Main Study - Information Sheet and Informed Consent Form

Sponsor / Study Title:	**Intra-Cellular Therapies, Inc. / "A Randomized, Double-blind, Placebo-controlled, Single Site Study to Evaluate the Efficacy of Lumateperone for the Treatment of Major Depressive Disorder (MDD) and early life trauma in Adult Patients Aged 21 to 70 Years"**
Protocol Number:	**STUDY00008399**
Principal Investigator: (Study Doctor)	Julie Farrington, MD Assistant Professor at The University of Texas at Austin and Clinical Trials Director
Telephone:	512-495-5566 833-882-2737 (24 hours)
Address:	Dell Medical School 1601 Trinity Street Austin, TX 78712 USA

This information sheet has 4 parts:

- PART 1 – Summary
- PART 2 – Study Information
- PART 3 – Protecting Your Personal Information
- PART 4 – Consent Form

PART 1 – Summary

What you should know this study?

The purpose of this clinical research study is to understand how effective and safe an investigational study drug called lumateperone is and whether it works to reduce the severity of depressive symptoms in adults with Major Depressive Disorder (MDD) and early life trauma.

- If you choose to take part, you will be asked to come to a study center for up to 8 visits. This will take about 9 weeks, or just over 2 months.
- While taking part in this study, you may experience side effects. These may range from mild to very serious and can be different for each person.
- You may or may not receive any benefit from taking part in this study.

Taking part in this clinical research study is voluntary. You do not have to take part. If you join the study, you can stop taking part at any time. Please take time to read this entire information sheet.
Ask any questions before deciding whether to take part in this study.

PART 2 – Study Information

Introduction

You are invited to take part in a clinical research study. A clinical research study is a medical investigation designed to answer specific questions about a potential new drug. All new drugs must undergo thorough testing in clinical

research studies before doctors can prescribe them to people. Without clinical research studies, no new drugs would be developed, and few medical advances would be made.

It is important that the subjects in clinical research studies are diverse and that all kinds of people are represented. Certain conditions or diseases can affect people differently based on their age, sex, race/ethnicity. By including a diverse range of people in studies, we may learn more about how a potential new medication works in a specific group of people and how safe it is.

To help you decide if you want to take part in this study, you should understand:

- The purpose of the study
- The procedures you may have while taking part
- The possible benefits and risks of taking part
- Any discomforts you may have; and
- The precautions that will be taken for your safety.

Please read this information sheet and consent form carefully. Feel free to share and discuss it with others. Please ask the study doctor about anything that is not clear, or if you would like more information. After you have read everything and all of your questions have been answered, if you decide that you want to take part, you will be asked to sign and date the informed consent form. You will be given a signed and dated copy of the form to keep. The original will stay at the study center.

This study is sponsored by Intra-Cellular Therapies, Inc., referred to as the "Sponsor" throughout this information sheet. Being the study Sponsor means that Intra-Cellular Therapies, Inc. is funding and is responsible for this study.

Why have I been invited to take part?

You have been invited to take part in this study because you have been diagnosed with Major Depressive symptoms and have experienced early life trauma/abuse.

Do I have a choice?

Yes. Taking part in this study is totally up to you.

- You can decide whether you want to continue to take part or not.
- You do not have to take part to receive treatment for your condition.
- If you decide not to take part, it will not affect your rights and you will still be able to continue receiving standard medical care for your condition.
- You can leave (withdraw from) the study at any time.
- Your decision not to take part or withdraw from this study will involve no penalty or loss of benefits to which you are otherwise entitled.

How many people will take part in this study?

This study will include about 50 subjects.

What is the purpose of the study?

The main aim of this clinical research study is to understand whether the investigational study drug, lumateperone, can reduce the severity of depression in adults who have been diagnosed with major depressive disorder and who have experienced early life abuse.

This study is a Phase 4 study. The purpose of Phase 4 studies is usually to:

- Expand on the information already obtained from previous phases, which principally look at safety.
- Conduct ongoing safety surveillance and optimize use of the drug.

What is the investigational study drug?

Lumateperone is approved by the FDA to be used in the United States for the treatment of:

- Schizophrenia in adults, and
- Major depressive episodes associated with bipolar disorder in adults, and

- As an adjunctive therapy for adults with Major Depressive Disorder An adjunctive therapy is given in combination with other treatments to help improve outcomes.

While lumateperone is approved, we are conducting more studies to continue to understand how it works in a larger group of people.

A possible benefit of taking lumateperone is a reduction in the severity of your depressive symptoms.

