for HIV or Hepatitis, you will not be included in the study.
- An alcohol breath test will be performed; the results will be kept with your study chart and will not be discarded. If you test positive, you may not be included in the study.
- A urine drug screen will be performed; the results will be kept with your study chart and will not be discarded. If you test positive, you may not be included in the study.
- A physical exam will be performed.
- Study entry criteria will be reviewed.

Screening does not guarantee entry into the study. Entry into the study will depend upon the results of your screening evaluation and the opinion of the study doctor. If you qualify to be in the study, you will return to the study center within 30 days of the screening visit for the in-patient part of the study. The in-patient part may last up to 23 days and 22 nights if you qualify for all portions of the study. If you are asked and agree to take part in the extended in-patient period of the study, your inpatient part may last up to 30 days and 29 nights.

In-Patient Visit (Up to 23 Days/22 nights total)

Enrollment/Baseline (Day -1)
You will be asked to return to the study center the day before receiving your first dose of challenge drug during the in-patient period.

The following procedures will be performed at check-in:

- Study entry criteria will be reviewed.
- The list of prescription or non-prescription medications taken from the previous visit will be updated.
- Any changes in your health will be updated.
- An assessment of methamphetamine and other drug use for the past 30 days will be done.

- Vital signs will be collected after you have been lying down for 5 minutes. Vital signs include pulse, respiration (breathing) rate, blood pressure, oral temperature, and pulse oximetry.
- An ECG will be performed after you have been lying down for 5 minutes.
- A physical examination will be performed.
- Routine clinical laboratory tests such as blood hematology, serum chemistry and urinalysis will be conducted. Approximately two teaspoons of blood will be collected. For women, a blood sample for a pregnancy test will also be collected.
- A urine drug screen; if you test positive, you may not be eligible to continue with the study. The results will be kept with your study chart and will not be discarded.
- An alcohol breath test; if you test positive, you will not be eligible to continue with the study. The results will be kept with your study chart and will not be discarded.
- Telemetry will be monitored continuously for at least 4 hours. Telemetry is the continuous monitoring of vital signs such as heart rate, blood pressure, and breathing and also looks at the electrical activity of your heart.

If you do not continue to meet the study requirements after admission procedures are performed, you will not be able to continue in the study.

In-patient Stay - Days 1, 2 and 3
You will receive the challenge drugs as outlined in this consent form. The following procedures will be completed:

- An IV catheter used for blood collection and challenge drug administration will be inserted into a vein. You will have two IV catheters placed on Day 1.
- Vital signs including pulse, respiration (breathing) rate, blood pressure, oral temperature, and pulse oximetry will be taken after you have been lying down for 5 minutes multiple times.
- ECG will be performed after you have been lying down for 5 minutes multiple times.
- Telemetry will be monitored continuously for at least 8 hours after METH Challenge dosing.
- A physical exam will be performed on Day 2.
- PK blood samples (a blood sample taken to measure the amount of drug in your blood) will be collected approximately 18 times. A little over ½ teaspoon of blood will be collected each time.
- A blood sample to test for an immune reaction to the study drug will be collected on Day 3. About one teaspoon of blood will be collected.
- Routine clinical laboratory tests such as blood hematology, serum chemistry and urinalysis will be conducted on Day 2. Approximately two teaspoons of blood will be collected.

- All your urine starting just prior to the METH Challenge through 36 hours after dosing will be collected for urine PK samples. Urine PK samples are to see how much methamphetamine gets into your urine.
- You will complete questionnaires several times about the way you are feeling and about the challenge drug. The questionnaires take approximately five to ten minutes to complete each time.
- You will be asked about any changes in your health.
- You will be asked about any changes in your medications.

After all the study-related procedures are completed on Day 3, the study doctor will determine if you may continue to the treatment phase of the study. If the study doctor determines that you cannot continue in the study, you will be asked to complete the early termination procedures (see End of Study Visit/ Early Termination section below). You will be discharged from the study center on Day 3 or when the study doctor feels it is okay for you to leave.

Depending on the results of the METH Challenge, you may be asked to continue on to the treatment phase of the study. If you continue into this part of the study, you will stay in the study center. You will spend up to 23 days total in the study center during the in-patient stay, if you complete the treatment phase. If you are asked and agree to take part in the extended in-patient period, you will spend up to 30 days total in the study center during the in-patient stay.

In-patient Treatment Phase – Days 4 through 22
You will receive the challenge and study drug treatments as outlined in this consent form on Days 4, 5, 12 and 19.

