An Experimental Therapeutics Study of a Monoclonal Antibody Against Interleukin 17A in Patients With Treatment-Resistant Depression
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STUDY INFORMATION:

Study Title: An Experimental Therapeutics Study of Ixekizumab, a Monoclonal Antibody Against Interleukin 17A, on Anhedonia, Reward Circuit Function, and Blood Brain Barrier Physiology in Patients with Treatment-Resistant Depression

Study site(s): School of Medicine at Mount Sinai, Mount Sinai Hospital

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SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. You can agree to join or not. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and if all of your questions about the research study are answered. If you do join the study, the research team must share any new information with you that may change your mind about taking part.

The purpose of this research study is to determine whether researchers can develop new therapies for the treatment of depression by acting on the immune system.

Recent scientific research has suggested that the immune system, which usually fights diseases, is disturbed in depression. This study is looking at the effects of the medication ixekizumab in patients with depression whose current depression symptoms have not improved following two prior treatments. Ixekizumab is a commercially available medication that is approved by the FDA (The United States Food and Drug Administration) to treat autoimmune diseases like plaque psoriasis and some forms of arthritis The drug works by binding to a protein called interleukin 17a and reducing inflammation. This drug is not approved by the FDA for depression.

If you choose to take part, you will be asked to complete six study visits for up to 12 weeks and take three doses of the study drug.

We also want to know whether people with depression have problems with their brain activity. To do this, we will ask you to undergo a brain scan to take high-resolution images of your brain both before and after receiving treatment with the study drug ixekizumab.

During the study visits, we will:

- Assess your physical health,

- Assess your depression symptoms,
- Collect blood to measure immune proteins, and
- Complete a brain scan to measure brain activity.

If you choose to take part, the main risks to you are (1) discomfort or pain during or after the blood draw, including bruising, infection, and dizziness or feeling faint after your blood has been taken; (2) having claustrophobic reactions in the MRI scanner, which means that you may experience feelings of being trapped, feel as if the walls are closing in, or feel discomfort because of being in a small place for a period of time. If you do have metal objects of any kind in your body, you will not be able to participate for matters of your own safety: metal objects cannot be in an MRI scanner because the scanner acts as a magnet, and this can cause you danger; (3) reaction to Gadolinium (MRI dye), which may be itching, nausea, breathing problems, vomiting, or a metallic taste. These reactions are very rare and usually occur in people who already have severe lung disease.

Other risks that may occur on the study drug ixekizumab are potential side effects such as headaches or upset stomach, allergic reactions, increased chance of minor infections or Inflammatory Bowel Disease (IBD) or worsen existing tuberculous infections. The study drug may also potentially harm a pregnancy or fetus in ways that are unknown.

You may benefit from taking part in this research. Some potential benefits are improvement in your symptoms of depression. However, participating in the study may not benefit you and no benefit is in any way guaranteed as a result of your participation.

Instead of taking part in this research, you may consider treatments such as medications (approved medications include fluoxetine, sertraline, etc.) or cognitive behavioral therapy that have been shown to be effective as treatment for depression.

If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

This research study will be fully explained to you by a member of the study team. Feel free to ask all the questions you want before you make a decision about whether or not to participate. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

You may qualify to take part in this research study because you are a medically healthy individual with a diagnosis of Major Depressive Disorder and your symptoms have not improved after two prior treatments during your current episode.

Your participation in this research study is expected to last up to 12 weeks.

There are up to 20 people expected to take part in this research study at the Depression and Anxiety Center at the Icahn School of Medicine at Mount Sinai.

Funds for conducting this research are provided by the Hope for Depression Research Foundation.

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.

DESCRIPTION OF WHAT IS INVOLVED:

If you agree to participate in this research study, here is what may be involved:

After receiving complete disclosure about the research and being given the opportunity to fully review the consent form, you will also be given the opportunity to ask questions. If you choose to take part in the study, you will be asked to sign this written consent form.