The study drug (lumateperone) will be provided as capsules to be swallowed once daily at about the same time, with or without food, for a total of 6 weeks. The first dose (given at visit 2/baseline) will be administered at the site under supervision of the study doctor. You will receive 42 mg capsules of study drug or placebo.

As part of this study, the study drug is being compared with a placebo. The placebo capsule looks like the study drug capsule and is taken in the same way, but the placebo contains no active ingredients. A placebo is used to understand if any effects seen in the study are likely to have been caused by the study drug.

You have a 1 in 2 chance of being randomly assigned (like flipping a coin) to receive the placebo or lumateperone. This means that you have the same chance of getting the placebo as you do the study drug. Both the placebo and lumateperone will be called the "study drug" in the rest of this form. Neither you nor your doctor will be told which study drug you are receiving. However, the study doctor would be able to find out if there is an emergency.

MRI Scanning (brain scanning): You may not participate in the brain scanning part of the study if you have braces or metal implants or fragments (due to routine MRI restrictions), if you are claustrophobic (afraid of small spaces), or if you have a neurological disorder.

If the results of the interview indicate that there is a reason that you cannot participate in the brain scanning, we will tell you so. MRI scans will be done at Dell Medical School in the Health Discovery Building at the University of Texas at Austin. You will be asked not to drink any alcohol or use any other non-prescribed medications that could change brain function within 24 hours of the MRI scanning session. You will also be asked not to drink caffeinated beverages (coffee, tea, cola drinks) or smoke cigarettes the morning of the MRI scanning session.

The MRI scanning phase of the study should last about one hour. You will lie down on a cot. The cot will slide inside of the MRI machine, which is a large tube-shaped magnet, until your head is within the machine. The MRI machine will make a loud clanking noise when it takes pictures. During the MRI session you will lie quietly and watch video(s). Pictures of your brain will be taken during the MRI session. You will be able to talk to the staff at all times during the scanning session and can be taken out of the MRI magnet at any time. If it is not possible to complete the full MRI scanning session in one hour we will tell you and arrange for a second scanning session on another day within two weeks.

What will happen to me during the study?

The study involves up to 8 visits and you may be in this study for just over 2 months.

In summary, the visit schedule is as follows:

- Screening period (about 2 weeks – 1 visit)
- Baseline visit & Study treatment period (about 6 weeks – 6 visits)
- Follow-up (about 1 week – 1 visit)

If you are taking certain medications not allowed in this study, they will be tapered down and discontinued during the screening period, under the supervision of the study doctor. You will not be allowed to take any other medications during the time you are in the study unless these are approved by the study doctor. If you are currently taking any psychiatric medications and the study doctor thinks it is unsafe for you to stop taking these medications, you will not be eligible for the study.

Some medications and supplements, available on prescription or over the counter, can affect the levels of study drug in your body; this reaction is called a "drug–drug interaction." To monitor this, it is very important that you tell the study doctor about all medications and supplements that you are using at the start of the study and during your participation in the study.

For your safety, you should not start any new medications or stop any of your regular medications during the study unless you first check with the study doctor.

You must not drink alcohol or take cannabis or any other illegal drugs for the duration of the study. This is also for your safety.

Information about each study period is described below. The tests and assessments that are done at each visit are shown in Table 1. Remember that you are signing and dating this form during your ongoing participation in this study. Any of these visits that have been completed will not be repeated.

Screening period (about 2 weeks)

If you agree to take part in this study, you will sign and date this Information Sheet and Consent Form. You will then have tests and procedures to ensure that the study is right for you. You will also undergo a clinical interview that assesses mental and physical health as well as any MRI contraindications that may prevent you from having an MRI due to your safety. After the screening visit and if found eligible, an fMRI scan will be performed prior to your first dose of medication.

Baseline visit (1 day)

If you qualify for the study, you will have a second visit. During this visit, you will have a few initial tests and will be given your first dose of study drug (which will contain **either** lumateperone **or** placebo). After this, you will be given a supply of study drug to take at home once each evening. The study team will advise you about how best to take the study drug.

Study treatment period (about 6 weeks)

The study treatment period will consist of up to 6 visits to the study center. Each visit (once weekly) is expected to last about 2 hours. Some visits, such as the baseline visit and visit(s) 4, 7, and 8, could take an additional 1.5 hours due to the blood testing performed, which will evaluate your body's reaction to the study drug.