The following procedures will be completed:

- An IV catheter used for blood collection and challenge and study drug administration will be inserted into a vein. You will have two IV catheters placed on dosing days.
- Vital signs including pulse, respiration (breathing) rate, blood pressure, oral temperature, and pulse oximetry will be taken after you have been lying down for 5 minutes multiple times.
    - When you are dosed on Day 4 with either placebo or study drug you will be asked to remain in a lying down or semi-reclining position for the entire 2 hour dosing period. During this dosing period of two hours vital signs will collected while you are in a lying down or semi-reclining position.
- ECG will be performed after you have been lying down for 5 minutes multiple times.
- Telemetry will be monitored continuously for at least 8 hours after each IXT-m200 and METH Challenge dosing.
- A physical exam will be performed multiple times.

- PK blood samples (a blood sample taken to measure the amount of drug in your blood) will be collected approximately 63 times, with the most on any one day being about 15 times. A little over ½ to one teaspoon of blood will be collected each time.
- A blood sample to test for cytokines will be collected prior to dosing on Day 4. Additional samples may be collected if necessary after dosing if you develop an infusion related reaction. Cytokines help to regulate the immune system. They are created in response to a stimulus such as inflammation. Approximately a little over 5 teaspoons of blood will be collected each time.
- Routine clinical laboratory tests such as blood hematology, serum chemistry and urinalysis will be conducted multiple times. Approximately two teaspoons of blood will be collected each time.
- All your urine starting just prior to each METH Challenge through 36 hours after dosing will be collected for urine PK samples. Urine PK samples are to see how much methamphetamine gets into your urine.
- You will complete questionnaires several times about the way you are feeling and about the challenge drug. The questionnaires take approximately five to ten minutes to complete each time.
- You will be asked about any changes in your health.
- You will be asked about any changes in your medications.
- You will be asked questions about your history of suicide and suicidal thoughts on Day 22 only unless you take part in the extended in-patient stay.

Once all the study procedures have been completed on Day 22 and the study doctor thinks that you are medically stable, you will be discharged from the study center unless you have been asked to take part in the extended in-patient stay (see details below). You will return to the study center weekly for outpatient visits.

In-patient Extended Period (Day 22 through Day 29):
If you are asked to stay in the study center for the extended in-patient stay, you will remain in the study center from Day 22 through Day 29. You will receive the challenge drugs as outlined in this consent form.

The following procedures will be completed:

- An IV catheter used for blood collection and challenge drug administration will be inserted into a vein. You will have two IV catheters placed on Day 26.
- Vital signs including pulse, respiration (breathing) rate, blood pressure, oral temperature, and pulse oximetry will be taken after you have been lying down for 5 minutes multiple times.
- ECG will be performed after you have been lying down for 5 minutes multiple times.

- Telemetry will be monitored continuously for at least 8 hours after the METH Challenge dosing.
- A physical exam will be performed multiple times.
- PK blood samples (a blood sample taken to measure the amount of drug in your blood) will be collected approximately 19 times. A little over ½ to one teaspoon of blood will be collected each time.
- Routine clinical laboratory tests such as blood hematology, serum chemistry and urinalysis will be conducted on Day 27. Approximately two teaspoons of blood will be collected.
- A blood sample to test for an immune reaction to the study drug will be collected on Day 28. About one teaspoon of blood will be collected.
- All your urine starting just prior to the METH Challenge through 36 hours after dosing will be collected for urine PK samples. Urine PK samples are to see how much methamphetamine gets into your urine.
- You will complete questionnaires several times about the way you are feeling and about the study drug. The questionnaires take approximately five to ten minutes to complete each time.
- You will be asked questions about your history of suicide and suicidal thoughts on Day 29 only
- You will be asked about any changes in your health.
- You will be asked about any changes in your medications.

Once all the study procedures have been completed on Day 29 and the study doctor thinks that you are medically stable, you will be discharged from the study center. You will return to the study center weekly for outpatient visits.

Outpatient Follow-up Visits (Days 28, 35, 42, 49, 56 and 63)
You will return to the study center for weekly follow up visits after you have been discharged from the study center during the in-patient period. If you participated in the extended in-patient period, you will not complete the Day 28 follow up visit.

