Permission to Take Part in a Human Research Study

Do not sign this consent if today's date is later than the stated expiration date above.

Title of Research Study: *Testing the ability of JNJ-18038683, a selective serotonin (5-HT)7 antagonist, to improve cognition and reduce residual depressive symptoms in stable bipolar patients*

Investigator: *Herbert Meltzer, MD*

Supported By: This research is supported by Northwestern University and Janssen Research and Development, LLC

Financial Interest Disclosure:

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Key Information:

The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you have been diagnosed with bipolar I or II disorder and may be having difficulty with memory, attention, or concentration.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

This study is being conducted in order to determine if an investigational drug, JNJ-18038683, improves mental function and is safe in people who have bipolar disorder and are taking other medications for their illness. Mental function is how your brain works and includes your mood, memory and how you think and concentrate. An investigational drug is one that is not approved for sale by the US Food and Drug Administration (FDA) or any other regulatory or health agency. This study compares an experimental drug to a placebo. A placebo is an inactive substance made to look/taste like an active medicine. The placebo in this study looks like JNJ-18038683 but has no drug or other active ingredient in it. You will receive either the study medication, JNJ-18038683, or the placebo during this study. Researchers use a placebo to see if the study drug works better or is safer than not taking anything.

How long will the research last and what will I need to do?

We expect that you will be in this research study for up to 10 weeks, including the screening period.

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If you participate, you will be closely followed by asking you about any side effects you experience, your vital signs, (BP, heart rate, respiratory rate, temperature), electrocardiograms, and clinical lab tests.

If you decide to participate, you will be in this study for up to 8 weeks (56 days) after the screening period with a safety follow-up phone call 4 weeks (28 days) after the completion of the study. The screening period can last up to 2 weeks (14 days). The total length of your participation is up to 14 weeks (98 days). After the initial screening visit (Visit 1), you will be asked to return to the research site at least 6 more times to take part in additional study procedures.

These procedures include but are not limited to: Physical and mental health questions, height and weight measurement, electrocardiograms, physicals examinations, blood samples, urine samples, pregnancy tests, questionnaires about our thinking, concentration, and memory; your thoughts/intentions to do harm to yourself and others; and your mood, feelings, thoughts, and symptoms.

You will also be contacted by phone at weeks 3, 5, and 7 of the study during the study to ask if you have had any health problems, have started any new medications, and to answer a questionnaire about our thoughts/intentions to do harm to yourself and others; and your mood, feelings, thoughts, and symptoms.

More detailed information about the study procedures can be found under the section **What happens if I say "Yes, I want to be in this research"?**

Is there any way being in this study could be bad for me?

While taking JNJ-18038683 you may experience side effect. It is important for you to let the study team know of any changes in your health. For more information on known side effects see **"Is there any way being in this study could be bad for me? (Detailed Risks)"**
In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death. The risk of this type of drug includes a risk of sexual problems, mood changes, nervousness, and experiencing thoughts of hurting yourself which may be life threatening.
If you start experiencing thoughts of hurting yourself or if you have any plan to do so, please call 911 immediately for assistance, in addition, the study staff should be notified of these issues as well. Please report any concerns at all study visits (on site or via phone).

More detailed information about the risks of this study can be found under **"Is there any way being in this study could be bad for me? (Detailed Risks)"**

Will being in this study help me any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include improvement of your mental functioning (mood, thinking, concentration, and memory) and providing scientific information that may benefit others in the future. The results of your screening evaluation can be made available to your regular doctor at your written request.

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What happens if I do not want to be in this research?

Participation in research is completely voluntary. You decide whether or not to participate. If you choose to not participate, there will be no penalty to you or loss of benefit to which you are entitled.

There is not an approved treatment for improving mental function in bipolar disorder. You may choose not to participate in this study.

During the study, you will remain on the current treatment you receive for bipolar disorder. For other available alternative treatments for bipolar disorder symptoms, please contact your doctor.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

Whom can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team.

You can call us with your questions or concerns.

Dr. Herbert Meltzer is the person in charge of this research study. You can call him at 312.503.0309 during Monday through Friday, from 8:30 am to 5:00 pm.

You can also call Katie Nikolajuk at 312-503-9076 with questions about this research study.

For problems arising evenings or weekends, you may call the Stone Institute psychiatric emergency number at 312-926-9670.

If you have any illness or injury during your time on this study, you should call us promptly.

If you experience an emergency, please call 911 immediately for assistance.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:

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

How many people will be studied?