During the study treatment period, you will continue to take the study drug once a day at home, with or without food in the evening. You will receive enough study drug to last until your next visit. You will be asked to bring the used and unused drug packages with you to each visit during the study treatment period so that the study team can count the number of capsules remaining and evaluate if you have taken the correct number of study drug doses. If they find that you have not taken the correct number of capsules, the study team will discuss this with you.

Follow-up (1 day, about 1 week after Visit 7)

About 1 week after you have stopped taking the study drug (which will be after Visit 7, unless you stopped taking the study drug earlier for any reason), you will have one last visit to the study center for final assessments as well as an fMRI scan.

If you stopped taking the study drug earlier than scheduled (called "Early Termination"), you will still be asked to return to the study center for this follow-up visit.

Table 1: The assessments you will have at each visit. You can read more about these assessments on the following pages.

Study Phase	**Screening Period**	**Double-blind Treatment Period**						**Safety Follow-up Period**
Visit Number	**1 (Screening)**	**2 (Baseline)**	**3**	**4**	**5**	**6**	**7**	**8/ET[2]**
Study Week	**Week -2**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**

Study Day	**Up to 15 days prior to baseline**		**(± 2 days)**					
Informed consent	X							
I/E criteria	X	X						
Medical history and demographics	X							
Physical examination	X						X	
Vital signs	X	X	X	X	X	X	X	X
12-lead ECG	X			X			X	
Clinical laboratory tests								
Blood Tests	X	X	X	X			X	X
Urine Drug Screen and Breath Alcohol Test	X	X						
Serum/Urine Pregnancy test	X	X						
Study Assessments								
Assessments and Questionnaires	X	X	X	X	X	X	X	X
EMA App Surveys	X	X	X	X	X	X	X	X
Study drug dispensing		X	X	X	X	X		
Study drug compliance			X	X	X	X		
fMRI		X						X
Prior/concomitant medication	X							
Adverse events								

BMI = body mass index; ECG = electrocardiogram; ET = early termination

If you agree to continue taking part in this clinical research study, you will have the following procedures, tests, and assessments, as listed in Table 1:

- **Pre-visit overnight fast:** You will be asked to fast (have no food or drinks, except water) for at least 8 hours before the study center visits when blood and urine will be taken, except for the screening visit.
- **Physical examination:** The study doctor will check your general appearance, heart, breathing, nerves, reactions, skin, and other relevant parts of your body.

- **Electrocardiogram (ECG):** The study doctor will place sticky pads on your chest, arms, and legs. The pads are connected by wires to a machine that checks the rhythm and activity of your heart. As well as the listed ECGs, you may also have additional unscheduled ECGs if the study doctor thinks it is needed.
- **Vital signs and weight:** Your body temperature, heart rate, breathing rate, blood pressure, and weight will be measured.
- **Height, body mass index (BMI) and waist circumference:** A member of the study center team will measure your height and waist circumference. Your BMI will also be calculated at certain visits.
- **Blood tests:** The total planned amount of blood that may be taken from you over the course of this study will be approximately 58 mL (12 teaspoons or 4 tablespoons). The blood samples will be collected to:
    - Check your overall health.
    - Test for certain infections caused by viruses, called hepatitis B and hepatitis C (this test will be done only in the screening period). The study doctor may be required by law to report the result of these tests to the local health authority.
    - Some of these tests are to understand how the study drug is absorbed and distributed in the body as well as how it is metabolized and eliminated from the body.
    - The study doctor may choose to perform any unscheduled blood test if they feel that it is required.
    - This study will not use your blood samples to look at all or some parts of your DNA
- **Urine tests:** Samples of urine will be tested to:
    - Check your overall health.
    - Look for cannabis and illegal drugs,
    - The study doctor may choose to perform any unscheduled urine test if they feel that it is required.
- **Breathalyzer**: Your will be asked to blow into a machine (breathalyzer) to test to see if you have taken any alcohol.
- **Questionnaires and interviews:** Throughout the study, you will be asked a series of questions to evaluate your psychiatric symptoms, how you are feeling, and your general health. In addition to interviews, you will also fill out questionnaires about your quality of life.

If you are female, have menstrual periods and can get pregnant, you will also have the following additional assessments:

> **Pregnancy tests:** This will be done using a urine or a blood sample taken at the study center. If you become pregnant, you must tell the study doctor immediately and you will stop taking part in the study. This is because the effect of the study drug on pregnancy and unborn children is unknown. Please see the "**Harm to the unborn child**" section of this document for more information. Additional tests may be needed, based on the study doctor's decision.