- ***Screening Visit (3-5hrs, can occur over multiple days)***

  A study team member will ask questions about your health and complete tests to see if you are eligible for this study. This is called the "screening visit" and the following examinations will be completed during this visit, with the expectation of this taking about 3 to 5 hours:

  - Medical, Psychiatric, and Personal History: Research personnel will ask you questions about your medical and psychiatric history, medications you have taken, and your family psychiatric history. You will also be asked if you have any planned surgeries or other medical procedures.
  - Clinical Interviews: Research personnel will conduct assessments to determine the presence of any current or past psychiatric symptoms.
  - Questionnaires: The research staff will ask that you complete self-report questionnaires to evaluate any symptoms of depression, anxiety, and stress.
  - Physical examination: A study doctor or nurse will check you for general signs of disease.
  - Vital signs: Your heart rate, blood pressure, respiratory rate, height, and weight will be recorded.
  - Blood draw: A blood sample (13ml, approximately 1 tablespoon) will be drawn from a vein in your arm. This blood sample will be used for routine clinical laboratory test (blood count, electrolytes, thyroid function, liver function, etc.).

- Urine sample: You will be asked to pee into a cup. This urine sample will be used for routine analysis, testing if you are pregnant, and to test for illegal drugs. If you test positive for pregnancy or illegal drugs, you may be unable to participate in the study. Results from your urine drug test will be filed in your research record and will not be entered into your medical record.

If you are already participating in and/or have already completed screening assessments under the screening protocol "A Screening Protocol for Adult Patients with Mood and Anxiety Disorders, Chronic Medical Conditions, and Healthy Volunteers" (GCO: 06-0945; PI Dr. Murrough), and these assessments have been completed within 1 month of signing the consent for this protocol, you do not need to repeat these assessments.

Some of the study screening procedures may be conducted remotely over a HIPAA-compliant virtual platform. The screening period may last from 1 day up to 4 weeks. If you meet all eligibility criteria you can go on to the next phase.

- **Visit 1** ***(Week 0, 3-5 hours, can occur over two days up to 5 days apart)***

  - Clinical Interviews: Research personnel will conduct assessments to determine the presence of psychiatric symptoms and any changes in your medical history.

  - Questionnaires: The research staff will ask that you complete self-report questionnaires to evaluate any symptoms of depression, anxiety, and stress.

  - Vital signs: Your heart rate, blood pressure, respiratory rate, height, and weight will be recorded.

  - Urine sample: You will be asked to pee into a cup. This urine sample will be used to test if you are pregnant and to test for illegal drugs. Results from your urine drug test will be filed in your research record and will not be entered into your medical record.

  - MRI scan: You will be asked to participate in a brain scan and a behavioral task. The details of the MRI procedures are outlined in the next section.

  - Blood draw: A blood sample (36 ml, approximately 2.5 tablespoons) will be drawn from a vein in your arm. This blood sample will be used for immunological analysis.

  - You will receive the first injection of the study drug.

You may elect to participate in the MRI scan portion of the visit first up to 5 days earlier than the remainder of this visit. Due to scheduling restrictions, we may also ask you to come in on two separate days to complete all of the visit procedures.

Magnetic Resonance Imaging (MRI) with Contrast

All of the described procedures are for research purposes. To study the brain, you will undergo a 60-minute MRI scan with a 3 Tesla (3T) MRI scanner machine (Biograph mMR) present at the Icahn School of Medicine at Mount Sinai in the Hess Building. The 3T MRI scanner uses a strong magnet to collect images of the brain.

Prior to the scan, you will be asked a series of questions to confirm MRI eligibility. These questions assess your prior history in order to minimize risks associated with contra-indications to MRI and include questions regarding metal objects, pregnancy, etc. If you are pregnant or have an electrical or metal device inside of you, you will not be eligible to participate in the study. Prior to beginning any of the MRI procedures, you will be asked to urinate into a cup. This urine sample will be used to test for illegal drugs. If you test positive for any illegal drugs, you will be unable to participate in the MRI scan and exited from the study. Results from your urine drug test will be filed in your research record and will not be entered into your medical record. Your urine will also be tested for pregnancy.