We expect about 60 people in total. Northwestern University and Beacon Medical Group Behavioral Health South Bend will be the sites conducting the research.

What happens if I say "Yes, I want to be in this research"?

You must give written consent to participate before any of the following tests are performed. The following procedures or tests will be done during the study. All study procedures and tests will take place at either the Northwestern University Feinberg School of Medicine suites at either

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680 N. Lake Shore Drive, Suite 1520, Chicago, Illinois, 60611 or the Stone Mental Health Center at 446 E Ontario St, Rooms 6-344 and 6-343, Chicago, IL 60611.

These procedures and tests are to establish your eligibility for the study, safety and effects of the study drug.

- Physical and mental health questions. You will be asked questions about your:
  - Current and past health
  - Age
  - Drug use (including prescription, over-the-counter, and other drugs). You may be asked to stop taking some medications. You should discuss the risk of stopping any medication with your doctor.
- Height and weight measurement: how tall you are, the size of your waist, and how much you weigh.
- Electrocardiograms (ECGs), a painless way to measure your heart rhythm and check for heart problems.
- Physical examinations will be done. Examinations will not include pelvic or breast examinations in females, genital examinations in males, or rectal examinations.
- Blood pressure, temperature, pulse, and breathing rate will be measured.
- Blood samples will be drawn to check your health before and during the study.
- Blood will be taken at three (3) different times over the course of the study. Approximately two and a half (2.5) tablespoons (about 36 mL) of blood will be drawn over the course of the study. A needle stick will be used for the blood draws.
- Serum pregnancy will be done at screening visit if you are a woman and can have children
- Urine pregnancy test will be done at baseline visit: a pregnancy test will only be performed if you are a woman and can have children.
- Urine samples will be collected and tested to:
  - Check your health
  - Test whether certain drugs, including illegal substances, are present in your body
  -

During the study, the study staff will perform interviews where they will ask you questions and have you perform tasks. These questions and tasks are described below.

- The study staff will ask you questions and have you perform tasks to test your thinking, concentration, and memory.
- You will be asked for any thoughts/intentions to do harm to yourself or others. Please share with your doctor any thoughts you have to do harm to yourself or others.
- You will also be asked about your mood, feelings, thoughts, and symptoms. These questions will help the study doctor and study staff to understand the severity of your bipolar disorder, whether it has become worse or better, how it affects your life, and your everyday activities.
- A study staff member will assess your movements (the way you move and whether you have movements you cannot control).
- Blood pressure, temperature, pulse, and breathing rate will be measured.

You will be randomly assigned to 1 of 2 groups (like drawing names out of a hat or flipping a coin).

Group 1: Placebo – After 1 week of 1 tablet per day, 2 tablets once per day by mouth

Group 2: study drug – After 1 week of 1 tablet (10 mg) per day, 2 tablets, each containing 10 milligrams of JNJ-18038683, once per day by mouth.

The treatment you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what treatment you get. Neither you nor the study doctor will know which treatment you are getting, but the information about which group you are in (whether you are receiving placebo or the study drug) can be made available to the study doctor in the case of an emergency.

A Safety Follow-up phone call will take place 4 weeks after the final visit.

If you choose to be in this study, you have the right to be treated with respect, including respect for your decision whether or not you wish to continue or stop being in the study. You are free to choose to stop being in the study at any time.

Any new findings developed during the course of this research that may affect your willingness to continue in this study will be shared with you.

If you want to speak with someone who is not directly involved in this research, or have questions about your rights as a research subject, please contact the Northwestern University Institutional Review Board (IRB) Office. You can call them at 312-503-9338.

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

In this form, both JNJ-18038683 and placebo will be called "study drug." The study drug will be available to you only during your participation in the study. You must return all study drug at the end of the study. After the study is over, Northwestern University will not continue to provide you with the study drug. Your doctor will discuss your future medical care options with you.

While you are in this study, you will continue to take your regular medications as prescribed by your doctor. If you start a new medication while in the study, you and the study doctor will talk about if it affects your ability to continue participating. This includes medications that do not require a prescription (over-the-counter medications, vitamins, dietary supplements, etc.). Your study doctor may discuss stopping certain medications with your other doctors. If it is determined that you need a medication not allowed in this study, you might need to discontinue your participation in this study.

What happens if I say "Yes", but I change my mind later?

You can leave the research at any time it will not be held against you.

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.

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Detailed Risks: Is there any way being in this study could be bad for me?