What will happen to any samples I give?

The study doctor and the study team will collect blood and urine samples from you as described in this Information Sheet and Consent Form. Collected samples will be given a code using your subject identifier, so that the sample can be traced back to you but will not contain anything that may identify you directly. Blood collection will take place at the Clinical pathologies lab in the Health Transformation Building,

Health Transformation Building / HTB 1st floor and 9th floor locations

Hours:

1st floor - 8 AM - 5 PM; closed 11:30 for lunch hour

9th floor - 8:30 AM to 5:00 PM; closed 12:30 PM for lunch hour

By signing and dating this Information Sheet and Consent Form you are allowing the study doctor and study team to provide these samples and interviews to the Sponsor and third parties working with the Sponsor. You are also allowing the study doctor, the study team, the Sponsor, and third parties working with the Sponsor to use the samples and interviews collected from you to conduct the study.

The Sponsor may continue using the study data and samples after the study is over. If you withdraw from study treatment in the study, the study data and samples collected, including study data and samples collected during any follow-up visits after your withdrawal from study treatment, will remain part of the study. You will not be able to

request the withdrawal of your information from the study data, as the study sponsor requires that any information collected up to the point of your withdrawal cannot be removed from the study.

Information regarding the quality or content of the interviews may be shared with the study Sponsor; however, nothing that could identify you will be used or shared. Information from the interviews may also be shared with the study doctor.

There are no plans to share any money or profits with you if your sample(s) lead to inventions or discoveries that can be sold.

What will I have to do?

If you decide to continue to take part in this study, it is important that you agree to the following:

- You will need to follow the instructions from the study doctor and study team, and you will need to take the study drug as directed.
- You must not take part in any other studies while taking part in this study
- You should ensure that you store the study drug at room temperature at home, out of the reach of children.
- You must not consume grapefruits, grapefruit juices, alcohol, cannabis, or any illegal drugs during the study. This is because these substances may interfere with the study drug.
- You should fast (not have food or drinks, except water) for at least 10 hours before certain study center visits.
- If you have periods and are sexually active, you must agree to use an acceptable method of birth control from the screening period until the end of the follow-up. The study doctor will discuss this with you. If you or your partner become pregnant during the study, you should inform the study doctor immediately.
- If you have your first period during the study, the study doctor will have a discussion with you to talk about the contraception that is required until the end of the follow-up period.
- You must tell the study doctor about all medications you are currently taking and any changes to them.
- You must also inform the study doctor of any changes in your health and any side effects that you may have during the study.

What are the possible risks of taking part in the study?

There are risks in taking part in this study. Your condition could get better, it could get worse, or it could stay the same. Taking this study drug may also involve risks to your health, now or in the future, that are not yet known.

You might have side effects or be at risk for symptoms, illnesses, and/or complications from the study drug and procedures used in this study. These may range from mild to very serious and can be different for each person. You may have some, none, or all of these while taking part in the study.

Risks of the study drug

There are several potential risks associated with taking part in this research study. Your depressive symptoms associated with major depressive disorder may not improve, and they could even get worse if you take part in this study. Each of the most common risks and side effects are discussed here. Please ask the study doctor if you have any questions or concerns about these risks.

During this study, you may take lumateperone.

The most frequent side effects observed of lumateperone include:

- Headache
- Somnolence/sedation (sleepiness/drowsiness)
- Dizziness
- Nausea (feeling like you need to throw up)
- Dry mouth
- Diarrhea
- Vomiting
- Insomnia

- Fatigue (tiredness)
- Upper respiratory tract infection

Other potential risks of lumateperone include:

- Rhabdomyolysis: A severe form of muscle injury that may be life threatening. There has been one case of an adult patient who developed rhabdomyolysis in a clinical trial while taking lumateperone. Tell your doctor immediately if you are experiencing muscle pain, weakness, or dark urine.
- Tardive dyskinesia (TD): Tell the study doctor if you cannot control the movements of your face, tongue, or other body parts. These could be signs of a serious and sometimes permanent side effect, called TD. TD can develop even after a person has been taking lumateperone for a short time at low doses.
- Neuroleptic malignant syndrome (NMS): Tell the study doctor immediately if you have a high fever, stiff muscles, confusion, sweating, or changes in pulse, heart rate, or blood pressure. These can be symptoms of a rare but potentially fatal side effect called NMS.
- Metabolic changes: Hyperglycemia (high blood sugar) and dyslipidemia (abnormally elevated cholesterol or fats [lipids] in the blood).
- Leukopenia, neutropenia, and agranulocytosis (low white blood cell count): Low white blood cell counts have been reported with antipsychotic drugs, including quetiapine. This may increase your risk of infection. Very low white blood cell counts may occur, which can be fatal.
- Orthostatic hypotension and syncope: You may feel lightheaded or faint when you rise too quickly from a sitting or lying position.
- Tachycardia (fast heartbeat) without standing.
- Akathisia: intense agitation or restlessness that may be very unpleasant.
- Seizures
- Potential for cognitive and motor impairment.