The following procedures will be completed at each visit:

- The list of prescription or non-prescription medications taken from the previous visit will be updated.
- Any changes in your health will be updated.
- An assessment of methamphetamine and other drug use for the past 30 days will be done.
- Vital signs will be collected after you have been lying down for 5 minutes. Vital signs include pulse, respiration (breathing) rate, blood pressure, oral temperature, and pulse oximetry.
- A physical examination will be performed.
- Routine clinical laboratory tests such as blood hematology, serum chemistry and urinalysis will be conducted. For women, a blood sample for a pregnancy test will also be collected. Approximately two teaspoons of blood will be collected.

- A PK blood sample (a blood sample taken to measure the amount of drug in your blood) will be collected. About one teaspoon of blood will be collected.
- A blood sample to test for human antibody against IXT-m200, will be collected on Days 28 and 63. About one teaspoon of blood will be collected.
- A urine drug screen. The results will be kept with your study chart and will not be discarded.
- An alcohol breath test. The results will be kept with your study chart and will not be discarded.

Outpatient Follow-up Visits (Days 84 and 105)
The following procedures will be completed at each visit:

- The list of prescription or non-prescription medications taken from the previous visit will be updated.
- Any changes in your health will be updated.
- An assessment of methamphetamine and other drug use for the past 30 days will be done.
- Vital signs will be collected after you have been lying down for 5 minutes. Vital signs include pulse, respiration (breathing) rate, blood pressure, oral temperature, and pulse oximetry.
- A physical examination will be performed.
- Routine clinical laboratory tests such as blood hematology, serum chemistry and urinalysis will be conducted. Approximately two teaspoons of blood will be collected. For women, a blood sample for a pregnancy test will also be collected.
- A PK blood sample (a blood sample taken to measure the amount of drug in your blood) will be collected. About one teaspoon of blood will be collected.
- A urine drug screen. The results will be kept with your study chart and will not be discarded.
- An alcohol breath test. The results will be kept with your study chart and will not be discarded.

End-of-Study Visit (Day 126) / Early Termination Visit
You will return to the study center for the last visit on Day 126 or in the event you discontinue from the study early. The following procedures will be completed:

- The list of prescription or non-prescription medications taken from the previous visit will be updated.
- Any changes in your health will be updated.
- An assessment of methamphetamine and other drug use for the past 30 days will be done.
- Vital signs will be collected after you have been lying down for 5 minutes. Vital signs include pulse, respiration (breathing) rate, blood pressure, oral temperature, and pulse oximetry.

- A physical examination will be performed.
- Routine clinical laboratory tests such as blood hematology, serum chemistry and urinalysis will be collected. Approximately two teaspoons of blood will be collected. For women, a blood sample for a pregnancy test will also be collected.
- A PK blood sample (a blood sample taken to measure the amount of drug in your blood) will be collected. About one teaspoon of blood will be collected.
- A blood sample to test for an immune reaction to the study drug will be collected. About one teaspoon of blood will be collected.
- A urine drug screen. The results will be kept with your study chart and will not be discarded.
- An alcohol breath test. The results will be kept with your study chart and will not be discarded.

Once the above procedures have been completed, your participation in the study will end unless you experience a change in your health that needs to be monitored.

Study Restrictions

In order to be in this study, you must agree to refrain from the substances and activities listed in the chart below for the specified timeframes.

Medication, Substance or Activity	**Specified Timeframe or Limit**
Strenuous activities, such as exercise or sports	At least 72 hours prior to dosing of study drug and for at least 48 hours after.
Recreational drug use	From screening, throughout the study
Treatment with any prescription medications, other than oral contraceptives, or over-the-counter nutritional supplements	Within 14 days prior to the first dose of study drug and throughout the inpatient stay (until Day 22 or Day 29 if taking part in the extended in-patient stay).
Any approved prescription anti-obesity drug or any over-the-counter medication for weight loss	Within a period of 90 days prior to the first dose of study medication and throughout the study.
Ingestion or use of any investigational medication or device	Within 30 days prior to the first dose of study drug and throughout the study.
Alcohol	Limit consumption to approximately 1 drink per day for women and 2 drinks per day for men while in the study. 1 alcoholic drink is defined as 12 oz. beer, 4 oz. wine, or 1 oz. distilled spirits.
Smoking and use of tobacco-containing products or nicotine-	Must be able to refrain from use for at least 3 hours on dosing days and limit

containing products	use to no more than 4 cigars or pipes of tobacco per day or no more than 30 cigarettes or equivalents per day.
Blood plasma or platelets donation	Within 30 days prior to screening and throughout the study
Egg or sperm donation	From screening until 90 days after the last dose of study drug(s)

Roles and Responsibilities
As a study volunteer, you will have the following responsibilities:

- Follow the study guidelines as instructed by the study staff and the study doctor.
- Tell the study doctor of any illnesses or injuries, side effects, or any problems that occur during your participation in the study.
- Tell the study doctor or study staff of any new medications (prescription or over-the-counter) that you start taking after signing this consent form.
- Return to the study center as instructed by the study staff.