To study the Blood Brain Barrier (BBB), a protective cell barrier around the brain, the study doctor would like to request your consent to use a dye called gadolinium, which will be injected into your blood during the scan. This is often called “contrast”. The dye is given through a small tube in a blood vessel (vein) in the back of the hand or forearm. This tube will be inserted by one of the nurses or a certified technologist. Inserting the tube into your vein may cause minimal discomfort. Gadolinium is considered a safe, FDA-approved contrast agent used routinely in MRI scanning to make certain brain tissue brighter in the MRI images. The FDA has recently issued a warning about contrast agents which contain gadolinium paying particular attention to some participant(s) who have acute or chronic kidney disease. Any participant(s) who is considering having a MRI with contrast will be provided with a blood test at screening to measure their serum creatinine and calculate the GFR (a measure of kidney function) to determine that it is safe to have the MRI contrast agent. The creatinine is a waste product in your blood that comes from muscle activity. It is normally removed from your blood by your kidneys, but when kidney function slows down, the creatinine level rises. We will use the results of your serum (from either a finger-stick or blood draw) creatinine test to calculate your glomerular filtration rate (GFR). The GFR tells us your kidney function. If your test shows that your GFR level is too low, one of the study personnel or the nurse present will tell you of your kidney test result. You may then wish to consult with your own doctor. If you meet the required criteria, you will be given a standard clinical dose, approximately 20 to 40 mL (or between 1-3 tablespoons) of contrast and then scanned at your baseline visit 1. At the end of the scan, the tube in your vein will be removed.

Once eligibility is confirmed, preparation for the MRI study will involve removing all metallic objects (such as watches, keys, chains, hair pins, glasses, jewelry, coins, etc.), items with magnetic data (credit cards), and other valuables. You will change out of any street clothing that is incompatible with the MRI study and into scrubs or hospital gowns that will be available during your visit. You will be given the opportunity to use the bathroom. You will then be escorted to the MRI room and positioned on the MRI bed. You will be asked to lie still on the MRI bed for up to one hour while the MRI machine gathers data. This will be a single scan session. During the scan, a researcher in Dr. Murrough’s team

or a trained technician will be present to talk with you throughout the scan and to oversee the scan. During this time, you will not be exposed to x-rays, but will be exposed to a strong magnetic field and radiofrequency magnetic fields. You will hear repetitive tapping noises that arise from the MRI scanner. We will provide earplugs or headphones that you will be able to wear during the scan. The space within the large magnet in which you lie is narrow. While lying in the scanner you will be asked to hold completely still, and padding such as a cushion may be used to stabilize your head. If you feel uncomfortable for any reason, you may choose to stop the scanning procedure at any time.

Because this project involves the use of a medical device, it is necessary that we make a note of your participation in the electronic medical record. That way anyone treating you will be aware of your participation and may be able to avoid any unfortunate outcomes that could arise if your research participation were unknown. All MRI scans will be reviewed by a licensed radiologist. In the event that an abnormality is detected, Dr. Murrough will communicate this to you, in consultation with a radiologist. Medical referral will be offered if it is considered necessary.

- **Visit 2** ***(Week 2, approximately 2 hours)***
    - Clinical Interviews: Research personnel will conduct assessments to determine any changes in your psychiatric symptoms or medical history.
    - Questionnaires: The research staff will ask that you complete self-report questionnaires to evaluate any symptoms of depression, anxiety, and stress.
    - Vital signs: Your heart rate, blood pressure, respiratory rate, height, and weight will be recorded.
    - Urine sample: If you are of childbearing potential, you will be asked to pee into a cup. This urine sample will be used to test if you are pregnant. If you test positive for pregnancy, you may be unable to participate in the study.
    - You will receive the second injection of the study drug.

- **Visit 3** ***(Week 4, approximately 2 hours)***
    - Clinical Interviews: Research personnel will conduct assessments to determine any changes in your psychiatric symptoms or medical history.
    - Questionnaires: The research staff will ask that you complete self-report questionnaires to evaluate any symptoms of depression, anxiety, and stress.

- Vital signs: Your heart rate, blood pressure, respiratory rate, height, and weight will be recorded.

- Urine sample: If you are of childbearing potential, you will be asked to pee into a cup. This urine sample will be used to test if you are pregnant. If you test positive for pregnancy, you may be unable to participate in the study.

- You will receive the third injection of the study drug.

- **Visit 4** ***(Week 6, 4-6 hours)***

  - Clinical Interviews: Research personnel will conduct assessments to determine any changes in your psychiatric symptoms or medical history.

  - Questionnaires: The research staff will ask that you complete self-report questionnaires to evaluate any symptoms of depression, anxiety, and stress.

  - Vital signs: Your heart rate, blood pressure, respiratory rate, height, and weight will be recorded.