There may be other side effects of lumateperone that have not yet been observed or reported. Ask the study doctor about any side effects that you do not understand.

It is likely that you will experience none or one or more of the symptoms listed above. It is also possible that you may experience other symptoms or side effects that are unforeseen or have not been observed frequently in connection with use of the study drug. Lumateperone has been approved for use in adults for the treatment of depressive episodes associated with bipolar disorder and major depressive disorder. When testing a compound in a different age group and medical diagnosis, it is possible that unexpected side effects could occur, and this includes side effects that are potentially life-threatening.

You will be monitored closely for any side effects during the study. At all times over the course of the study, you are strongly urged to promptly contact the study doctor or study team if you think you are experiencing a side effect. If you want to contact the study doctor or study team about symptoms you notice after you have left the study center, you can call them at the telephone number listed on the first page of this form. If any of your symptoms or side effects are unexpected (have not been described to you in this Information Sheet and Consent Form), are severe or alarming, or if you have any desires or thoughts of harming yourself or others, you are required to report them to the study doctor immediately, day or night.

If you are having suicidal thoughts or feel in crisis, call the study doctor at the telephone number listed on the first page of this form. You can also call or text the National Suicide & Crisis Lifeline at 9-8-8 or 1-800-273-TALK (8255). The Lifeline numbers are answered 24 hours a day every day of the year by a skilled, trained counselor. You can also present to a healthcare provider, your local emergency room, or call 9-1-1 to be connected to local emergency services.

If you receive placebo (the inactive substance) as part of this study and during the washout period (discontinuation of certain medications), your symptoms of depression may not improve or may get worse.

Allergic reaction

As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash

- Wheezing and difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the study doctor and study team if you have any of these symptoms. Any side effects or other health issues occurring during the study will be followed up by the study doctor.
Any side effects or other health issues occurring during the study will be followed up by the study doctor.

You should exercise caution and wait until you know how the study drug affects you before you drive, operate machinery, or need to be alert.

The study drug must be taken only by you. It must be kept out of the reach of other people.

Risks from study procedures

Privacy: There is a low risk of loss of confidentiality of your personal information. While every effort will be made to protect the confidentiality of your information, absolute confidentiality cannot be guaranteed. However, steps have been taken to help make sure this will not happen. You will read more about the protection of your personal information in Part 3 of this information sheet.

ECG: Some areas where the electrodes (sticky patches) will be placed may need to be shaved. The test is painless, but the electrodes may irritate your skin.

Blood Pressure & Heart Rate: Your arm might feel a little uncomfortable when the blood pressure cuff gets tight.

Blood tests: Drawing blood may cause discomfort, bruising, and very rarely, infection at the puncture site, or damage to a vessel or a nerve. You may also experience dizziness, nausea, or fainting during the blood-taking procedure. Please tell the study doctor or study team if you do not feel well after having your blood drawn.

Questionnaires and interviews: Some of the questions that you may be asked during the study may be sensitive, which can be distressing for some people. If you feel uncomfortable as a result of the study questionnaires or an interview, please tell the study doctor or a member of the study team.

Fasting: Fasting could cause dizziness, headache, stomach discomfort, or fainting.

MRI Scan: No serious ill effects have been reported to date from facilities in the United States operating with a magnetic field strength of 3 Tesla (the magnetic field strength used in this study); these types of magnets are widely used for clinical practice. Since the study involves entering a confined space, you may not be able to participate if you have a history of claustrophobia or if you experience anxiousness when entering the magnet tube.

The risks due to exposure to the magnet itself are primarily related to the slight possibility of a sensation of dizziness or nausea as you move in and out of the magnet or move your head in the magnet. The magnet is thought to be able to exert a force on the fluid within the semicircular canals near the ears, thus possibly giving a sensation of dizziness. The sensations go away if your head is not in motion or if you are not moving in/out of the magnetic field. Less than 10% of subjects experience this dizziness, which generally lasts 1-2 minutes or less. You will be exposed to noise from the machine for which earplugs and/or earphones are provided. There are no other known risks to being in the magnetic field.