Note: You may be removed from the study because of inappropriate conduct, not following instructions or violation of study protocol or the study center rules.

What are the potential risks of being in the study?

In this study, you will receive IXT-m200, Methamphetamine HCl and placebo.

IXT-m200 Risks*:*
IXT-m200 is a chimeric (meaning part mouse, part human) monoclonal antibody. Risks of monoclonal antibodies include the following:

- Allergic reactions, such as hives or itching
- Flu-like signs and symptoms, including chills, fatigue, fever, and muscle aches and pains
- Nausea, vomiting
- Diarrhea
- Skin rashes
- Low blood pressure

One study has been conducted with IXT-m200 in healthy male and females to date. In this first clinical study, of 42 participants (17 females) 32 received IXT-m200 of doses up to 20 mg/kg and 10 participants receiving placebo (saline).

There were no serious adverse events or serious adverse reactions during the conduct of the study. One participant had an infusion reaction halfway through the IXT-m200 infusion. The participant experienced 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. No further symptoms were noted, and the participant required treatment for bronchitis but fully recovered after the incident.

There are possible risks associated with binge use of METH (high doses of METH taken in a short period of time) after receiving IXT-m200. IXT-m200 may increase the concentration of METH in the blood or tissues when large doses of METH are used. While IXT-m200 is in your system, you may react differently to typical doses of methamphetamine, and this reaction may change over time. It is possible that binge use of METH after receiving IXT-m200 could be extremely dangerous and possibly life-threatening.

The METH risks listed below may be worse following a dose of IXT-m200 until it leaves your body (up to about 3 or 4 months after dosing).

Methamphetamine Risks:
Use of methamphetamine can have cardiovascular risks such as the following:

- Elevation of blood pressure
- Fast heart rate and palpitation
- Fatal cardiorespiratory arrest (sudden stoppage of heart's ability to pump blood) has been reported, mostly in the context of abuse/misuse.

Methamphetamine use can also include risks of the following:

- psychotic episodes for example hallucinations
- dizziness
- dysphoria (state of unease or generalized dissatisfaction with life)
- overstimulation
- euphoria
- insomnia
- tremor
- restlessness
- headache
- worsening of motor and phonic tics (involuntary muscles movements) and Tourette's syndrome
- diarrhea
- constipation
- dryness of mouth
- unpleasant taste
- hives
- impotence and changes in libido (sexual drive)
- frequent or prolonged erections
- rhabdomyolysis (a condition in which damaged skeletal muscle breaks down rapidly)
- hair loss

Methamphetamine may impair your ability to perform potentially hazardous activities, such as driving a car or operating heavy machinery.

Tolerance, extreme psychological dependence and severe social disability can develop during chronic (long-lasting) use of methamphetamine. Tolerance results in the need for increasing doses to maintain a desired effect.

Abruptly discontinuing use of methamphetamine after prolonged use of high doses can result in extreme fatigue, mental depression and changes in sleep. Signs of chronic use of methamphetamine can cause severe skin lesions, insomnia, irritability, hyperactivity, and personality changes and psychosis. Abuse and/or misuse of methamphetamine have resulted in death. Fatal cardiorespiratory arrest has been reported in the context of abuse and/or misuse of methamphetamine.

Placebo Risks:
Placebo is an inactive substance that is unlikely to cause side effects.

Allergic Reaction Risks*:*
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.

It is important that if you should feel any side effects, you tell the study staff or study doctor immediately. **If it is an emergency or if you cannot contact the study staff or study doctor, you should call 911 immediately.**

<u>Other Potential Risks*:*</u>

Blood Draw and IV Risks*:*
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 your stay at the study center, you will have blood drawn either from a vein using a needle or through an IV catheter (a small plastic tube that is temporarily inserted into your vein with a needle). You will also have the challenge and study drugs given through an IV catheter. You may have an IV in place for several hours during each treatment day. You will have about two and a half cups of blood drawn during the entire study. If you take part in the In-Patient Extended period, you will have less than three total cups of blood drawn during the entire study. For comparison, a standard Red Cross blood donation is equal to about

two cups of blood. You may need to return for additional unexpected visits or additional laboratory tests.