  - Physical examination: A study doctor or nurse will check you for general signs of disease.

  - Blood draw: A blood sample (45 ml, approximately 3 tablespoons) will be drawn from a vein in your arm. This blood sample will be used for routine laboratory test (blood count, electrolytes, thyroid function, liver function, etc.) and analysis of immune proteins.

  - Urine sample: You will be asked to pee into a cup. This urine sample will be used for routine analysis, testing if you are pregnant, and to test for illegal drugs. Results from your urine drug test will be filed in your research record and will not be entered into your medical record.

  - MRI scan: You will be asked to participate in another brain scan, the same as the one you would have completed at Visit 1.

- **Exit Visit 5** ***(1-2 hours, Week 8)***

  - Clinical Interviews: Research personnel will conduct assessments to determine any changes in your psychiatric symptoms or medical history.

- Questionnaires: The research staff will ask that you complete self-report questionnaires to evaluate any symptoms of depression, anxiety, and stress.

This study exit visit will be conducted entirely remotely over a HIPAA-compliant virtual platform, two weeks following the last in-person visit (Visit 4).

Randomization

This is a single-arm, open-label study. All participants will receive the study drug.

Pregnancy

If you can possibly get pregnant, a urine test for pregnancy will be done before you begin the study and the pregnancy test will be repeated at each visit.

You cannot be included in the study if you are or become pregnant, as the study drug could harm your fetus. You also should not be in the study if you are producing milk to feed a child as the study drug could harm your baby.

Therefore, practicing effective birth control is important. No individual birth control is 100% effective.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use effective birth control. Unless you are sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual activity),
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

Birth control methods (other than abstinence and sterilization) are only effective if you use them properly, start them at least one month before you begin the research study, and continue using them throughout the research study and for six months after the research study ends. If you are unsure whether the method of birth control you use is approved to use while you are in this study, you should ask the Lead Researcher before you begin the study. If you are less than one-year post-menopausal, you could still become pregnant. If you or your partner becomes pregnant, or may be pregnant, at any time during the trial, *you must tell a person from the research team immediately. The team may stop the study drug and refer you/your partner to an obstetrician/gynecologist for follow-up.*

Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no

longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Semen/Sperm:

Drugs can be found in semen and alter sperm. Since you are taking part in a study using experimental drugs or treatments, it is recommended that 1) you use a condom, 2) you do not get a partner pregnant or expose them to semen, and 3) you do not donate semen. These recommendations apply both while you are taking the study drug, and for 6 months after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or semen even after you stop taking the study drug. You are encouraged to tell your partner(s) and/or their doctor(s) that you are participating in this clinical trial.

Future Contact:

The researchers may wish to use your personal contact information to contact you in the future. Do you give the researchers permission to **contact you** in the future to request the collection of additional information about you, discuss how your private information, study data and/or samples might be used, or discuss possible participation in another research study?

Please initial your choice: Yes_____ No_____

If "Yes", please indicate your preferred method of contact: (initial all that apply)

[ ] Email [ ] Phone [ ] Letter [ ] Text

USE OF YOUR DATA AND/OR SPECIMENS:

The researchers would like your permission to keep your personal information (such as, name, address, date of birth, social security number), study data and/or samples (blood, tissue, urine, saliva, or any other body matter) to use or share in future studies. You can still be part of the study if you do not allow us to use or share them. Please select Yes or No to each of the questions below. To decline all future uses/sharing please select 'No' each time..

(1) Will you allow the researchers to store your information and/or specimens to use in future research studies?

Please initial your choice: Yes_____ No_____

If you select No, please stop here and move to the next section, '**Your Responsibilities If You Take Part in This Research**' section below."

If yes, please continue to the next question and tell us how your personal information, study data and/or samples may be used in future research studies.

(2) The researchers can store your information and/or specimens in one of two ways:

a) Anonymously (no one will know who the information and/or specimens came from). If you choose this option, you can't change your mind. So, if you wanted to have your information and/or specimens destroyed in the future, the team could not do it as they would not know which information and/or specimens were yours.
b) Linked to your identity (using a code that can show the information came from you personally). In this case you could ask for your information and/or specimens to be destroyed in the future if you want that to happen.