Magnetic items move in a high magnetic field and by doing so, can be dangerous. The Biomedical Imaging Centers (BIC) at the University of Texas at Austin is careful to maintain an environment safe from these objects. We require you to do the same, being careful to ensure that you carry no metallic items into the MRI room. You will be asked to change into MRI-approved clothing for the MRI scans.

We want you to read and answer very carefully the questions on the MR Safety Questionnaire related to your personal safety. Take a moment now to be sure that you have read the MR Safety Questionnaire and be sure to tell us any information about you that you think might be important.

Electrical shocks: During the MRI scan you will complete a task during which you will receive mild electrical shocks. Prior to entering the scanner, you will select a level of shock that is annoying and mildly uncomfortable but not painful. If the shocks become too uncomfortable or distressing for you, you can stop the MRI scan at any time by alerting the research staff.

Harm to the unborn child: Currently, we are not fully aware of the effects of the study drug on unborn babies, or on people who are pregnant or breastfeeding. If you can become pregnant, use of the study drug may lead to new, side effects that we currently do not know about, and this may involve risks to your unborn baby. Because of this, subjects who can have children will have pregnancy tests (blood and/or urine) during the study. Sexually active subjects who can become pregnant must be using an effective form of birth control from the screening visit until the end of the follow-up. The study doctor will discuss effective birth control methods with you.

If you become (or your partner becomes) pregnant during the study, you should immediately tell the study doctor. If you become pregnant, you will have to stop taking the study drug. Your pregnancy and health will be followed carefully by the study team. Female partners of male subjects who become pregnant will be asked to provide consent for the study team to follow their pregnancy and health until the end of the pregnancy.

What are the possible benefits of taking part in this study?

If you are receiving the study drug, it is hoped that the study drug will be of medical benefit to you, but this cannot be guaranteed. There may not be any direct benefit for you. If you are receiving the placebo, it is not expected that you will receive medical benefit from this study. Information from this study may help researchers understand major depressive episodes associated with major depressive disorder and develop new tests or medications to help other people with this condition in the future.

What if new information about the study becomes available?

The study doctor will contact you if any important new information becomes available that might affect your health or willingness to continue in the study. The study doctor will explain and discuss this new information with you. If you decide to continue in the study, you may be asked to sign and date a new consent form. If you decide to leave (withdraw from) the study, the study doctor will make arrangements for your future care.

What happens when the research study ends?

If you have received the study drug, there is no guarantee that you will continue to receive it after you have finished taking part in the study. The care you receive after the study has ended may involve a different drug or treatment, which the study doctor considers to be the best treatment for you.

Will I have to pay to take part in the study?

There will be no cost to you for taking part in this study. You will be provided with all study drug, examinations, and medical care related to the study without charge.

Will I be paid to take part in the study?

You will receive a stipend of $50 for each study visit you complete. In addition, you will receive an extra $50 for Visit 2 and Visit 8 if you complete the imaging procedures scheduled during those visits. This means you may receive additional compensation for participating in specific procedures that require more time or effort.

All stipends will be provided through Tango Cards, which can be redeemed for a variety of gift cards or charitable donations.

Payment received as compensation for participation in research is considered taxable income to the research subject. If payment to an individual is equal to or exceeds $600 in any one calendar year, The University of Texas at Austin is required to report this information to the Internal Revenue Service (IRS). If the compensation you receive from participation in this research in combination with all other compensation received from The University of Texas at Austin is equal to or exceeds $600 in the current calendar year, you must provide IRS 1099 related information.

What happens if I am injured while taking part in the study?

In case of an injury, please contact your study doctor at the telephone number provided on page 1 of this form. If you are not able to reach the study doctor at the telephone number listed, please contact your family doctor. If it is an emergency, go to the closest emergency department.

Any compensation payable for any injury caused to you by taking part in this study will be in line with local guidelines. The Sponsor will pay for the cost of medical treatment for any injury that is directly due to administration of the study drug or protocol specified procedures.. The Sponsor will not compensate you if your injury has happened because a procedure has been carried out that is not in line with the study plan or where the study doctor has acted negligently.

If you have medical insurance, please check with your insurance company that taking part in this study will not affect your policy. Your insurance provider may not offer coverage for injuries or illnesses resulting from research participation. You should check with your insurance company about any such payments.