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.

If you have any questions about the use, storage and destruction of samples collected, ask study staff.

ECG Risks:
An ECG measures how your heart is beating. The test takes a few minutes and is not painful. The study staff will put electrodes (sticky patches) on your skin. The patches might cause irritation, redness, and/or itchiness. To make the patches stick, you may have to have some of the hair shaved off of your skin.

Blood Pressure Measurement Risks
Temporary discomfort and bruising caused by repeated inflation of the blood pressure cuff may happen.

Confidentiality Risks*:*
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.

Unknown Risks*:*
In addition to the risks already mentioned, there may be other risks that are unknown and can't be predicted.

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.**

Reproductive Risks:
The effects of the study drug(s) on a fetus (unborn baby) are unknown.

If you are male, you must be sterile (for example a vasectomy) or agree to use a condom and spermicide in addition to your female partners using an acceptable form of birth control (as described below) or abstain from sexual relations

throughout the study. You must also agree not to donate any sperm for 90 days after the last dose of study drug(s).

If you are female and become pregnant while in this research study, an injury that we don't know about could occur to the fetus. You may not be in this study if you are pregnant, are trying to get pregnant or are breastfeeding. Women will be tested for pregnancy during the study. In order to take part in this research study, if you are able to get pregnant, you should not have sexual intercourse or you must use a method of birth control that is acceptable to you and the study doctor during the study until the end-of-study follow up visit. Women who are surgically sterile or who have been post-menopausal for at least one year will be considered unable to become pregnant and do not need to use additional birth control. If you become pregnant during the study, you must tell the study doctor immediately. The study drug will be stopped, and your participation in the drug administration phases of the study will end. We will ask you to continue to participate in the follow-up parts of the study.

Acceptable methods of birth control for this study include the following:

- oral contraceptive pills
- contraceptive patches
- vaginal ring
- diaphragm
- sponge
- condom with spermicide
- hormone injection
- intrauterine device
- vasectomized partner

If you or your partner becomes pregnant during the study you should tell the study doctor immediately. Please also tell the doctor who will be taking care of you/your partner during the pregnancy that you took part in this research study. The study doctor will ask if you/your partner or your pregnancy doctor is willing to provide updates on the progress of the pregnancy and its outcome. You and your partner are not required to provide this information. If you/your partner agree, this information will be provided to the study sponsor for safety monitoring follow-up.

You will be informed of new information relating to the study.
All new findings discovered during the course of this study that may influence your decision to stay in this study will be given to you by your study doctor as they become available.

Does being in this study provide any benefit?
This study is for research purposes and is not designed to offer you any treatment. There is no direct benefit to you for being in this study.

Are there any alternatives to participating in the study?
No therapeutic or other health benefits will result from participating in this study, so your only alternative is to not participate in the study.

Whom do you contact in the event of an emergency?
If you experience an adverse event (undesirable reaction) or a study-related injury during the course of the study, you should immediately contact Dr. Lynn Webster at (801) 269-8200 or (801) 892-5151 (if during non-business hours).

If you seek emergency care, or if you are hospitalized, please alert the doctor who is treating you that you are enrolled in a study being conducted by Dr. Lynn Webster.

If it is an emergency or if you cannot contact the study staff or study doctor, you should call 911 immediately.

What happens if you have a study-related injury?
If you experience a research injury, Pharmaceutical Research Associates, Inc. will provide or arrange for medical treatment. For serious, related injuries, please call 911. For related injuries that are not serious, contact Dr. Webster at 801-269-8200. InterveXion Therapeutics, LLC will cover the reasonable physician fees and medical expenses necessary for treatment of the injury that are not covered by your medical and hospital insurance coverage. A research injury is any physical injury or illness caused by your direct participation in the study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered to be a research injury. There are no plans to offer you any payment for such things as lost wages, expenses other than medical care required for a research injury, or pain and suffering. To help avoid injury, it is required that you follow all study directions provided by the study staff. You are not giving up any of your legal rights by signing this form.

If you are treated for a research injury that is paid for by InterveXion Therapeutics, LLC or its representative, your name, date of birth, gender, and Medicare Health Insurance Claim Number or Social Security Number will be collected to determine your Medicare status. If you are a Medicare beneficiary, InterveXion Therapeutics, LLC will report the payment and information about the study you are in to the Centers for Medicare & Medicaid Services, in accordance with CMS reporting requirements. InterveXion Therapeutics, LLC will not use this information for any other purpose.