How would you like your information and/or specimens stored? Please initial **ONE** choice below:

I would like my information and/or specimens stored anonymously _____

I would like my information and/or specimens stored with a link to my identity through the use of a code_____

(3) Do you give the researchers permission to keep the information and/or specimens, so they could use them in future studies that are **directly related** to the purpose of the current study?

Please initial your choice: Yes_____ No_____

(4) Do you give the researchers permission to keep the information and/or specimens indefinitely, so they could use them for future studies that are **not related** to the purpose of the current study (for example a different area of research)?

Please initial your choice: Yes_____ No_____

(4.1) From time to time, researchers outside of medicine and related sciences would like to use information and/or specimens. This might be in the fields such as anthropology, human origins, mapping human migration patterns. Do you give permission for researchers **outside the field of medicine** to use your information and/or specimens?

Please initial your choice: Yes_____ No_____

a. If the future research in a different area can be done without having to know that the information and/or specimens came from you personally, that will be done.

b. If the future research in a different area requires that it is known specifically who information and/or specimens came from, then one of the following will be done:

I. If you allowed the researchers to contact you in the future, they may be able to contact you to explain why your information and/or specimens is needed and what will be done with it. Your permission will be asked to use your data and/or samples in that research project.

II. If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical (for example, because you have moved), your information and/or specimens may still be used. The Institutional Review Board (IRB) will be asked for permission to use the data and/or samples linked to your identity. The IRB can give permission for researchers to use and share identifiable health information without contacting you, but only if it determines that sharing the data and/or samples will not be more than minimal risk to you or your privacy. The IRB is a committee of doctors and scientists and nonscientists, including people not associated with this hospital or medical school, whose job it is to protect people who participate in research.

(5) Do you give permission to have your information and/or specimens given **to other researchers,** including those at Mount Sinai, other medical or scientific institutions and for-profit companies, for use in research within the limits you have chosen above?

Please initial your choice: Yes_____ No_____

(6) Do you give permission to have portions of your information and/or specimens deposited in large public databases (repositories) for use in research with the limits you may have chosen above? Please read the paragraphs below which explains repositories, then initial your choice:

To do more powerful research, it is helpful for researchers to share data and/or samples from the people they study. They do this by putting information and/or specimens into a repository. A repository is where something is stored safely for a specified period of time. Data and/or samples from one study may be stored in a repository along with information and/or specimens from other studies. Sample repositories are commonly called biobanks, while data repositories are commonly called databases. Researchers can then use the information and/or specimens from multiple studies to learn even more about health and disease. If you agree to take part in this study, some of your genetic and health information might be placed into one or more scientific databases, but they will not share your direct identifiers (for example, name, address, date of birth). These databases are maintained by either Icahn School of Medicine at Mount Sinai, another institution, the federal government, or private companies. Any researcher who wants to do a study using data and/or samples from the repository must apply for permission. There are different ways of reviewing such requests. Researchers with an approved study may be able to see and use your data, along with that from many other people. Researchers may use your samples for genetic sequencing and other experimental testing. Researchers will always have a duty to protect your privacy and to keep your information confidential, but there are always risks associated with data and/or sample collection and sharing. They are described in more detail in the Risks section.

Researchers will use a Global Unique Identifier, a computer-generated ID, which cannot be linked back to your identity. This is so any data collected from you is linked to one unique ID, so the database can make sure your data is secure and is not accidentally duplicated if you take part in research at multiple sites.

Please initial your choice: Yes _____ No _____

Whether or not you have allowed us to share your information and/or specimens, the researchers at Mount Sinai will keep information and/or specimens collected about you during this research study to use in future research studies consistent with the wishes you expressed above.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things:

- Come to all study visit appointments and be available for any telephone appointments
- Complete questionnaires yourself and participate in interviews several times
- Do not participate in other medical research studies
- Take the study drug at the prescribed dose and time.
- Tell the study doctor about any health problems you have during the study
- Tell the study doctor about any new medicine you take during the study
- Do not take any other drugs or remedies unless the study doctor has approved them beforehand. This includes prescription drugs and over the counter medicine (including vitamins and herbal remedies) that you buy without a prescription.
- Use effective birth control; examples of effective birth control include barrier contraception (for example condoms), oral contraceptive pills or intrauterine devices.
- Do not get pregnant or cause your partner to become pregnant
- Do not take illegal drugs; examples of illegal drugs include marijuana, cocaine, heroin or other narcotic substances.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

Being in this study will not cost you anything extra. If you agree to take part in this study, you will be paid a total of $600 for your time and effort/ You will receive a check for $75 upon completing the screening visit. You will receive $150 for Visit 1 upon completing the MRI scan and all visit assessments. You will receive a check of $100 for each of the other treatment visits (Visit 2 and Visit 3). You will receive an additional $150 for Visit 4 upon completing the second MRI scan and all visit assessments. In addition, you will receive a check of $25 for completing the study exit procedures.