Overall, seven completed clinical studies in 405 individuals (245 men and 160 women) have been completed with the study medication. In general, side effects (adverse events) were mild to moderate in severity; the investigational drug was well tolerated at doses of up to 20 mg/day for up to 7 weeks treatment in both men and women. This dose (20 mg/day) is similar to the dose that you will be receiving if you choose to participate in this study. There have been no deaths reported with the use of the study drug. Most side effects were mild to moderate in severity.
This research may hurt you in the following ways:

In a previously completed clinical trial with the study drug which evaluated JNJ 18038683, active comparator escitalopram, and placebo, the most common side effects (>5%) reported were similar in all treatment groups:

- headache
- nausea
- nasopharyngitis (stuffy nose and sore throat)
- insomnia
- somnolence (sleepiness)
- dyspepsia
- dizziness
- dry mouth
- constipation
- diarrhea
- vomiting
- back pain
- upper respiratory tract infection
- palpitations
- fatigue

The side effects that were reported more frequently in the JNJ-18038683 treatment group compared with the placebo or escitalopram groups included:

- dyspepsia (upset stomach)
- constipation
- upper respiratory tract infection
- palpitations

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death. The risk of this type of drug includes a risk of experiencing thoughts of hurting yourself which may be life threatening. In addition, there may be changes in your mood such as euphoria (a feeling or state of intense excitement and happiness), sexual problems, nervousness, and/or inappropriate affect (emotions that do not properly fit a circumstance, such as smiling in reaction to a tragedy, or failing to show emotion at a time when an emotional reaction would normally be called for).

<u>If you start experiencing thoughts of hurting yourself or if you have any plan to do so, please call 911 immediately for assistance, in addition, the study staff should be notified of these issues as well. Please report any concerns at all study visits (on site or via phone).</u>

There have been no reports of death with use of study drug thus far.

Also, there have been a fewevents associated with syncope (temporary loss of consciousness caused by a fall in blood pressure) and orthostatic hypotension (temporary lowering of blood pressure, usually related to suddenly standing up) and in several studies these events were severe and/or serious and led to early discontinuation from study. There was one adverse event of elevated blood levels of creatine kinase, an enzyme present in the body muscles, which was not related to investigational drug JNJ 18038683

Risks Associated With Blood Draws

During this study, blood samples will be taken from a vein in the arm with a sterile needle. For blood samples drawn by needles, several sites of blood drawing on both arms may be required. Risks associated with having blood drawn include pain, bruising, swelling, or infection at the site where the needle is inserted. Rarely, some people feel lightheaded or faint.

Risks Associated with Interviews, Tests, and Questionnaires

There is the possibility that you might find the evaluations stressful. The likelihood of this occurring is low and for most of the evaluations, you can stop and take as many breaks as you wish.

This study involves the use of your identifiable, personal information and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: **"What happens to the information collected for the research?".**

What do I need to know about reproductive health and/or sexual activity if I am in this study

The procedures in this research may affect a pregnancy or fetus in the following ways: The effect of the study drug on human sperm and eggs has not been studied. The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death. Therefore, both men and women should not attempt pregnancy and women should not be pregnant or breast-feeding while taking part in this study

If you are sexually active, both men and women should use at least one effective means of birth control while participating in this research study. According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable but least effective methods of birth control include male condoms (with or without spermicide) and female condoms.

If you or your partner become pregnant while participating in this research study or for 6 months after you complete the study, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other treatment options will be discussed with you at that time if necessary. You are encouraged to use condoms to protect against sexually transmitted diseases.

If you or your partner [are/is] considered to be postmenopausal, you are not required to use contraception while participating in this research study. Postmenopausal women rarely become pregnant. If you or your partner become pregnant while participating in this research study or for

6 months after you complete the study, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other treatment options will be discussed with you at that time if necessary.

Will it cost me anything to participate in this research study?

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

There will be no costs to you for being in this study.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include: include improvement of your mental functioning (mood, thinking, concentration, and memory) and providing scientific information that may benefit others in the future. The results of your screening evaluation can be made available to your regular doctor at your written request.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution.

Monitors, auditors, the IRB, the Northwestern University Office for Research Integrity, the US Office of Research Integrity, the US Office for the Protection of Human Research Protections, the US Food and Drug Administration may be granted direct access to your medical records to conduct and oversee the research. 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.

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

Data Sharing

De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Can I be removed from the research without my OK?