This study involves HIV-related information. The release of any HIV-related information to InterveXion Therapeutics, LLC does not permit InterveXion Therapeutics, LLC to re-disclose such information without your consent, unless permitted or required to do so under applicable state law. If you receive

Medicare, by signing this consent, you specifically authorize InterveXion Therapeutics, LLC and its representatives to disclose your HIV-related health information to CMS for the purpose of complying with reporting requirements.

By signing this consent form, you are not giving up any legal rights that you would otherwise have. You are not prevented from seeking to collect compensation for injury related to malpractice, negligence, or misconduct on the part of those conducting the study.

Will it cost you anything to be in this study?
There will be no cost to you for the study doctor's time, medicines, study procedures, or supplies related to this study. The challenge and study drugs used in the study will be given to you at no cost. The sponsor, InterveXion Therapeutics, LLC will pay for the study doctor's time, study procedures, and supplies related to this study.

Will you be compensated for being in this study?
You will be reimbursed for time and travel associated with being in this study.

If you follow all instructions and complete the entire study, you will receive the study completion amount. If you are dropped from the study due to circumstances beyond your control, such as medical reasons or technical problems, you will be compensated based on the number of completed visits.

Any missed visits or failure to meet scheduled visits will be considered non-compliance. If you miss a scheduled visit, you will not be eligible to receive the full amount stated below and you will not receive any compensation for the missed visit(s).

If you are dropped from the study because of non-compliance or you choose to withdraw from the study, you will be asked to undergo the Early Termination procedures. You will receive a pro-rated compensation amount based on the study visits that you completed.

You will receive all compensation you are due within 30 days after your last completed visit.

Visit	Per Day	Sub-Total
Screening	50.00	50.00
Check-in (Day -1)	200.00	200.00
In-patient METH Challenge (Day 1, 5, 12 and 19)	300.00	1200.00
In-patient Period (Days 2 and 3)	200.00	400.00
In-patient Treatment (Day 4)	300.00	300.00
In-patient Treatment Period (Days 6-11, 13-18 and	200.00	2800.00

20-21)		
Discharge Treatment Period (Day 22)	150.00	150.00
Follow up Visits (Days 28, 35, 42, 49, 56, 63, 84, 105 and 126)	150.00	1350.00
Completion Stipend (on Day 126)	1100.00	1100.00
Total		**$7550.00**

If you take part in the extended inpatient period you will receive the additional compensation listed below:

Extended In-patient Compensation	**Per Day**	**Sub-Total**
Extended In-patient METH Challenge (Day 26)	300.00	300.00
Extended In-patient Period Days 22 and 28	50.00	100.00
Extended In-patient Period (Days 23-25 and Day 27)	200.00	800.00
Discharge Extended In-patient Period (Day 29)	150.00	150.00
Completion Stipend (on Day 126)	350.00	350.00
Total		**$1700.00**

Once you are enrolled, if the PRA medical team requires you to return to the clinic for additional physical examinations, blood, urine or ECG testing after you have completed your participation in the study, you will be compensated an additional amount for your time and travel; the amount will range between $50 to $100 depending on the procedures.

Financial compensation for such things as lost wages, disability, or discomfort due to study-related injury is not offered. There will be no financial compensation for any medical expenses due to personal injury caused by you.

This compensation will be considered earned income and will be reported to the IRS, as required by law. You will receive a 1099 Form. If you do not know what this form is, please ask the study staff.

Do you have to be in this study?
Being in this study is voluntary. This means you can decide if you do or do not want to be in the study. If you decide to be in the study, you can stop at any time. If you decide that you no longer want to be in the study, you will be asked to complete Early Termination procedures.

You can take a copy of this consent form home with you, so you can read and talk about it with other people before you sign it. If you decide to be in this study, you will be asked to sign and date this form. You will also get a copy of the signed and dated form.

You can withdraw your consent to be in this study, at any time, without penalty or loss of benefits.

If you decide to withdraw from the study and want to leave the clinic after you have recently taken a study drug that may cause side effects like drowsiness or fuzzy thinking, you will be asked to stay at PRA until it is physically safe for you to leave. If you insist on leaving PRA before the PRA study staff has determined it would be physically safe for you to leave, you will be asked to sign a separate Against Medical Advice Form.