The study team may cover travel or treatment related costs (i.e. car service, train, ferry) in addition to the compensation listed above of up to $150 per study. Please provide the study team with all travel receipts so that you may be reimbursed. Reimbursement for travel or treatment related costs will be provided in the form of a check.

It can take up to 6 weeks to prepare and give you a check for study participation. If you do not get a check by then, you can first contact the research team. If further assistance is needed, please contact Mount Sinai's Program for the Protection of Human Subjects at (212) 824-8200.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally, this happens if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

If you are unable to complete the entire study, the payment will be prorated for the part you have completed. We will pay you based on your completion of the following visits:

Study Visit	Compensation
Screening	*$75*
Visit 1	*$150*
Visit 2	*$100*
Visit 3	*$100*
Visit 4	*$150*
Study Exit	*$25*
Total	***$600***

POSSIBLE BENEFITS:

It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may include a potential reduction in depression symptoms. Potential benefits to others may include increasing scientific knowledge and understanding of depression to further advance research and treatment developments. Note that the study drug provided at no cost during a study may not be available for free, or at all, when the research ends.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

- Risks associated with study drug:
  - May cause headaches or stomach upset
  - May result in an allergic reaction
  - The study drug may increase your chances of minor infections
  - May worsen existing tuberculous infections
  - May, in rare cases, increase the likelihood of developing Inflammatory Bowel Disease (IBD)
  - Suicidal ideation and behavior have occurred in patients with a similar drug
  - This study drug may harm a pregnancy or fetus in ways that are unknown. You should not become pregnant or impregnate a woman while on this research study. Please read the acceptable methods of birth control found under the Description of What's Involved section of this document.
- Psychological risks - during the psychiatric interviews and questionnaires, participants will possibly be exposed to the discomfort of being asked personal questions they may find distressing. You may choose to not answer any questions that make you uncomfortable. The risks and discomforts associated with answering questionnaires are minimal.
- Risks for the following study procedures:
  - Blood Draw: The risks of a blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw.
  - fMRI: The risk associated with the fMRI procedure is very small. No short-term risks have been reported for fMRI. An fMRI does not involve exposure to radiation. Some people have claustrophobic reactions in the fMRI scanner, which means that they may experience feelings of being trapped, feel as if the walls are closing in, or feel discomfort because of being in a small place for a period of time. A member of the study team will be present to reassure you and aid in relaxing, but should you wish it, the fMRI scanning can be stopped immediately. If you have any surgical clips or metallic prostheses (such as an artificial hip or knee), or shrapnel (metal fragments) in your body, you will not be able to participate in this study. Metal objects cannot be in an fMRI scanner because the scanner acts as a magnet, and this can cause you danger. If you do have metal objects of any kind in your body, you will not be able to participate for matters of your own safety.
  - MRI with Contrast: Gadolinium (MRI dye) is routinely used in medical imaging. As described in the MRI safety literature, it is a substance that is not normally absorbed

into the tissues of the body. Once it is injected, it will stay in the blood stream and will be eliminated a few hours later in the urine. Some patients very rarely have a reaction to this dye, which may be itching, nausea, breathing problems, vomiting, or a metallic taste. These reactions are very rare and usually occur in people who already have severe lung disease. A safety questionnaire will be given to you before the injection to make sure you are safe to have the dye injection. If you are not a candidate for this dye, the MRI scan can be done without it. A recent FDA warning has been issued that states participant(s) with kidney problems must not be given contrast because it may lead to debilitating and potential fatal disease that involves the skin, muscles, and internal organs. Patients with kidney disease can develop skin thickening that may prevent bending and extending joints, resulting in decreased mobility of joints. The chance of developing nephrogenic systemic fibrosis (NSF) is extremely low in individuals with normal kidney function. In addition, patients may experience scarring that has spread to other parts of the body such as the diaphragm, muscles in the thigh and lower abdomen, and the interior areas of lung. There is a slight chance of an allergic reaction from the contrast which has a less than 1 in 300,000 chance that this will be severe.