Compensation for an injury resulting from your participation in this research is not available from The University of Texas at Austin except as provided by law. You are not waiving any of your legal rights by participating in this study.

During the MRI scans, there is a small chance that the researchers may see a problem that might be medically important. This is unlikely, but if the researchers see a potential problem they will send your images to the Biomedical Imaging Center's (BIC) Safety Panel where they will be reviewed by the Medical Director or a designated qualified radiologist. If anything that might be medically significant is observed the Medical Director will contact you to discuss the findings. Since the scans themselves are not equivalent to a medical diagnostic MRI, the images will not be shared with you or your physician.

What alternative treatments are available?

Taking part in this study is voluntary – you do not have to take part in this study to be treated for your condition. The study doctor will discuss with you any other treatment options or medications that may be available for you, including their risks and benefits. If you decide not to take part in this study, it will not affect your ability to receive medical care.

Can I withdraw from the study?

If you join the study, you can stop taking part at any time without giving a reason. This will not affect your future treatment or your relationship with the study doctor. If you want to stop taking part in the study, you should tell the study doctor immediately. For your safety, you will be asked to return to the study center for an end-of-study assessment and to return all unused study drug and empty packaging. You may also be asked for permission to be contacted at a later date by your family doctor to check on your condition since leaving the study.

If you decide to withdraw from the study, no new information or samples will be collected from you. The information and samples that have already been collected will still be used for the study.

Are there any other reasons why I may need to stop taking part?

The Sponsor or study doctor may also decide that you should stop receiving the study drug or stop taking part in the study completely. They may decide that you should stop even if you want to continue, for the following reasons:

- You are no longer eligible to take part
- You do not follow study instructions
- There are safety concerns
- The study is stopped by the Sponsor or a regulatory authority for any reason.

If the study is stopped, you will be told, and the study doctor will arrange for your care to continue.

What will happen to the results of this study?

The results of this study will be used to make informed clinical decisions for developing this potential new study drug.

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.

The results of this study may also be shared publicly, for example, by publishing within scientific papers or as presentations at scientific meetings. You will not be identified in any publications, presentations, or announcements.

In the future, we might remove the details that can identify you from the information and samples you give us. After that, your information and samples could be used for other research by our study team or other researchers without asking you for additional consent.

Who has reviewed the study?

All human research studies are reviewed by an independent group of people, called an Institutional Review Board (IRB), to protect the safety, rights, well-being, and dignity of subjects. This study has been reviewed by the UT IRB who considers the risks and benefits of the study during their review. Their approval does not guarantee that taking part in this study is without risk.

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 such as:

- Whom 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 research subject;
- Eligibility to participate in the study;
- The study doctor's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

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 treating 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 subjects. If you have any questions about your rights as a research subject, contact:

The University of Texas at Austin Institutional Review Board

Phone: 512-232-1543

Email: irb@austin.utexas.edu

Please reference the following number when contacting the Study Subject Adviser: STUDY00008399

PART 3 – Protecting Your Personal Information

Every effort will be made to maintain the confidentiality of your study records. All information learned through this study will be available only to investigators working on the study and the scientists working with them. However, if you wish us to discuss the results of the interview with your physician please ask

us and we will do so. Otherwise, the results of the interview will be known only to the investigators of the study.

In all records of this study you will be identified by a number and letter code, and only the researchers will know your name. Any information obtained during this study and identified with you will remain confidential and will be disclosed only with your permission. All identifying information (name, birthdate, etc.) will be kept separate from data obtained from interviews, saliva and physiology monitoring (heart rate, temperature), and imaging. If the results of this study are reported in medical journals or at meetings, you will not be identified by name, or by any other means without your specific consent. Your identity will remain confidential unless disclosure is required by law.

Will my taking part in this study be kept confidential?

Any information about you that is collected during this study will remain confidential by using appropriate measures to protect your privacy and personal information.

The information collected about you for this study will be identified only by your subject ID number. Your subject ID number is a code used to protect your identity and keep your involvement in the study confidential. This is known as "coded data." Your full name, or any other information that could be used to directly identify you, will not be included in the coded data. Only the study doctor and authorized personnel will have access to the information that can link you to your subject ID number.

What personal information will be collected and used?

The study doctor and study team will collect personal information from you for the purposes of this study. This personal information will include:

- Sensitive information about your physical and mental health, and your general condition
- Information such as your name, address, telephone number, date of birth, sex, race, ethnicity, and other demographic information
- Information related to the tests and procedures done in the study, including any blood or urine samples taken from you during the study.