Can you be removed from the study without your permission?
Your study doctor may end your participation in this study for any of the following reasons:

- If you develop a side effect or medical condition that may place you at risk of more complications by staying in the study or if you need a medicine not allowed in this study;
- If you become disruptive during the study;
- If you do not follow the study doctor's or study staff's instructions;
- If you become pregnant;
- If you are unable to take the doses;
- If you are unable to keep your scheduled appointments;
- If the study is cancelled by InterveXion Therapeutics, LLC, Midlands IRB or by the FDA; the Midlands IRB is an independent ethics committee that reviews the conduct of human research studies.
- For administrative reasons.

Who will have access to your study and/or medical information?
As part of this study, your personal and medical information will be collected, including the following:

- Your name
- Address
- Birth date
- Medical records
- Information gathered for this study
- Records about the study (such as drugs or treatments)

In addition to the people directly involved with the study, other people may see your information. These people and organizations include the following:

- Pharmaceutical Research Associates, Inc., InterveXion Therapeutics, LLC and/or its representatives
- People hired by InterveXion Therapeutics, LLC to review the study information

You do not have to give us permission to use and give out your information. However, if you do not give us this permission, you cannot be in this study.

All of your study data will be kept in secure location(s) and may be held and processed on computers.

Your medical records and signed consent form may also be reviewed and copied. Because of the need to release information to some groups, absolute confidentiality cannot be guaranteed. These groups are

- InterveXion Therapeutics, LLC, the study sponsor
- Food and Drug Administration
- Midlands IRB
- Other governmental agencies, both foreign and domestic.
  Study data may be transferred to other countries for processing, including countries not covered by data protection legislation

Although the results of this study may be presented at meetings and in publications, your identity will be kept private.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the study staff cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The study staff will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government if that information is to be used for auditing or evaluation of federally-funded projects or for information that must be disclosed in order to meet the requirements of the FDA.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about you or your involvement in this study. If an insurer, employer, or other person obtains your written consent to receive study information, then the study staff may not use the Certificate to withhold that information.

The Certificate of Confidentiality does not prevent the study staff from disclosing voluntarily, without your consent, information that would identify you as a participant in the study under the following circumstances: intent to harm yourself or others and child abuse.

PERSONS TO CONTACT FOR QUESTIONS, CONCERNS, OR COMPLAINTS

If you have any questions, concerns or complaints about this study, contact Lynn Webster at (801) 269-8200, Monday-Friday between 8:00 am-5:00 pm or after hours at (801) 892-5151.

If you have questions about your rights, general questions, complaints or concerns about this research, or questions about your rights as a person taking part in this study, call the Midlands Independent Review Board (MLIRB) at (913) 385-1414 or (800) 636-4445. If, at any time during or after your participation in this research, you would like information or to offer input about your research experience, you can call the Midlands IRB at the number above or you can go to the Midlands IRB website at www.mlirb.com and give us your comments. Either way you do not have to give us your name, if you do not want to.

You have the right to ask any questions concerning the potential and/or unknown hazards of this study, at any time. If you have any questions concerning your participation in this study, or if at any time you feel you have experienced a research-related injury or a reaction to the study drug, contact Lynn Webster at (801) 269-8200, Monday-Friday between 8:00 am-5:00 pm or after hours at (801) 892-5151.

LEGAL RIGHTS

You will not lose any of your legal rights to which you are otherwise entitled by signing this consent form.

SUBJECT'S STATEMENT
CONSENT

By signing this form you are agreeing to the following:

- That you have read this Informed Consent form or someone read it to you.
- This form describes the purpose and nature of this study.
- You have had time to review this information.
- You have been offered a chance to ask questions.
- You received satisfactory answers to your questions.
- If you do not take part in the study, you will not lose any benefits.
- If you leave the study, you will not lose any benefits.
- If you leave the study, you will not lose any legal rights.
- Your participation in this study is completely voluntary.

You will receive a copy of this signed and dated Informed Consent Document for your records.

You agree to participate in this study.

_____ _____
Print Participant's Name Date

_____ Time Signed __ __ : __ __
Study Participant (signature)

_____ _____
Print Name of person who explained this study Date

_____ Time Signed __ __ : __ __
Person who explained this study (signature)

AUTHORIZATION TO USE AND DISCLOSE MEDICAL INFORMATION

A federal regulation known as the Privacy Rule gives you certain rights concerning the privacy of your health information. The Privacy Rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Researchers covered by this rule are required to get your authorization (permission) to use and disclose (share with others) any health information that could identify you. Under this federal law, your records cannot be used or disclosed by Pharmaceutical Research Associates, Inc. for research purposes unless you sign this form. You may not take part in this study unless you sign this form.