The person in charge of the research study can remove you from the research study without your approval. Possible reasons for removal include if your symptoms of bipolar disorder get worse, you lose the ability to consent, or if the study is harming you

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

What else do I need to know?

If you become ill or are injured as a result of this study (medications, devices or procedures), you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

The hospital will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If you agree to take part in this research study, we will pay you up to $280 for your time and effort. You will get $40/visit for taking part in this research study. All visit payments will be made via a check that will be mailed to you. Processing for checks can take approximately 4 weeks after each visit. If you withdraw from the study, you will be paid for the portions that you completed, depending upon how many visits were done.

You will be given assistance for expenses related to parking, taxi or public transportation. Parking for study participation will be provided to the participant by the study through University Services. You will not be responsible for parking expenses. You will be provided with a validation ticket, which will allow you to park for free if you park at one of two Northwestern Memorial Hospital parking garages:

- Huron-St. Clair Self Park located at 222 E. Huron Street, Chicago, IL 60611, or
- Erie-Ontario Self Park located at 321 E. Erie St, Chicago, IL 60611

Expenses for taxis will be reimbursed by cash at the end of each visit, as long as reimbursement receipts are received.
If public transportation is used, single-use CTA cards will be provided for transportation to and from each visit.

Up to $20 per visit will be provided to cover your transportation and parking expenses.

$10 will be provided to cover lunch expenses for visits lasting over 4 hours.

The Accounting Services at Northwestern University will be given your name, address, and Social Security Number in order to issue a check for your study participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

HIPAA Authorization

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- Results of physical examinations
- Medical history
- Lab tests, or certain health information indicating or relating to a particular condition
- Records about study medication or drugs
- Substance abuse information: Results of drug tests

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- Mental Health information: Diagnosis, previous treatment, medication history

You have the right to inspect and copy the mental health and developmental disabilities records that will be collected as part of this study.

This consent expires on December 31,2060. After this date, Northwestern University may not gather new information about you, use or disclose your personal health information collected in this study for any purpose other than the research study described in this consent unless Northwestern University obtains permission to do so from you. Illinois State Law permits use and disclosure of your mental health information only to the extent specified in this document.

The following clinical providers may give the researchers information about you: all current and previous health care providers, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH).

Once we have the health information listed above, we may share some of this information with the following offices or entities outside of Northwestern University and its clinical partners (or affiliates): the Northwestern University Institutional Review Board Office and Office for Research Integrity; the US Office of Research Integrity; the US Office for Human Research Protections; the US Food and Drug Administration.

Any research information shared with outside entities will not contain your name, address, telephone or social security number or any other personal identifier unless disclosure of the identifier is necessary for review by such parties or is required by law or University policy [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office].

The following entities may receive your health information:

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board (a committee which is responsible for the ethical oversight of the study),
- Clinical affiliates, including but not limited Northwestern Memorial Hospital (NMH), or Northwestern Memorial Physicians Group (NMPG). Your participation in this clinical trial will be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.
- Clinical affiliates, including but not limited to Northwestern Memorial Hospital (NMH), for purposes including, but not limited to, the affiliate's provision of care to you and/or the affiliate's scheduling of appointments and/or billing activities.
- Janssen Research and Development, LLC with whom Northwestern University shares a collaborative research agreement. Janssen is the manufacturer of the study medication, JNJ-18038683 and the placebo.
- Other University research centers and University contractors who are also working on the study.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).

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- Research results from the study may be shared with research partners working with the Northwestern University. Research results shared with research partners working with Northwestern University will not contain personal identifying information.

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

However, Illinois law does not allow the re-release of HIV/AIDS, genetic testing, mental health and developmental disabilities information by the receivers of the information except in precise situations allowed by law.

Also, Federal Confidentiality Rules, 42 CFR Part 2, prohibit making any further disclosure of substance use disorder information unless further disclosure of this information is expressly permitted by written consent of the person to whom it pertains or as otherwise permitted by 42 CFR Part 2.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will expire December 31 2060.

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing. To revoke your authorization, write to:

- PI's Name: Herbert Meltzer, MD
- Institution: Northwestern University
- Department: Psychiatry and Behavioral Sciences
- Address: 680 N. Lake Shore Drive Suite 1520, Chicago, IL 60611

You do not have to authorize the use or disclosure of your health information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

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Signature Block for Capable Adult:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

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

_____ _____
Signature of Witness to Consent Process Date

_____
Printed Name of Person Witnessing Consent Process