This study will collect information about your race and ethnicity.

If you agree to give this information, your race and ethnicity will be collected and entered into the same database where the other data about you will be entered, stored, and protected during this study. This will be coded data linked to your subject ID number.

You can request a copy of your personal data. To ensure that the study meets regulatory standards, you will not be able to review some of the personal data or receive a copy of it until the study ends. You may also object to any further processing of your personal information.

To discuss your rights or for further information, please contact the study doctor using the contact details provided on the first page of this form.

Who will have access to my personal information?

All study data will be kept for approximately 15 years after the end of this study, or as required by U.S regulations. After this time your coded data will be deleted or the code that links your coded data to your personal data at the study center will be destroyed.

Your personal information will be accessible to the study doctor and study team to conduct the study. To ensure the study is being conducted properly, access may also be granted to the following:

- ITI or its designee (any company they use to oversee or conduct the study)
- The Sponsor's designated company overseeing this study
- Other people and groups assisting with the study [i.e., Laboratories for testing biospecimens, etc.].
    - Lab vendor will receive blood samples

- EMA Wellness
- UT Institutional Review Board
- Data Monitoring Committee
- Study monitors
- Other companies or agencies working with (or owned by) the Sponsor
- Your family doctor, as necessary.

The study information collected about you that leaves the study center (your coded data) may be processed by:

- The study Sponsor and their representatives
- Other researchers for medical or scientific research
- Health authorities and possibly ethics committees
- The Institutional Review Board,
- Data monitoring committee (DMC): A group that oversees study information and safety.

Your protected health information may be further shared by the groups above. These groups are committed to keeping your health information confidential. In each case your identity will be protected.

Under certain situations, we may break confidentiality. If during the study we learn about child abuse or neglect, we will report this information to the appropriate authorities including the police and/or the Texas Department of Family and Protective Services.

Texas Education Code, Chapter 51, Subchapters E-2 and E-3, requires reporting incidents of sexual assault, sexual harassment, dating violence, or stalking committed by or against a person who was a student enrolled at or an employee of UT Austin at the time of the incident. However, the researchers working on this study have been designated as confidential employees. This means that if we learn about any incidents of sexual assault, sexual harassment, dating violence, or stalking, we are only required to report the type of incident reported and the date we learn about the incident. We will not report any information that could identify you.

The study doctor or study team may also need to share your full name and contact information with companies working with the Sponsor, in order to:

- Reimburse you for the time, effort, and certain expenses related to study participation.

There is a risk of loss of confidentiality in research studies. Reasonable efforts will be made to protect you and your health information to the extent possible.

If you withdraw from the study, no new information will be collected for study purposes unless the information concerns a side effect related to the study. All information that has already been collected for study purposes, and any new information about a side effect related to the study, will be sent to the study sponsor.

PART 4 – Consent Form

By signing and dating this consent form, I confirm the following:

- I have read the information sheet for the above study and have had enough time to think about taking part.
- I have had enough time to ask questions and I am satisfied with the answers given.

- I voluntarily agree to take part in this study, to follow the study requirements, and to provide the information the study doctor, nurses or other staff members ask from me.
- I understand that my taking part in this study is confidential and that I am free to withdraw from this study at any time, without giving a reason and without my medical care or rights being affected.
- I agree that if I decide to withdraw and leave the study, the information and data collected about me up to the point when I withdraw may continue to be used.
- I understand I will receive a signed and dated copy of this information sheet and consent form to keep for myself.
- I agree to my samples being taken and used as described in this information sheet.
- I understand I may also be contacted at a later date for my permission in connection with this or any related sub-study.

By signing and dating this document, I agree to take part in this study, as set out in this information sheet and consent form. I have been told that I will receive a signed and dated copy of this Consent and Authorization for my records.

Printed Name of Subject

Signature of Subject | Date

Study Doctor/**Authorized Designee:**

- ✓ I have fully and carefully explained the study to the subject named above and confirm that, to the best of my knowledge, they clearly understand the nature, risks, and benefits of taking part in this study.
- ✓ I confirm that I gave them adequate opportunity to ask questions about the study, and that I answered all the questions they asked correctly and to the best of my ability.
- ✓ I confirm that they have not been forced into giving consent, and that they have given their consent freely and voluntarily.
- ✓ I confirm that they will receive a signed and dated copy of this information sheet and consent form.
- ✓ I certify that I am not aware of any objections to participating in the clinical study previously expressed by the subject

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent | Date