If you sign this Form, you will be agreeing to the disclosures described below:

This section, called an "Authorization," explains how your health information will be used and disclosed and describes your rights.

Your personal health information may be used or disclosed in order to conduct this study, as necessary for your study-related procedures or payment for such procedures, to allow Pharmaceutical Research Associates, Inc. to conduct its normal business operations, and to ensure that information related to the study is available to the parties that need it for research purposes. The sponsor, InterveXion Therapeutics, LLC, may add your information to research databases so that it can study better measures of safety and effectiveness, study other therapies for patients, develop a better understanding of disease, or improve the effectiveness of future clinical trials.

This personal health information may include, but is not limited to, your name, address, telephone number, date of birth, government-issued identification number, and medical records and charts, including the results of all tests and procedures performed during the study.

The study data that InterveXion Therapeutics, LLC requests does not include your name, address, or social security number. Instead, the study doctor uses your initials and assigns a code number to your records that are sent to InterveXion Therapeutics, LLC Your records will be assigned a code number. Your personal health information will be kept as confidential as possible under the law; however, absolute confidentiality cannot be guaranteed.

Your medical records will be reviewed or copied at Pharmaceutical Research Associates, Inc., InterveXion Therapeutics, LLC and/or its representatives and may be reviewed or copied by regulatory authorities or other oversight bodies, including the Midlands IRB, for this study. The purpose of these reviews is to make sure the study is being conducted properly and that the data are being collected correctly, or for other purposes, allowed by law.

Some or all of the test results and other information will be reported to InterveXion Therapeutics, LLC. InterveXion Therapeutics, LLC and its representatives will analyze this information. Their findings may be reported to the U.S. Food and Drug Administration (the FDA) or other regulatory agencies in the United States and foreign countries.

The Midlands IRB may also review your records.

Except for the disclosures described above, they will not disclose your records to other parties. Once your health data has been shared with authorized users, it may no longer be protected by Federal privacy law.

In no event will you be identified by name in any published reports about this study or in any other scientific publications or presentations.

You have the right to request access to your personal health information from the study doctor. To ensure the scientific integrity of the study, you may not be able to review some of your records related to the study until after the study has been completed.

Your study records may be kept at Pharmaceutical Research Associates, Inc. indefinitely following the completion of the study. You may not have the right to review your records while the study is in progress. You will be able to review your records after the study has been completed.

This Authorization does not expire; however, you have the right to revoke this authorization at any time by giving written notice to the study doctor. The study doctor's and Pharmaceutical Research Associates, Inc. contact information is:

Pharmaceutical Research Associates, Inc.
1255 East 3900 South
Salt Lake City, UT 84124

If you revoke this authorization, you will not be permitted to continue in this study. Neither Pharmaceutical Research Associates, Inc., nor InterveXion Therapeutics, LLC will be able to use or disclose your personal health information from this study except to the extent that they have already relied on this information to conduct the study.

Under federal law, your study records cannot be used or disclosed for research purposes unless you sign this authorization. You may refuse to sign this authorization; however, you may not take part in the study unless you sign this authorization. If you revoke this authorization, you will not be able to stay in the study. If you drop out of the study, you do not have to revoke this authorization. If

you drop out and decide to revoke your authorization, the information that has already been collected in your study record may continue to be used and disclosed as described above. If you cancel this Authorization, Pharmaceutical Research Associates, Inc. and InterveXion Therapeutics, LLC will no longer use or disclose your personal health information under the Authorization for this study, unless the study doctor needs to use or disclose some of your personal health information to preserve the scientific integrity of the study. Information given to InterveXion Therapeutics, LLC before you cancel this Authorization may still be used by InterveXion Therapeutics, LLC. No new information will be added.

You have read, in a language that you understand well, the above information. The content and meaning of this information has been explained to you. You hereby voluntarily consent and offer to take part in this study and authorize the use and disclosure of your medical information.

You have not forfeited any of your legal rights by signing this authorization. You will receive a copy of the signed and dated form.

Your signature on this form will authorize (give permission for) Pharmaceutical Research Associates, Inc. to collect and use information that can identify you.

Statement of Authorization
I have read this form, and its contents were explained. My questions have been answered. I voluntarily agree to allow the 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 this form.

_____
Printed Name of Study Participant

_____ _____
Signature of Study Participant Date

Statement of Person Explaining Authorization

I have carefully explained to the subject the nature and purpose of this form. I have been available to answer any questions that the subject has had about this form.

Printed Name of Person Explaining Authorization

Signature of Person Explaining Authorization | Date