- Group Risks - Although we will not give researchers your name, we will give them basic information such as your race, ethnic group, and sex. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or even promote discrimination.
- Privacy Risks - Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk. If your private information was misused it is possible you would also experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.
- Insurance Risks – There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers of over 15 people to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.
- Financial Risks – Participants will not be charged for any study procedures. If a participant is injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to the participant or their insurance in the ordinary manner and they will be responsible for all treatment costs not covered by their insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. You may contact the investigator for more information.

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.

This study is not a substitute for comprehensive treatment for MDD. Instead of being in this research study, your choices may include treatments such as medications or cognitive behavioral therapy that have been shown to be effective as treatment for MDD. These alternatives are available to you at Mount Sinai and elsewhere and will be described to you fully prior to agreeing to participation in this study.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to the participant or their insurance in the ordinary manner and they will be responsible for all treatment costs not covered by their insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. You may contact the investigator for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff.

If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the study doctor can collect information from your routine medical care. If you agree, this data will be handled the same as research data.

If you decide you don't want your samples and/or data to be used for research anymore, you can contact the researcher and ask to have your samples and/or data removed from future use. If any samples or data have already been shared without your identity, it won't be possible to retrieve them because no one will know who you are. Samples and data that have already been used will not be affected by your decision. Any samples and/or data that are still linked to your identity by a code the researcher has will be withdrawn so that no future sharing of your samples and/or data will take place. If your samples have already been deposited in an external repository, the study team will request that your samples be removed.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the

investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns, or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Principal Investigator at phone number 212-585-4640.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research participant(s).
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be shared with others?

As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address, dates directly related to you (birth, admission, discharge, etc.), e-mail addresses, social security number, and medical records number. The researchers will also get information from your medical record. During the study, the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses,
- conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- reviewing mental health records

Why is your protected health information being used?
Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The Principal Investigator may also use and share the results of these tests and procedures to treat you in collaboration with others in the Mount Sinai Health System.

The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects is responsible for overseeing research on human participant(s), and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?
As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- The foundation sponsor and/or their representative (who will use the results for submissions to the Food and Drug Administration): The Hope for Depression Research Foundation

- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.

In almost all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. The Certificate of Confidentiality obtained from the Department of Health and Human Services will not be used to prevent disclosure to local authorities of child abuse and neglect, or harm to self or others. It is possible that a sponsor or their representatives, a data coordinating office, or a contract research organization, will come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. They are authorized to remove information with identifiers if necessary to complete their task. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information? Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will be able to access your medical records. Your information will be available should an emergency arise that would require your treating physician to know this information to best treat you.

Do you need to give us permission to obtain, use or share your health information?
NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission

to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your protected health information.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Certificate of Confidentiality:

To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services. This is intended to ensure that your identity as a participant in this research study will not have to be disclosed as a result from a subpoena, for the purpose of identifying you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings other than to the FDA or OHRP as identified above.

The research staff will not share any of your research information or biospecimens with anyone who is not a member of the research team, including any family members or friends, other than to those identified above. However, you should know that if we learn that you or someone else is threatened with serious harm, such as a child or an elderly person being abused, the investigators may notify the

appropriate authorities if necessary to protect you or others. A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. This means that you and your family must also actively protect your own privacy. If an insurer or employer learns about your research participation, and you agree that they can have your research information, then the researchers may not use the Certificate of Confidentiality to keep this information from them.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

ADULT PARTICIPANT:

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of participant(s) Time	Printed Name of participant(s)	Date	

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

Signature of consent delegate	Printed Name of consent delegate	Date	Time

WITNESS SECTION:
When a witness is required to observe the consent process, it should be documented below (for example, when participant(s)is illiterate, visually impaired, or this document accompanies a short form consent).

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant(s), and that consent was freely given by the participant(s).

_____	_____	_____	_____
Signature of Witness	Printed Name of Witness	Date	Time